FUNCTIONAL AAV CAPSIDS FOR INTRAVITREAL ADMINISTRATION

CROSS-REFERENCE

[0001] The present application claims the benefit of U.S. Provisional Application No. 63/284,962, entitled "FUNCTIONAL AAV CAPSIDS FOR INTRAVITREAL ADMINISTRATION," filed on December 1, 2021, and U.S. Provisional Application No. 63/346,295, entitled "FUNCTIONAL AAV CAPSIDS FOR INTRAVITREAL ADMINISTRATION," filed on May 26, 2022, which applications are each herein incorporated by reference in their entireties for all purposes.

BACKGROUND

[0002] Recombinant adeno-associated viruses (rAAV) provide the leading platform for *in vivo* delivery of gene therapies. Current clinical trials employ a limited number of AAV capsids, primarily from naturally occurring human or primate serotypes such as AAV1, AAV2, AAV5, AAV6, AAV8, AAV9, AAVrh.10, AAV4rh.74, and AAVhu.67. These capsids often provide suboptimal targeting to tissues of interest, both due to poor infectivity of the tissue of interest and competing liver tropism. Increasing the dose to ensure infection of desired tissues can lead to dose-dependent liver toxicity. In addition, use of naturally-occurring capsids presents an immunological memory challenge – pre-immune patient populations are excluded from treatment and repeat dosing in a previously immune naïve patient is often not possible. Thus, there is a need for additional AAV capsids for use in gene therapy, in particular capsids that confer upon the rAAV high infectivity for specific tissues, such as ocular tissues.

SUMMARY OF THE INVENTION

[0003] Described herein is a system for high throughput engineering of functional AAV capsids with altered tropism for various tissues, and using this system, have identified capsid variants with increased tropism for target tissues, such as eye tissues.

[0004] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence of SEQ ID NO: 5014 and further comprises at least one substitution relative to SEQ ID NO: 9; and wherein the 581 to 589 region comprises one or more basic amino acid residues.

[0005] In some aspects, the 581 to 589 region comprises more basic amino acid residues than acidic amino acid residues. In some aspects, the acidic amino acid residues are selected from the

group consisting of D and E. In some aspects, the basic amino acid residues are selected from the group consisting of K, R, and H.

[0006] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581-589 region of the VP capsid polypeptide comprises a sequence of SEQ ID NO: 5014, wherein X^1, X^2, X^3, X^4, X^5, or X^6 of SEQ ID NO: 5014, or any combination thereof is K or R.

[0007] In some aspects, X^1 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 1726, 374, 1442, 933, 1748, 4142, 1434, 1358, 1191, 3732, 4110, 4039, 4411, 4506, 4270, 4156, 3780, 4036, 4030, 4016, 1550, 3899, 1247, 1855, 1181, 3919, 1639, 3664, 1244, 4140, 3930, 4117, 4189, 4001, 3799, 3643, 3619, 1240, 1686, 1479, 1307, 1575, 4296, 1665, 3871, 4135, 1605, 4408, 3604, 1274, 4149, 1313, 3741, 1938, 3709, 1727, 3893, 1280, 3622, 1784, 3834, 1752, 1983, 1743, 3979, 4461, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 1857, 2510, 2316, 1904, 1219, 1486, 1512, 1481, 1516, 3820, 3789, 4252, 4047, 4330, 4082, 4094, 1574, 1248, 4078, 1872, 1426, 3785, 3687, 4318, 4243, 3866, 3704, 4172, 1621, 4315, 1192, 1513, 1856, 2476, 3324, 2769, 2678, 1561, 3296, 375, 2343, 2348, 376, 377, 1395, 1584, 4093, 4453, 3940, 3778, 4374, 4210, 4009, 4264, 4339, 4368, 1738, 378, 1610, 4194, 4474, 4013, 4266, 1771, 1759, 1922, 3860, 3832, 1349, 1381, 3663, 1642, 1185, 4356, 3932, 1233, 4212, 3858, 1198, 4192, 3611, 1919, 1819, 3790, 3712, 1969, 4095, 1887, 4468, 1720, 4247, 934, 1790, 2002, 1657, 1663, 1336, 3894, 1554, 1494, 1405, 3576, 4314, 3695, 1851, 1850, 4362, 1815, 3845, 4511, 3656, 3638, 1406, 1596, 4454, 1443, 1661, 935, 4504, 1359, 1734, 3650, 1910, 1305, 1648, 3831, 4435, 1208, 1988, 4451, 1993, 1986, 3849, 1718, 4068, 1835, 1425, 1428, 1282, 4380, 1658, 1452, 1687, 4024, 379, 4072, 3791, 4491, 4323, 4014, 1304, 1440, 1511, 1981, 1676, 1547, 4422, 1283, 3861, 1383, 3644, 3691, 4259, 1749, 1418, 1176, 4216, 1924, 1421, 1387, 3992, 4423, 4253, 1618, 1871, 1256, 3748, 4119, 1297, 1586, 1251, 1299, 1954, 4450, 3990, 4029, 4097, 3890, 3796, 1389, 3711, 4344, 1578, 1476, 4343, 1202, 4413, 4384, 3808, 1647, 1475, 3892, 3674, 1739, 3926, 3595, 1943, 3756, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 3781, 1535, 1210, 4492, 4365, 4118, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 4350, 4334, 3821, 1932, 3929, 4171, 1258, 3824, 3631, 4465, 4494, 1320, 1398, 3828, 1204, 1223, 1284, 1685, 3773, 4209, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916,

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[0008] In some aspects, X^2 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 285, 1626, 299, 3809, 4271,

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[0009] In some aspects, X^3 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289,

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[0011] In some aspects, X^5 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4177, 742, 16, 17, 18, 745, 3477, 1548, 2982, 3426, 3073, 3169, 747, 3362, 4942, 23, 28, 2038, 3660,

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[0012] In some aspects, X^6 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551,

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513, 3636, 514, 1699, 1027, 1366, 4950, 4027, 3478, 2959, 1293, 3197, 1595, 3413, 518, 1032, 1033, 1675, 1797, 2315, 521, 1999, 3759, 1215, 4122, 1730, 3966, 1035, 4973, 528, 3911, 3289, 1821, 530, 532, 1874, 533, 1038, 538, 539, 3767, 1929, 3683, 1338, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 3720, 4351, 4414, 3453, 3254, 1649, 544, 4240, 3580, 1046, 548, 549, 2598, 552, 553, 3819, 1259, 4062, 554, 2841, 3515, 1433, 1323, 4301, 555, 558, 3738, 1567, 559, 1054, 1270, 3857, 2175, 1257, 1238, 3662, 561, 1058, 563, 1061, 4203, 1899, 3981, 1062, 1303, 4116, 1946, 3620, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 1401, 4438, 1895, 1264, 1912, 573, 3939, 4170, 4056, 1271, 1521, 1221, 1451, 3934, 4080, 4352, 1700, 3739, 1419, 1811, 3950, 1690, 3716, 1569, 1437, 1674, 4337, 1285, 4268, 1183, 3881, 3938, 4198, 4416, 4229, 4292, 4193, 4325, 4375, 4432, 4215, 3944, 4195, 4223, 1540, 4455, 4512, 1723, 3750, 4070, 4104, 4235, 1863, 4346, 1881, 1814, 4443, 3761, 1587, 3592, 576, 4469, 1275, 1950, 4129, 1296, 1551, 3733, 4111, 3993, 4108, 1287, 1713, 1556, 1736, 1995, 1705, 1861, 4120, 4417, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 3928, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1757, 4299, 1773, 1364, 1462, 4007, 3729, 3665, 3722, 1691, 1712, 1624, 1751, 1394, 3924, 3952, 581, 2003, 1559, 1250, 1555, 4114, 1818, 1076, 4448, 1078, 1786, 3354, 1832, 3432, 2891, 1903, 4459, 589, 1563, 1084, 591, 592, 594, 595, 1858, 596, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 4439, 3852, 3997, 3847, 4050, 3377, 4424, 4143, 4493, 3492, 1412, 4017, 4477, 1794, 602, 4263, 3072, 2009, 1754, 3888, 603, 604, 1368, 3827, 4103, 1571, 1438, 611, 1093, 612, 1094, 3701, 4389, 614, 615, 1332, 1715, 4369, 1652, 1541, 1921, 1733, 1373, 1870, 619, 4218, 1798, 1702, 1384, 3700, 1788, 1600, 624, 2473, 1423, 2771, 1339, 3875, 3070, 2015, 2557, 2795, 2906, 2103, 3299, 3118, 4576, 1103, 1614, 1947, 631, 4479, 3766, 1107, 635, 1813, 636, 2431, 637, 1109, 639, 3706, 1110, 640, 642, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1568, 1766, 3221, 2643, 2739, 3920, 647, 1801, 4279, 3762, 1637, 1509, 648, 1117, 1119, 2965, 2695, 3293, 4722, 1121, 653, 1122, 3264, 655, 656, 657, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3537, 3994, 1319, 4467, 1623, 660, 1123, 664, 1126, 1128, 1129, 1130, 670, 1527, 671, 1772, 1137, 5005, 1933, 1731, 1793, 3342, 1140, 1141, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 1920, 4999, 1544, 703, 4031, 4305, 1636, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 4028, 3989, 704, 1493, 1902,

1152, 4182, 707, 708, 709, 4476, 1375, 713, 714, 1841, 4234, 1154, 1314, 4096, 718, 719, 720, 2063, 1311, 721, 4217, 1627, 1158, 1953, 1201, 3787, 729, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 2423, 1745, 1973, 3807, 4307, 1169, 1454, or 1781.

[0013] In some aspects, X^7 of SEQ ID NO: 5014 is R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 740, 15, 742, 743, 17, 22, 24, 1836, 32, 36, 2450, 39, 752, 753, 1998, 3059, 2519, 757, 48, 1952, 50, 52, 760, 2389, 54, 2346, 58, 4086, 1660, 1966, 768, 2402, 772, 71, 72, 2453, 3882, 775, 1806, 3669, 1356, 2132, 81, 84, 85, 87, 4040, 88, 1885, 782, 783, 784, 785, 94, 788, 2173, 98, 2007, 102, 113, 799, 4848, 1444, 4821, 2329, 115, 119, 2290, 123, 806, 128, 134, 812, 145, 817, 154, 2149, 821, 167, 171, 4596, 183, 830, 191, 194, 2071, 195, 4920, 831, 2223, 207, 3901, 211, 212, 213, 215, 224, 4782, 845, 846, 849, 850, 854, 247, 248, 2245, 255, 261, 264, 265, 1477, 270, 874, 876, 279, 882, 1930, 285, 286, 886, 2119, 2468, 887, 888, 4138, 297, 3844, 302, 893, 307, 308, 2155, 1431, 2312, 900, 1635, 906, 2799, 2128, 2918, 1363, 4251, 2622, 3333, 3474, 3614, 2732, 3166, 3151, 3088, 2883, 3318, 2645, 2733, 3213, 3782, 1844, 2523, 2520, 2997, 2681, 3035, 3279, 2764, 3480, 2787, 1808, 3101, 3689, 4147, 1762, 1976, 340, 1594, 2439, 348, 4498, 1518, 1782, 926, 357, 359, 932, 363, 369, 1873, 3780, 4140, 4001, 3709, 3834, 1752, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 3820, 4330, 1872, 3687, 4318, 375, 4210, 3860, 4212, 3695, 1851, 4504, 1910, 1428, 4323, 4422, 4259, 1176, 3711, 4365, 4383, 3969, 4128, 3802, 3863, 3821, 4171, 3824, 4462, 3760, 3753, 2783, 3880, 3943, 4163, 4178, 4199, 3724, 3670, 4482, 3692, 4430, 4316, 3645, 3690, 3589, 3730, 4426, 3851, 4429, 1335, 1717, 1997, 1975, 4280, 4006, 3900, 4298, 4388, 1341, 1350, 1909, 4412, 4407, 4281, 4167, 1893, 3585, 4015, 1747, 4286, 3826, 1473, 1914, 3984, 4495, 4184, 3977, 1707, 4074, 4003, 3915, 1410, 1498, 940, 4131, 4357, 1925, 1466, 1611, 1530, 4168, 4245, 4075, 3987, 1679, 4306, 3869, 3768, 393, 2265, 3618, 4433, 947, 399, 401, 402, 4139, 1352, 406, 415, 418, 420, 4919, 431, 4044, 976, 433, 434, 435, 442, 3873, 3411, 3985, 987, 1485, 2262, 457, 458, 4425, 466, 467, 468, 1468, 474, 1008, 1012, 1016, 4518, 1697, 490, 3616, 2247, 2302, 499, 500, 501, 509, 2110, 512, 1797, 520, 525, 3966, 1038, 537, 1041, 3683, 2165, 542, 4331, 3129, 1044, 4351, 3453, 1047, 1323, 4301, 557, 3738, 559, 1270, 3857, 1056, 2186, 1057, 1059, 565, 566, 3981, 567, 3620, 4002, 3666, 3939, 1221, 1397, 1437, 4337, 4268, 3938, 4292, 4215, 3750, 3633, 4070, 3592, 1827, 3839, 4395, 3855, 3665, 1624, 2395, 1818, 586, 587, 1903, 1080, 1081, 1082, 589, 1084, 1085, 594, 596, 4439, 3997, 1962, 1087, 4777, 606, 607, 610, 1094, 4389, 1603, 1095, 616, 618, 622, 1104, 4536, 3706, 2481, 3100, 3200, 3621, 4179, 1432, 4381, 643, 1115, 644, 2307, 2477, 652, 657, 658,

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[0014] In some aspects, (a) X^3 of SEQ ID NO: 5014 is a basic amino acid residue, (b) X^6 of SEQ ID NO: 5014 is a basic amino acid residue, or (c) X^3 of SEQ ID NO: 5014 is a basic amino acid residue and X^6 of SEQ ID NO: 5014 is a basic amino acid residue. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 739, 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 52, 760, 53, 762, 4659, 54, 3925, 55, 3654, 56, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 2399, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 75, 1312, 4501, 76, 77, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 1180, 92, 785, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 794, 795, 104, 105, 106, 1849, 108, 4736, 1579, 110, 1906, 113, 1444, 1344, 116, 802, 117, 118, 2158, 121, 803, 804, 1463, 805, 122, 2058, 124, 125, 127, 4994, 807, 132, 809, 810, 133, 1978, 812, 135, 136, 137, 138, 813, 4673, 140, 815, 1326, 141, 142, 143, 144, 145, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 151, 152, 153, 154, 155, 819, 820, 157, 821, 159, 160, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 180, 826, 827, 181, 828, 182, 183, 4641, 829, 184, 185, 186, 187, 188, 189, 830, 191, 192, 193, 194, 195, 196, 1391, 197, 2223, 200, 201, 202, 203, 204, 205, 832, 833, 206, 834, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 215, 1896, 1522, 3490, 838, 2241, 217, 218, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 226, 227, 230, 231, 842, 232, 233, 235, 844, 236, 237, 2150, 851, 852, 853, 1536, 240, 854, 242, 243, 244, 245, 246, 247, 855, 4634, 249, 250, 251, 252, 253, 254, 255, 857, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 869, 870, 271, 871, 872,

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4179, 4398, 3959, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1585, 1568, 1766, 3221, 2643, 2739, 4629, 3920, 4603, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4590, 648, 1117, 4800, 4724, 4674, 1119, 2965, 2695, 3293, 4722, 1121, 4784, 653, 1122, 3264, 655, 656, 657, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3537, 3994, 1319, 4467, 1623, 660, 4714, 4812, 1123, 664, 2138, 1126, 1128, 1129, 1130, 670, 1527, 671, 1772, 1133, 2196, 1136, 1137, 5005, 1933, 1731, 1793, 3342, 1140, 1141, 4525, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 4756, 4859, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2194, 1920, 4999, 1544, 703, 4031, 4305, 1636, 1393, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 4715, 704, 1493, 1902, 1152, 4824, 4182, 707, 708, 709, 4732, 4476, 1375, 713, 714, 715, 1841, 4234, 1154, 1314, 4096, 4895, 718, 719, 720, 2063, 1311, 721, 4903, 4885, 4217, 1627, 2116, 1158, 724, 5013, 4894, 1953, 1201, 3787, 729, 2485, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4976, 4294, 1582, 4587, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 4835, 4571, 2423, 1745, 1973, 1168, 3807, 4307, 1169, 1454, or 1781. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 35, 36, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 45, 756, 48, 1952, 3122, 2551, 3718, 3484, 3577, 759, 3960, 1378, 2994, 3080, 2589, 3681, 760, 762, 3925, 3654, 60, 4086, 1740, 1660, 62, 1966, 63, 768, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 1312, 4501, 76, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 4065, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 1180, 92, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 104, 105, 108, 1579, 110, 1906, 1444, 1344, 116, 802, 117, 118, 121, 803, 1463, 124, 807, 133, 1978, 812, 135, 136, 137, 138, 140, 1326, 141, 142, 143, 1634, 1302, 817, 818, 147, 148, 149, 151, 154, 155, 819, 820, 157, 165, 822, 168, 169, 170, 823, 1651, 173, 1483, 174, 825, 176, 180, 827, 181, 828, 184, 185, 186, 188, 189, 830, 192, 193, 194, 196, 1391, 197, 200, 201, 202, 203, 205, 832, 206, 834, 835, 836, 1334, 3901, 3312, 2649, 1450, 4386, 3028, 1446, 215, 1522, 3490, 217, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 230, 231, 842, 232, 233, 235, 851, 853, 1536, 240, 242, 243, 244,

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[0015] In some aspects, the basic residue is selected from the group consisting of K, R, and H.

[0016] In some aspects, X^3 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 760, 53, 3925, 55, 3654, 56, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 3882, 3713, 1942, 1312, 4501, 76, 77, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 90, 91, 779, 1180, 92, 785, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 794, 795, 104, 105, 106, 1849, 108, 1579, 110, 1906, 113, 1444, 1344, 116, 802, 117, 118, 121, 803, 804, 1463, 805, 122, 124, 125, 127, 807, 132, 809, 810, 133, 1978, 812, 135, 136, 137, 138, 813, 140, 815, 1326, 141, 142, 143, 144, 145, 1634, 1302, 817, 146, 818, 147, 148, 149, 151, 152, 153, 154, 155, 819, 820, 157, 159, 160, 163, 164, 165, 166,

822, 167, 168, 169, 170, 171, 823, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 826, 827, 181, 828, 182, 829, 184, 185, 186, 187, 188, 189, 830, 191, 192, 193, 194, 195, 196, 1391, 197, 200, 201, 202, 203, 204, 205, 832, 833, 206, 834, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 215, 1896, 1522, 3490, 838, 217, 218, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 226, 227, 230, 231, 842, 232, 233, 844, 236, 237, 851, 852, 853, 1536, 240, 854, 242, 243, 244, 245, 246, 247, 249, 250, 251, 252, 253, 254, 255, 857, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 264, 1241, 265, 266, 866, 1477, 267, 867, 869, 870, 271, 871, 872, 272, 1252, 273, 1591, 275, 1980, 276, 876, 877, 277, 278, 279, 1892, 1539, 880, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 282, 1799, 283, 1626, 1374, 287, 1620, 1290, 1354, 888, 291, 1956, 889, 292, 4324, 293, 4138, 891, 3903, 297, 3829, 3809, 4271, 3844, 1436, 1515, 1617, 1961, 304, 306, 1589, 4370, 308, 309, 894, 3646, 4059, 1431, 1331, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 898, 321, 322, 899, 1958, 901, 325, 902, 326, 1491, 329, 330, 905, 4484, 1756, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 1888, 4248, 1557, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 1345, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 2772, 3230, 3043, 2922, 3581, 3524, 2869, 2610, 3298, 2775, 3108, 2603, 3614, 2612, 2860, 3187, 3238, 3786, 4385, 3016, 3436, 2876, 2987, 3532, 3438, 3561, 3259, 2663, 2890, 3433, 3071, 3018, 2580, 2755, 3015, 2540,

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[0017] In some aspects, X^6 of SEQ ID NO: 5014 is K or R. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 1308, 3960, 1378, 2994, 3080, 2589, 3681, 51, 760, 762, 3925, 3654, 763, 59, 60, 4086, 1740, 1660, 62, 1966, 63, 2438, 768, 66, 67, 68, 3816, 2599, 2706, 72, 73, 74, 3865,

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[0018] In some aspects, (a) X^3 of SEQ ID NO: 5014 is not D, (b) X^6 of SEQ ID NO: 5014 is not D, or (c) X^3 of SEQ ID NO: 5014 is not D and X^6 of SEQ ID NO: 5014 is not D. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 2167, 52, 760, 53, 2389, 4755, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 2140, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2379, 81, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 4556, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 1579, 110, 1906, 111, 2428, 798, 2075, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4864, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 4533, 129, 130,

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[0019] In some aspects, (a) X^3 of SEQ ID NO: 5014 is not E, (b) X^6 of SEQ ID NO: 5014 is not E, or (c) X^3 of SEQ ID NO: 5014 is not E and X^6 of SEQ ID NO: 5014 is not E. In some aspects, the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 52, 760, 53, 2389,

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2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 2456, 4606, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 677, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 718, 1155, 719, 720, 2063, 1311, 721, 4642, 722, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 730, 731, 2024, 1846, 2507, 2368, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0020] In some aspects, X^3, X^6, and X^1 of SEQ ID NO: 5014 are basic amino acid residues. In some aspects, X^3, X^6, and X^4 of SEQ ID NO: 5014 are basic amino acid residues. In some aspects, X^3, X^6, X^1, and X^4 of SEQ ID NO: 5014 are basic amino acid residues.

[0021] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region of the VP capsid polypeptide comprises at least two basic amino acid residues and no more than one acidic amino acid residue.

[0022] In some aspects, the VP capsid polypeptide comprises one or more features selected from the group consisting of: (a) the 581 to 589 region comprises two or more basic amino acid residues, (b) X^3, X^6, X^1, or X^4 of SEQ ID NO: 5014, or any combination thereof are basic amino acid residues, and (c) the 581 to 589 region comprises no more than one acidic amino acid residue.

[0023] In some aspects, the VP capsid polypeptide comprises two or more of the features. In some aspects, the VP capsid polypeptide comprises three of the features. In some aspects, the acidic amino acid residue is D or E. In some aspects, the basic amino acid residues are K, R, or H.

[0024] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013.

[0025] In some aspects, the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013.

[0026] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 4513.

[0027] In some aspects, the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 2514 – SEQ ID NO: 4513. In some aspects, the 581 to 589 region confers increased retina tissue tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the retina tissue tropism is at least 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, or at least 500-fold higher than the wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1.

[0028] In some aspects, the 581 to 589 region further confers increased retinal pigment epithelium tissue tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the 581 to 589 region confers decreased photoreceptor tissue-tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the photoreceptor tissue comprises rod photoreceptor cells, cone photoreceptor cells, or a combination thereof. In some aspects, the VP capsid polypeptide comprises an amino acid sequence at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 98.5%, at least 99%, or at least 99.5% identical to SEQ ID NO: 1.

[0029] In some aspects, the VP capsid polypeptide has a sequence of SEQ ID NO: 2, wherein residues 581 to 589 of SEQ ID NO: 2 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$) correspond to the 581 to 589 region. In some aspects, the VP capsid polypeptide is capable of assembling into a recombinant viral capsid. In some aspects, the VP capsid polypeptide comprises at least one amino acid substitution as compared to each of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8. In some aspects, the 581 to 589 region comprises a net positive charge at pH 7.4.

[0030] In some aspects, the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region relative to a wild type VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the 581 to 589 region confers on a recombinant viral capsid assembled from the VP capsid polypeptide improved stability compared to a wild type AAV capsid comprising a peptide of SEQ ID NO: 1. In some aspects, the 581 to 589 region confers lower toxicity upon administration to a subject compared to a wild type VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region that contributes to reduced production of neutralizing antibodies relative to a wild type VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region that improves manufacturability relative to a wild type VP capsid polypeptide of SEQ ID NO: 1.

[0031] In various aspects, the present disclosure provides a recombinant viral adeno-associated virus (rAAV) capsid comprising a VP capsid polypeptide as described herein, wherein the rAAV capsid preferentially targets retina tissue.

[0032] In some aspects, the rAAv further comprises a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region.

[0033] In various aspects, the present disclosure provides a recombinant adeno-associated virus (rAAV), comprising a VP capsid polypeptide as described herein assembled into a recombinant viral capsid and a payload encapsidated by the recombinant viral capsid.

[0034] In some aspects, the rAAV preferentially targets retina tissue. In some aspects, the rAAV further comprises a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region. In some aspects, the payload encodes a therapeutic polynucleotide or a therapeutic peptide. In some aspects, the payload encodes a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, or an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof. In some aspects, the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA. In some aspects, the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor.

[0035] In various aspects, the present disclosure provides a pharmaceutical composition comprising a VP capsid polypeptide as described herein, a rAAV capsid as described herein, or a rAAV as described herein.

[0036] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues.

[0037] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513.

[0038] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide as described herein.

[0039] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region

comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues; and (ii) delivering the payload to the retina tissue.

[0040] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513; and (ii) delivering the payload to the retina tissue.

[0041] In various aspects, the present disclosure provides a method of delivering a payload to a retina tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide as described herein; and (ii) delivering the payload to the retina tissue.

[0042] In some aspects, the method comprises administering the rAAV via intravitreal administration. In some aspects, the method comprises administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration. In some aspects, the method further comprises expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload. In some aspects, the method further comprises producing a therapeutic effect upon expression of the payload. In some aspects, the therapeutic effect is produced upon administration of from 1×10^5 to 5×10^{14} rAAVs. In some aspects, the method comprises administering an amount of the rAAV sufficient to produce the therapeutic effect without producing a toxicity in the subject.

[0043] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues.

[0044] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85%

sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513.

[0045] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide as described herein.

[0046] In some aspects, the method further comprises expressing the payload in a retina tissue of the subject. In some aspects, the method further comprises producing a therapeutic effect in the subject.

[0047] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues; and (ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

[0048] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513; and (ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

[0049] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide as described herein; and (ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

[0050] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide as described herein; (ii) delivering the payload to a retina tissue of the

subject; and (iii) producing a therapeutic effect in the retina tissue, thereby treating the condition.

[0051] In some aspects, the method comprises administering the rAAV via intravitreal administration. In some aspects, the method comprises administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration. In some aspects, the condition is an ocular condition. In some aspects, the ocular condition is achromatopsia, macular degeneration, cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis. In some aspects, the ocular condition is Stargardt disease.

[0052] In some aspects, the method further comprises delivering the rAAV to a retina tissue with higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. In some aspects, the method further comprises delivering the rAAV to a retina tissue with higher tissue tropism than for photoreceptor tissue. In some aspects, the method comprises delivering the rAAV to a retina tissue with at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. In some aspects, the method comprises administering from 1×10^5 to 5×10^{14} rAAVs.

[0053] In some aspects, the payload encodes a therapeutic protein, therapeutic polynucleotide, a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof. In some aspects, the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA. In some aspects, the therapeutic protein is selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I, ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, and RS1. In some aspects, the therapeutic

polynucleotide targets an mRNA encoding a protein selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I, ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, or RS1. In some aspects, the payload encodes a therapeutic polynucleotide targeting ABCA1, ABCA4, or CRB1 or a transgene encoding ABCA1, ABCA4, or CRB1. In some aspects, the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor. In some aspects, the component of the CRISPR/Cas system comprises a Cas3, a Cas8, a Cas10, a Cas9, a Cas4, a Cas12, a Cas13, a guide RNA, or a combination thereof. In some aspects, the ADAR enzyme is ADAR1 or ADAR2. In some aspects, the transcriptional activator is VP64. In some aspects, the transcriptional repressor is KRAB.

[0054] In some aspects, the method further comprises expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload. In some aspects, the method comprises expressing the therapeutic polypeptide or the therapeutic polynucleotide at a higher level in a retina tissue compared to a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. In some aspects, the method comprises expressing the therapeutic polypeptide or the therapeutic polynucleotide in a retina tissue at a level that is at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher compared to the wild type AAV5 capsid. In some aspects, the method comprises producing a toxicity in the subject that is lower than a toxicity produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the method comprises producing a toxicity in the subject that is lower than a toxicity produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retina tissue. In some aspects, the method comprises producing a concentration of neutralizing antibodies in the

subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1. In some aspects, the method comprises producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV2 capsids. In some aspects, the method comprises producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV8 capsids. In some aspects, the method comprises producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV9 capsids. In some aspects, the method comprises producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retina tissue.

[0055] In various aspects, the present disclosure provides a rAAV capsid as described herein, a rAAV as described herein, or a pharmaceutical composition as described herein for use as a medicament.

[0056] In various aspects, the present disclosure provides a rAAV capsid as described herein, a rAAV as described herein, or a pharmaceutical composition as described herein for use in a method of treating an ocular condition.

[0057] In some aspects, the ocular condition is achromatopsia, macular degeneration, cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis. In some aspects, the ocular condition is Stargardt disease.

[0058] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513.

[0059] In some aspects, the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513.

[0060] In various aspects, the present disclosure provides a viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5

VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0061] In some aspects, the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0062] In various aspects, the present disclosure provides a recombinant viral adeno-associated virus (rAAV) capsid comprising a VP capsid polypeptide as described herein, wherein the rAAV capsid preferentially targets retinal pigment epithelium tissue.

[0063] In various aspects, the present disclosure provides a recombinant viral adeno-associated virus (rAAV) capsid comprising a VP capsid polypeptide as described herein, wherein the rAAV capsid preferentially targets choroid tissue.

[0064] In various aspects, the present disclosure provides a method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0065] In various aspects, the present disclosure provides a method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0066] In various aspects, the present disclosure provides a method of delivering a payload to a choroid tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and (ii) delivering the payload to the choroid tissue.

[0067] In various aspects, the present disclosure provides a method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589

region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and (ii) delivering the payload to the retinal pigment epithelium tissue.

[0068] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0069] In various aspects, the present disclosure provides a method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and (ii) expressing the payload in a retinal pigment epithelium tissue of the subject, thereby treating the condition in the subject.

INCORPORATION BY REFERENCE

[0070] All references cited herein are incorporated by reference to the same extent as if each individual publication, database entry (e.g., Genbank sequences or GeneID entries), patent application, or patent, was specifically and individually indicated incorporated by reference in its entirety, for all purposes. This statement of incorporation by reference is intended by Applicants, pursuant to 37 C.F.R. §1.57(b)(1), to relate to each and every individual publication, database entry (e.g., Genbank sequences or GeneID entries), patent application, or patent, each of which is clearly identified in compliance with 37 C.F.R. §1.57(b)(2), even if such citation is not immediately adjacent to a dedicated statement of incorporation by reference. The inclusion of dedicated statements of incorporation by reference, if any, within the specification does not in any way weaken this general statement of incorporation by reference. Citation of the references herein is not intended as an admission that the reference is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents.

BRIEF DESCRIPTION OF THE DRAWINGS

[0071] These and other features, aspects, and advantages of the present invention will become better understood with regard to the following description, and accompanying drawings where:

[0072] FIG. 1 is a schematic of the high throughput AAV capsid engineering system for identification of tissue-tropic sequences for intravitreal administration. A capsid library, selected for the ability to assemble into viral capsids, is administered to a non-human primate (NHP) by intravitreal administration. Tissues, including eye tissues such as retina, optic nerve, choroid, aqueous humor, and vitreous humor, are recovered, and the capsids accumulated in each tissue are sequenced. The resulting sequencing data are fed into a machine learning-powered bioinformatics pipeline to identify viral capsid polypeptide sequences and biophysical properties that promote tissue-specific transduction/infection.

[0073] FIG. 2A provides a side view (top panel) and top view (bottom panel) of key residues of known AAV capsids that have been shown to interact with target cells.

[0074] FIG. 2B illustrates salient features of the AAV capsid library described in **EXAMPLE 1**, showing the region of introduced diversity, with residue numbering corresponding to the numbering of amino acids in AAV5 VP1.

[0075] FIG. 3 is a bar graph showing viral genomes per milligram of tissue recovered from various eye tissues following NHP capsid library screening performed as illustrated in **FIG. 1**. Screening was performed independently in two non-human primates ("NHP1" and "NHP2").

[0076] FIG. 4 is a bar graph showing the number of unique variant capsid polypeptide sequences ("# of varAA") identified within various tissues from two NHPs ("NHP #1" and "NHP #2") administered a recombinant AAV library via intravitreal injection.

[0077] FIG. 5A – FIG. 5D are sequence logo plots depicting relative amino acid enrichment and depletion at each amino acid position of the 581 to 589 region in the retina from two NHPs administered a recombinant AAV library via intravitreal injection. **FIG. 5A** illustrates enrichment in retina versus other remaining eye tissues ("other") in example NHP1. **FIG. 5B** illustrates enrichment in retina versus other remaining eye tissues ("other") in a second example NHP2. **FIG. 5C** illustrates enrichment in retina versus vitreous/aqueous humor ("humor") in a first NHP. **FIG. 5D** illustrates enrichment in retina versus vitreous/aqueous humor ("humor") in a second NHP.

[0078] FIG. 6A and **FIG. 6B** are heatmaps showing relative amino acid enrichment in retina at each amino acid position of the 581 to 589 region (corresponding to positions 581-589 in the VP1 sequence) for a first (**FIG. 6A**) and second (**FIG. 6B**) NHP, administered a recombinant

AAV library via intravitreal injection. The enrichment shown is relative to "ST2", the diversity of the assembled capsid library pre-infusion.

[0079] FIG. 7 is a bar graph showing numbers of AAV capsid polypeptide variants observed in a primary screen of an engineered AAV capsid library. Counts are provided for the total number of variants found in either retina or RPE tissue ("total"), the number of variants found in only that tissue ("tissue_unique"), the number of tissue-unique variants found in more than one non-human primate ("multiple_nhps"), and the number of tissue-unique variants found in more than one replicate ("multiple_reps," includes variants found in multiple NHPs).

[0080] FIG. 8 is a violin plot comparing the predictive probability ("retina_score") of having retina-specific tropism for retina tissue-unique variants separated based on numbers of observations, either a single observation ("n") or multiple observations ("y"), within non-human primates ("multiple_nhps") or within all replicates ("multiple_reps").

[0081] FIG. 9 is a box and whisker plot showing the predictive probability ("Average ML Score") of having retina-specific tropism for all retina tissue-unique variants identified from the primary screen ("observed") or generated through machine learning models ("synthetic"). Subsets of observed retina variants found in multiple NHPs ("Multiple NHPs") or multiple replicates ("Multiple Replicates") are noted, along with synthetic variants generated using three distinct modeling strategies ("Input optimization", "Sample PWM", and "Sample uniform").

[0082] FIG. 10 is plot showing the predictive probability ("Average ML Score") of having retina-specific tropism for retina tissue-unique variants selected for inclusion in the secondary screen that were identified from the primary screen ("observed") or through machine learning models ("synthetic").

DETAILED DESCRIPTION OF THE INVENTION

[0083] Unless described otherwise, all technical and scientific terms used herein have the meaning commonly understood by one of ordinary skill in the art to which the invention pertains.

[0084] Unless otherwise stated, whenever a range is recited, the range is inclusive of the recited endpoints. For example, the region from amino acid residue 581 to amino acid residue 589 of SEQ ID NO: 1 includes amino acid residues 581 and 589.

[0085] "Homology" or "identity" or "similarity" can refer to sequence similarity between two peptides or between two nucleic acid molecules. Homology can be determined by comparing a position in each sequence which can be aligned for purposes of comparison. When a position in the compared sequence can be occupied by the same base or amino acid, then the molecules can

be homologous at that position. A degree of homology between sequences can be a function of the number of matching or homologous positions shared by the sequences. An "unrelated" or "non-homologous" sequence shares less than 40% identity, or alternatively less than 25% identity, with one of the sequences of the disclosure. Sequence homology can refer to a % identity of a sequence to a reference sequence. As a practical matter, whether any particular sequence can be at least 50%, 60%, 70%, 77.7%, 80%, 88.8%, 85%, 90%, 92%, 95%, 96%, 97%, 98% or 99% identical to any sequence described herein (which can correspond with a particular nucleic acid sequence described herein), such particular polypeptide sequence can be determined conventionally using known computer programs such the Bestfit program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, 575 Science Drive, Madison, Wis. 53711). When using Bestfit or any other sequence alignment program to determine whether a particular sequence is, for instance, 95% identical to a reference sequence, the parameters can be set such that the percentage of identity can be calculated over the full length of the reference sequence and that gaps in sequence homology of up to 5% of the total reference sequence can be allowed. The term percent "identity" or percent "homology," in the context of two or more nucleic acid or polypeptide sequences, refer to two or more sequences or subsequences that have a specified percentage of nucleotides or amino acid residues that are the same, when compared and aligned for maximum correspondence, as measured using one of the sequence comparison algorithms described below (e.g., BLASTP and BLASTN or other algorithms available to persons of skill) or by visual inspection. Depending on the application, the percent "identity" can exist over a region of the sequence being compared, e.g., over a functional domain, or, alternatively, exist over the full length of the two sequences to be compared. For sequence comparison, typically one sequence acts as a reference sequence to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters. For purposes herein, determination of percent identity and sequence similarity is performed using the BLAST algorithm, which is described in Altschul et al., *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov/). For example, where an amino acid sequence consisting of 9 residues is compared with another 9

residue amino acid sequence, if 8 residues match then the sequences have 88.8% identity, if 7 residues match then the sequences have 77.7% identity.

[0086] In some cases, the identity between a reference sequence (query sequence, e.g., a sequence of the disclosure) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program. In some embodiments, parameters for a particular embodiment in which identity can be narrowly construed, used in a FASTDB amino acid alignment, can include: Scoring Scheme=PAM (Percent Accepted Mutations) 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject sequence, whichever can be shorter. According to this embodiment, if the subject sequence can be shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction can be made to the results to take into consideration the fact that the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity can be corrected by calculating the number of residues of the query sequence that can be lateral to the N- and C-terminal of the subject sequence, which can be not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. A determination of whether a residue can be matched/aligned can be determined by results of the FASTDB sequence alignment. This percentage can be then subtracted from the percent identity, calculated by the FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score can be used for the purposes of this embodiment. In some cases, only residues to the N- and C-termini of the subject sequence, which can be not matched/aligned with the query sequence, can be considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence can be considered for this manual correction. For example, a 90-residue subject sequence can be aligned with a 100-residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence, and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C-termini not matched/total number of residues in the query sequence) so 10% can be subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched, the final percent identity can be 90%. In another example, a 90-residue

subject sequence can be compared with a 100-residue query sequence. This time the deletions can be internal deletions, so there can be no residues at the N- or C-termini of the subject sequence which can be not matched/aligned with the query. In this case, the percent identity calculated by FASTDB can be not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which can be not matched/aligned with the query sequence can be manually corrected for.

[0087] Peptide sequences for use in the present invention may comprises one or more substitutions, i.e. amino acid substitutions. The substitutions may be conservative amino acid substitutions. Therefore, peptide sequences for use in the present invention may include one or more conservative amino acid substitutions, such that the resulting sequence has a similar amino acid sequence and/or retains the same function. The skilled person is aware that various amino acids have similar biochemical properties and thus are "conservative". One or more such amino acids of a protein, polypeptide or peptide can often be substituted by one or more other such amino acids without eliminating a desired activity of that protein, polypeptide or peptide. Thus, the amino acids glycine, alanine, valine, leucine and isoleucine can often be substituted for one another (amino acids having aliphatic side chains). Of these possible substitutions it is preferred that glycine and alanine are used to substitute for one another (since they have relatively short side chains) and that valine, leucine and isoleucine are used to substitute for one another (since they have larger aliphatic side chains which are hydrophobic). Other amino acids which can often be substituted for one another include: phenylalanine, tyrosine and tryptophan (amino acids having aromatic side chains); lysine, arginine and histidine (amino acids having basic side chains); aspartate and glutamate (amino acids having acidic side chains); asparagine and glutamine (amino acids having amide side chains); and cysteine and methionine (amino acids having sulfur containing side chains). It should be appreciated that amino acid substitutions within the scope of the present invention can be made using naturally occurring or non-naturally occurring amino acids. For example, the methyl group on an alanine may be replaced with an ethyl group, and/or minor changes may be made to the peptide backbone. Whether or not natural or synthetic amino acids are used, it is preferred that only L- amino acids are present. Substitutions of this nature are often referred to as "conservative substitutions".

[0088] As used herein, "tropism" of a rAAV for a tissue may refer to the ability of a given rAAV to preferentially infect a given cell type or tissue. A degree of tropism may be determined by a ratio of an infection rate in a targeted tissue to an infection rate in a different, non-targeted tissue. As used herein, increased tropism for a given cell type or tissue, such as increased

tropism conferred by a 581 to 589 region, is determined relative to a wild type AAV5 capsid. As used herein, "detargeting" of a rAAV to a tissue may refer to the ability of a given rAAV to avoid infecting a detargeted tissue or cell type while infecting one or more other tissues or cell types. A degree of detargeting may be determined by a ratio of an infection rate in a detargeted tissue to an infection rate of a different, non-detargeted tissue. As used herein, increased detargeting for a given cell type or tissue, such as increased detargeting conferred by a 581 to 589 region, is determined relative to a wild type AAV5 capsid.

[0089] As used herein, "tissue tropism" refers to a preference of a virus having an engineered VP capsid polypeptide of the present disclosure to infect a given tissue or be enriched in or accumulate in a given tissue. A "tissue-tropic" rAAV may specifically target or infect a first tissue or set of tissues and may not target or infect a second tissue or set of tissues. For example, a "retinal tissue-tropic" rAAV may specifically target or infect retinal tissue and may not target or infect vitreous humor, aqueous humor, or other tissues. A "tissue-detargeted" rAAV may specifically avoid targeting or avoid infection of the detargeted tissue or set of tissues while infecting a second tissue or set of tissues. For example, a "liver-detargeted" rAAV may not target or infect liver tissue but may infect one or more other tissues, such as ocular, nervous, muscle, skin, bone, and/or other tissue. In another example, a "photoreceptor-detargeted" rAAV may not target or infect photoreceptor cells but may infect one or more other cell or tissue types, such as aqueous humor, retina, retinal pigment epithelium, optic nerve, vitreous humor, and/or other tissue or cells. In another example, a "choroid-detargeted" rAAV may not target or infect choroid tissue but may infect one or more other tissue or cell types, such as aqueous humor, retina, retinal pigment epithelium, optic nerve, vitreous humor, and/or other tissue or cells. Tissue tropism or tissue detargeting, when used as a relative term and depending on the context in which it is described herein, refers to an increase or decrease in tissue tropism of a given rAAV virion having a first capsid polypeptide in a first tissue as compared to a second tissue and/or refers to an increase or decrease in tissue tropism of a given rAAV virion having a first capsid polypeptide to an rAAV virion having a second capsid polypeptide. In some embodiments, the first tissue can be a group of tissues. In some embodiments, the second tissue can be a group of tissues. For example, the first tissue may be retinal tissue and the second tissue may be a different eye tissue (e.g., aqueous humor, choroid, optic nerve, vitreous humor, or remaining eye tissue). In another example, tissue tropism can refer to cellular homing, such as targeting a retinal pigment epithelial cell, a photoreceptor cell (e.g., rod cells, cone cells, or a combination thereof), or both.

[0090] In some embodiments, the rAAV virions of the present disclosure may also be referred to as preferentially targeting a given tissue or having tissue selectivity for a given tissue. For example, an rAAV virion that preferentially targets retinal tissue may specifically target or infect retinal tissue and may not target or infect vitreous humor, aqueous humor, or other tissues. As another example, an rAAV virion that has retinal tissue selectivity may specifically target or infect retinal tissue and may not target or infect vitreous humor, aqueous humor, or other tissues.

[0091] For simplicity throughout this disclosure, viral capsid protein is generally referred to as "VP." Viral capsid protein is referred to as VP1 when referencing AAV5 VP1 positional notation. In all cases, viral capsid sequences and mutations disclosed herein should be understood as pertaining to all isoforms of the capsid protein (VP1, VP2, and VP3), as a mixture of these isoforms assemble to form virions. The positional amino acid residue designations "581 to 589" are relative to the translational start of the VP1 polypeptide and should be adjusted accordingly to the relative start sites of VP2 and VP3. It should be understood that the present disclosure, when describing any particular VP1 sequence with mutations at particular amino acid residue positions, necessarily also encompasses corresponding mutations in VP2 and VP3. For example, any consensus sequence or specific sequence of a VP1 capsid protein having one or more mutations in the 581 to 589 region, corresponding to amino acid residues 581 to 589 of VP1, also encompasses VP2 and VP3 capsid proteins having said one or more mutations in an amino acid residue region in VP2 and VP3 corresponding to the amino acid residues of the VP1 581 to 589 region. For example, the amino acid residues of the 581 to 589 region of VP1 (SEQ ID NO: 1;

MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG
LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG
KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS
GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV
VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD
WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV
GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT
YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN
WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN
TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST
TAPATGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL) correspond to the amino acid residues of the

445 to 453 region of VP2 (SEQ ID NO: 10;
TAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAG
GGGPLGDNNQGADGVGNASGDWHCDSTWMGDRVVTKSTRTWVLPSYNNHQYREIKS
GSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLINNYWGFRPRSLRVKIFNIQ
VKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGY
ATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLAN
PLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRA
SVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSNTYALENTMIFNSQPANPGTTATY
LEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQEIVPGSVWMERD
VYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQ
YSTGQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRY
LTRPL) and to the amino acid residues of 389 to 397 region of VP3 (SEQ ID NO: 11;
MSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRVVTKSTRTWVLPSYNNHQY
REIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLINNYWGFRPRSLRVK
IFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQ
YGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFK
LANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGV
NRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSNTYALENTMIFNSQPANPGTT
ATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQEIVPGSVWM
ERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSS
FITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIG
TRYLTRPL). As used herein, “wild type 581 to 589 region” refers to a 581 to 589 region of VP1 having a sequence of ATGTYNLQE (SEQ ID NO: 9).

[0092] As used herein, “581 to 589 region” refers to a region or fragment of VP1 corresponding to amino acid residues 581 to 589 relative to the translational start of the VP1 polypeptide. The 581 to 589 region corresponds to amino acid residues 445 to 453 of VP2 and to amino acid residues 389 to 397 of VP3. The 581 to 589 region may confer tissue tropism or tissue preference to an AAV, and region variants may be engineered to confer tissue tropism or tissue preference to an rAAV formed from viral capsid polypeptides (VP1, VP2, and VP3) comprising the assembled variant. The VP1 with a generalized 581 to 589 region is provided in SEQ ID NO: 2
(MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG
LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG
KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS

GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST TAPX^{1}X^{2}X^{3}X^{4}X^{5}X^{6}X^{7}X^{8}X^{9}IVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLK HPPPMMLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYT NNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), in which the 581 to 589 region has a sequence of X^{1}X^{2}X^{3}X^{4}X^{5}X^{6}X^{7}X^{8}X^9 (SEQ ID NO: 5014); wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V.

[0093] It should be understood that the present disclosure includes polynucleotide sequences encoding for any sequence disclosed herein. For example, if an amino acid sequence is provided, the present disclosure also encompasses a polynucleotide sequence encoding for said amino acid sequence.

[0094] It should be understood that further embodiments include mutations in VP1, VP2, VP3, or any combination thereof that do not alter the desired properties (e.g., a particular tissue tropism) or affect viral assembly, as described herein.

[0095] An AAV virion is made of a capsid that may include the AAV5 VP capsid polypeptides disclosed herein (e.g., VP1, VP2, and VP3 capsid polypeptides).

Engineered Capsids and Capsid Polypeptides for Tissue Tropism

[0096] Described herein are engineered capsids, engineered capsid polypeptides, and 581 to 589 regions of capsid polypeptides that confer tissue tropism or preference (e.g., tissue-specific accumulation, tissue-specific infection, or both) to a viral capsid. In some embodiments, an engineered capsid may comprise one or more engineered capsid polypeptides assembled into a recombinant adeno-associated virus (rAAV) viral capsid. In some embodiments, an engineered capsid polypeptide may comprise a 581 to 589 region. The 581 to 589 region of viral capsid polypeptides, corresponding to amino acid residues 581 to 589 of the VP1 polypeptide, amino acid residues 445 to 453 of the VP2 polypeptide, and amino acid residues 389 to 397 of the VP3 polypeptide, is located at an AAV interface that likely interacts with host cells and tissues.

[0097] In some embodiments, an engineered capsid polypeptide may comprise a 581 to 589 region that confers increased tropism or preference for retina tissue relative to other ocular tissues as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a retina tissue-tropic capsid polypeptide may have increased tropism for retina tissue and may be de-targeted to photoreceptor tissue, as compared to a wild type AAV5 capsid polypeptide. In some embodiments, an engineered capsid polypeptide may comprise a 581 to 589 region that confers increased tropism or preference for retinal pigment epithelium (RPE) tissue relative to other ocular tissues as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a RPE tissue-tropic capsid polypeptide may have increased tropism for RPE tissue and may be de-targeted to photoreceptor tissue, as compared to a wild type AAV5 capsid polypeptide. In some embodiments, an engineered capsid polypeptide may comprise a 581 to 589 region that confers increased tropism or preference for choroid tissue relative to other ocular tissues as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a choroid tissue-tropic capsid polypeptide may have increased tropism for choroid tissue and may be de-targeted to photoreceptor tissue, as compared to a wild type AAV5 capsid polypeptide. In some embodiments, an engineered capsid polypeptide may comprise a 581 to 589 region that confers increased tropism or preference for RPE tissue and choroid tissue relative to other ocular tissues as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1).

[0098] Also described herein are methods of using engineered capsids comprising engineered capsid polypeptides with 581 to 589 regions for tissue-specific delivery of a payload (e.g., a polynucleotide, such as a transgene) encapsidated by the engineered capsid. Recombinant AAVs comprising VP capsid polypeptides with 581 to 589 regions engineered for tissue specificity may be used to specifically infect a target tissue. Using tissue-tropic rAAV viral capsids for payload delivery provides numerous advantages over using adeno-associated virus (AAV) viral capsids that lack tissue tropism including reduced toxicity, lower dose needed to produce a therapeutic effect, wider therapeutic window, and reduced immune response. Furthermore, tissue-specific payload delivery may improve tissue-specificity of therapies following local administration. For example, an ocular tissue-tropic rAAV viral capsid may be intravitreally administered to specifically deliver a payload to the eye for treatment of an ocular disease. Alternatively or in addition, an ocular tissue-tropic rAAV viral capsid may be administered by sub-retinal injection or topical mucosal administration (e.g., via eye drops) to deliver a payload

to the eye for treatment of an ocular disease. In some embodiments, an ocular tissue-tropic rAAV viral capsid may be administered systemically.

[0099] Ocular tissue tropism of the rAAV may reduce systemic effects (e.g., liver toxicity) from the therapy that may otherwise occur despite local administration. For example, an ocular tissue-tropic rAAV viral capsid may be engineered to target a specific ocular tissue (e.g., retinal tissue) while detargeting other ocular tissues (e.g., choroid, vitreous humor, or aqueous humor). Ocular tissue-tropic rAAV viral capsids may target a specific ocular cell type, such as retinal pigment epithelial cells or photoreceptor cells (e.g., rod cells, cone cells, or both). In some embodiments, an ocular tissue-tropic rAAV viral capsids may target a specific ocular cell type (e.g., retinal pigment epithelial cells) while detargeting one or more other ocular tissue or cell types (e.g., photoreceptor cells, choroid, vitreous humor, or aqueous humor). Such ocular tissue-specific rAAVs may enable specific targeting of regions within the eye for treatment of tissue-specific conditions, such as conditions of the retina, optic nerve, or choroid. In yet another example, an ocular tissue-tropic rAAV may accumulate in specific ocular tissue (e.g., retina) following intravitreal administration, sub-retinal injection, topical mucosal administration, or systemic administration. An ocular tissue-tropic rAAV may target a specific ocular cell type (e.g., retinal pigment epithelial cells, photoreceptor cells, or both) following intravitreal administration, sub-retinal injection, topical mucosal administration, or systemic administration. For example, a retina tissue-tropic rAAV may specifically accumulate in retina tissue and may be de-targeted from photoreceptor tissue. In another example, a RPE tissue-tropic rAAV may specifically accumulate in RPE tissue and may be de-targeted from photoreceptor tissue. In another example, a choroid tissue-tropic rAAV may specifically accumulate in choroid tissue and may be de-targeted from photoreceptor tissue. In another example, a choroid and RPE tissue-tropic rAAV may specifically accumulate in choroid and RPE tissue and may be de-targeted from photoreceptor tissue.

[0100] In some embodiments, a tissue-tropic capsid of the present disclosure may be ocular tissue-tropic. For example, an ocular tissue-tropic capsid polypeptide may confer increased tropism or preference for one or more ocular tissues (e.g., retinal tissue) as compared to a wild type VP capsid polypeptide (e.g., SEQ ID NO: 1). An ocular tissue-tropic capsid polypeptide may confer cellular homing to one or more ocular cell types (e.g., retinal pigment epithelial cells, photoreceptor cells, rod photoreceptor cells, cone photoreceptor cells, or combinations thereof).

[0101] An engineered capsid polypeptide of the present disclosure may comprise one or more amino acid substitutions relative to an AAV5 viral protein (VP) polypeptide (e.g., a VP1

polypeptide of SEQ ID NO: 1, a VP2 polypeptide of SEQ ID NO: 10, or a VP3 polypeptide of SEQ ID NO: 11). The engineered capsid polypeptide may comprise one or more amino acid substitutions relative to a VP1 polypeptide of any or all of SEQ ID NO: 3 – SEQ ID NO: 8. In some embodiments, the engineered capsid polypeptide may comprise a 581 to 589 region comprising one or more amino acid substitutions in a region of a VP polypeptide (e.g., a 581 to 589 region of VP1, VP2, VP3, or a combination thereof) corresponding to amino acid residues 581 to 589 of VP1 (e.g., SEQ ID NO: 1), amino acid residues 445 to 453 of VP2 (e.g., SEQ ID NO: 10), or amino acid residues 389 to 397 of VP3 (e.g., SEQ ID NO: 11). In some embodiments, the 581 to 589 region may be present in VP1, VP2, and VP3. An engineered viral capsid may be assembled from VP1, VP2, and VP3 polypeptides comprising a 581 to 589 region. In some embodiments, the 581 to 589 region may confer ocular tissue tropism or preference.

[0102] In some embodiments, an engineered capsid polypeptide of the present disclosure may comprise a 581 to 589 region that confers increased retina tissue-tropism or preference as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a 581 to 589 region that confers increased retina tissue-tropism may have a sequenced of any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513. In some embodiments, an engineered capsid polypeptide of the present disclosure may comprise a 581 to 589 region that confers increased RPE tissue-tropism or preference as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a 581 to 589 region that confers increased RPE tissue-tropism may have a sequenced of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, an engineered capsid polypeptide of the present disclosure may comprise a 581 to 589 region that confers increased choroid tissue-tropism or preference as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). For example, a 581 to 589 region that confers increased choroid tissue-tropism may have a sequenced of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

Capsid engineering methods

[0103] Disclosed herein is a system for high throughput engineering of engineered AAV capsids with modified function, including increased or decreased infectivity of desired tissues, such as increased targeting of ocular tissue (e.g., retinal tissue), decreased targeting of non-eye tissue, or selective targeting of a specific ocular tissue (e.g., retinal tissue) compared to other ocular

tissues (e.g., aqueous humor or vitreous humor), relative to a wild type AAV5 capsid (e.g., comprising a VP capsid polypeptide of SEQ ID NO: 1). In some embodiments, the engineered AAV capsids may exhibit cellular homing to specific ocular cell types (e.g., retinal pigment epithelial cells, photoreceptor cells, rod photoreceptor cells, cone photoreceptor cells, or combinations thereof). A general schematic of the process is shown in **FIG. 1**. However, it should be understood that the present disclosure also encompasses reasonable variations or extensions to the method that are understood to those of ordinary skill in the art. The method may begin with production of a capsid library with theoretical diversity of 5×10^{11} unique sequence variants. Higher or lower theoretical diversities are also encompassed herein. For example, a capsid library may have a theoretical diversity of from about 1×10^{3} to about 1×10^{20}. As shown in **FIG. 1**, the library may first be selected for the ability to assemble into viral capsids. The library may then be cloned into plasmids and transformed into bacteria. As shown in **FIG. 1**, the library plasmids may be subsequently screened for productive virion assembly in a production cell line. The assembled virions may then be administered intravitreally into non-human primates (NHP). In some embodiments, the assembled virions may be administered via sub-retinal injection, topical mucosal administration, or systemic administration. After a period of time sufficient for distribution, infection, and stable transduction, the NHP may be sacrificed, organs harvested, and sequences of AAV capsids in each tissue may be determined by deep sequencing. Eye tissues, including aqueous humor, choroid, retina, optic nerve, vitreous humor, and remaining eye tissue may be harvested for sequencing.

[0104] FIG. 2A provides a side view (top panel) and top view (bottom panel) of the surface of a prototype AAV virion, identifying residues of known AAV capsids, including AAV2, AAV5, AAV6, and AAV9, that have been shown in the research literature to interact with target cells. These target-interacting residues correspond to amino acids 581 to 589 in the AAV5 VP1 capsid protein.

[0105] FIG. 2B shows the salient elements of the library plasmid, illustrating rep and cap coding sequences positioned between AAV ITRs. In the illustrated embodiment, further described in **EXAMPLE 1**, variation is introduced into each of residues 581 to 589 of the AAV5 cap protein ("Library 581 to 589 region") that is present in assembled VP1, VP2, and VP3 polypeptides. Each of the 20 natural amino acids is introduced at each of the 9 positions of the 581 to 589 region, providing a theoretical library diversity of 20^{9} (20^9; approximately 5×10^{11}) unique sequence variants.

[0106] The 581 to 589 region targeted for engineering is the most likely to interact with target cell receptors, and relatively tolerant to changes without disrupting virion assembly. Unlike

earlier approaches that add unstructured peptides that protrude above the virion 3-fold axis of symmetry, the current approach introduces sequence diversity that alters the characteristics of the binding pocket. In addition, this approach may change the overall structure of the receptor-binding trimer, allowing for altered allosteric interactions outside the binding pocket (e.g., AAVR PKD1). Introduced diversity is non-random, thereby reducing missense and frameshifts of randomized libraries.

[0107] By cloning the polynucleotide encoding the capsid variants into the packaged viral genome (between the ITRs), the recombinant virions with variant capsids carry polynucleotides having their cognate mutation, so the unique variant providing the desired function can be identified by sequencing packaged virus or infected cells.

[0108] In some embodiments, the capsid is a capsid selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV 10, AAV11, AAV12, AAV13, AAV14, AAV15, AAV16, AAV-DJ, AAV-DJ/8, AAV-DJ/9, AAV1/2, AAV.rh8, AAV.rh10, AAV.rh20, AAV.rh39, AAV.Rh43, AAV.Rh74, AAV.v66, AAV.Oligo001, AAV.SCH9, AAV.r3.45, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65, AAV.7m8, AAV.PhP.eB, AAV.PhP.V1, AAV.PHP.B, AAV.PhB.C1, AAV.PhB.C2, AAV.PhB.C3, AAV.PhB.C6, AAV.cy5, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, AAV.HSC16, AAV.HSC17, or AAVhu68, (described in WO2020/033842, incorporated herein by reference in its entirety). For example, the capsid may be an AAV5 capsid. The hu68 capsid is described in WO 2018/160582, incorporated herein by reference in its entirety.

[0109] Such capsids may comprise a 581 to 589 region corresponding amino acid residues 581 to 589 of the AAV5 VP1, and as such analogous engineered VP capsids with desired tissue tropism, ability to assemble, and exhibit various other desired traits are encompassed herein. Thus, any one of the engineered AAV5 VP capsid polypeptides disclosed herein having a mutation or substitution in the 581 to 589 region corresponding to the 581 to 589 region of AAV5 VP1 may be inserted into the corresponding region in any one of the other AAV capsids described herein and the present disclosure encompasses such variants.

[0110] In some embodiments, the capsid is a derivative, modification, or pseudotype of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV 10, AAV11, AAV12, AAV13, AAV14, AAV15, AAV16, AAV-DJ, AAV-DJ/8, AAV-DJ/9, AAV1/2, AAV.rh8, AAV.rh10, AAV.rh20, AAV.rh39, AAV.Rh43, AAV.Rh74, AAV.v66, AAV.Oligo001, AAV.SCH9, AAV.r3.45, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65,

AAV.7m8, AAV.PhP.eB, AAV.PhP.V1, AAV.PHP.B, AAV.PhB.C1, AAV.PhB.C2, AAV.PhB.C3, AAV.PhB.C6, AAV.cy5, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, AAV.HSC16, AAV.HSC17, or AAVhu68,. For example, the capsid may be a derivative of AAV5.

[0111] In some embodiments, capsid protein is a chimera of capsid proteins from two or more serotype selected from AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV 10, AAV11, AAV12, AAV13, AAV14, AAV15, AAV16, AAV-DJ, AAV-DJ/8, AAV-DJ/9, AAV1/2, AAV.rh8, AAV.rh10, AAV.rh20, AAV.rh39, AAV.Rh43, AAV.Rh74, AAV.v66, AAV.Oligo001, AAV.SCH9, AAV.r3.45, AAV.RHM4-1, AAV.hu37, AAV.Anc80, AAV.Anc80L65, AAV.7m8, AAV.PhP.eB, AAV.PhP.V1, AAV.PHP.B, AAV.PhB.C1, AAV.PhB.C2, AAV.PhB.C3, AAV.PhB.C6, AAV.cy5, AAV2.5, AAV2tYF, AAV3B, AAV.LK03, AAV.HSC1, AAV.HSC2, AAV.HSC3, AAV.HSC4, AAV.HSC5, AAV.HSC6, AAV.HSC7, AAV.HSC8, AAV.HSC9, AAV.HSC10, AAV.HSC11, AAV.HSC12, AAV.HSC13, AAV.HSC14, AAV.HSC15, AAV.HSC17, AAVhu68, and AAV.HSC16 (described in WO2020/033842, incorporated herein by reference in its entirety). In certain embodiments, the capsid is an rh32.33 capsid, described in US Pat. No. 8,999,678, incorporated herein by reference in its entirety.

[0112] Such capsids may comprise a 581 to 589 region corresponding to 581 to 589 of the AAV5 VP1, and as such analogous engineered VP capsids with desired tissue tropism, ability to assemble, and exhibit various other desired traits are encompassed herein.

VP-encoding polynucleotides, vectors, and vector libraries

[0113] Accordingly, in a first aspect, polynucleotides are provided. The polynucleotides encode an adeno-associated virus (AAV) VP1 capsid polypeptide having the amino acid sequence of SEQ ID NO: 2, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from the 20 naturally occurring amino acids, using standard one letter codes, from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V. The sequence $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 corresponds to the 581 to 589 region of VP1. X^1 corresponds to a position 581 of the 581 to 589 region. X^2 corresponds to a position 582 of the 581 to 589 region. X^3 corresponds to a position 583 of the 581 to 589 region. X^4 corresponds to a position 584 of the 581 to 589 region. X^5 corresponds to a position 585 of the 581 to 589 region. X^6 corresponds to a position 586 of the 581 to 589 region. X^7 corresponds to a position 587 of the 581 to 589 region. X^8

corresponds to a position 588 of the 581 to 589 region. X^9 corresponds to a position 589 of the 581 to 589 region. The polynucleotide encodes a polypeptide that includes at least one mutation of the native AAV5 capsid and thus does not have the sequence of SEQ ID NO: 1. In addition, the polypeptide does not have the sequence of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8. In some embodiments, the VP1 capsid polypeptide comprises a 581 to 589 region. For example, a VP1 capsid polypeptide comprising a 581 to 589 region may comprise a sequence of SEQ ID NO: 1 in which residues 581 to residue 589 are replaced with a sequence of $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ (SEQ ID NO: 5014), wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V, and wherein the VP1 capsid polypeptide does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3 (MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST TAPATGTVNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), SEQ ID NO: 4 (MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST

TAPATGTYNTQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), SEQ ID NO: 5
(MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG
LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG
KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS
GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV
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WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV
GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT
YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN
WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN
TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST
TAPTTGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), SEQ ID NO: 6
(MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG
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KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS
GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV
VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD
WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV
GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT
YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN
WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN
TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST
TAPAAGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), SEQ ID NO: 7
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GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV
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WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV
GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT
YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN
WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN
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TAPATGAYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL), or SEQ ID NO: 8
(MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNG
LDRGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLG
KAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPS
GSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDRV
VTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRD
WQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVV
GNGTEGCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFT
YNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKN
WFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQGSN
TYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSST
TAPATGTVNTQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPM
MLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYN
DPQFVDFAPDSTGEYRTTRPIGTRYLTRPL).

[0114] In some embodiments, a polynucleotide of the present disclosure may encode an AAV VP1 capsid polypeptide having the amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513. In some embodiments, a polynucleotide of the present disclosure may encode an AAV VP1 capsid polypeptide having the amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0115] In some embodiments, the polynucleotide encodes an AAV VP1 capsid polypeptide that further comprises one or more mutations at an amino acid residue outside of the 581 to 589 region, with reference to SEQ ID NO: 1, wherein the resulting recombinant capsid is capable of forming an assembled virion that exhibits desired tissue targeting as compared to wild type AAV5 (SEQ ID NO: 1). The one or more mutations may confer increased tissue tropism or

preference (e.g., increased retinal tissue tropism) on the assembled virion as compared to a wild type AAV capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1).

[0116] In another aspect, a vector capable of replication in prokaryotic cells is provided, wherein the vector comprises the polynucleotide described immediately above. In typical embodiments, the vector is a plasmid encoding a replication competent AAV genome.

[0117] In a further aspect, a library is provided. The library comprises a plurality of vectors comprising the AAV capsid-encoding polynucleotides. In some embodiments, the vectors are plasmids, and the plurality of plasmids comprise a plurality of different AAV VP-encoding polynucleotides. The library may comprise a plurality of vectors encoding AAV VP1 capsid polypeptides having the amino acid sequence of SEQ ID NO: 2 comprising one or more amino acid variations in the 581 to 589 region.

[0118] In various embodiments, the library encodes at least 1×10^9 different AAV VP capsid polypeptides, at least 2.5×10^9 different AAV VP capsid polypeptides, at least 5×10^9 different AAV VP capsid polypeptides, at least 7.5×10^9 different AAV VP capsid polypeptides, at least 1×10^{10} different AAV VP capsid polypeptides, at least 2.5×10^{10} different AAV VP capsid polypeptides, at least 5×10^{10} different AAV VP capsid polypeptides, at least 7.5×10^{10} different AAV VP capsid polypeptides, at least 1×10^{11} different AAV VP capsid polypeptides, at least 2.5×10^{11} different AAV VP capsid polypeptides, or at least 5×10^{11} different AAV VP capsid polypeptides. The library may encode VP capsid polypeptides comprising 581 to 589 region variants.

[0119] In another aspect, prokaryotic cells comprising the vectors are provided. In some embodiments, the prokaryotic cell is an *E. coli* cell and the vector is a plasmid.

[0120] In a related aspect, libraries are provided, the library comprising a plurality of *E. coli* cells, wherein the plurality of cells comprise a plurality of plasmids, wherein the plurality of plasmids comprise a plurality of different AAV VP-encoding polynucleotides.

[0121] In some embodiments, the library encodes at least 1×10^9 different AAV VP capsid polypeptides, at least 2.5×10^9 different AAV VP capsid polypeptides, at least 5×10^9 different AAV VP capsid polypeptides, at least 7.5×10^9 different AAV VP capsid polypeptides, at least 1×10^{10} different AAV VP capsid polypeptides, at least 5×10^{10} different AAV VP capsid polypeptides, at least 7.5×10^{10} different AAV VP capsid polypeptides, at least 1×10^{11} different AAV VP capsid polypeptides, at least 2.5×10^{11} different AAV VP capsid polypeptides, or at least 5×10^{11} different AAV VP capsid polypeptides. The library may encode VP capsid polypeptides comprising 581 to 589 region variants.

VP polypeptides, peptide libraries

[0122] In another aspect, AAV VP1 capsid polypeptides are provided. The polypeptide has the amino acid sequence of SEQ ID NO: 2, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V. The polypeptide includes at least one mutation as compared to native AAV VP1, and thus does not have the sequence of SEQ ID NO: 1. In addition, the polypeptide does not have the sequence of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

[0123] In some embodiments, the polypeptide further comprises one or more mutations at an amino acid residue outside of the 581 to 589 region, with reference to SEQ ID NO: 1, wherein the resulting recombinant capsid is capable of forming an assembled virion that exhibits desired tissue targeting as compared to a wild type AAV5 comprising a VP capsid polypeptide of SEQ ID NO: 1.

[0124] In a further aspect, libraries are provided, the libraries comprising a plurality of polypeptides as described immediately above, the plurality having different primary amino acid sequences. A library may comprise a plurality of polypeptides of SEQ ID NO: 2 comprising one or more amino acid variations in the 581 to 589 region.

[0125] In some embodiments, library comprises at least 1×10^9 different AAV VP capsid polypeptides, at least 2.5×10^9 different AAV VP capsid polypeptides, at least 5×10^9 different AAV VP capsid polypeptides, at least 7.5×10^9 different AAV VP capsid polypeptides, at least 1×10^{10} different AAV VP capsid polypeptides, at least 2.5×10^{10} different AAV VP capsid polypeptides, at least 5×10^{10} different AAV VP capsid polypeptides, at least 7.5×10^{10} different AAV VP capsid polypeptides, at least 1×10^{11} different AAV VP capsid polypeptides, at least 2.5×10^{11} different AAV VP capsid polypeptides, or at least 5×10^{11} different AAV VP capsid polypeptides. The library may comprise VP capsid polypeptides comprising 581 to 589 region variants.

[0126] In certain embodiments, the library comprises at least from about 1×10^5 to at least about 5×10^{11} different AAV VP capsid polypeptides. In certain embodiments, the library comprises at least about 1×10^5, at least about 2×10^5, at least about 3×10^5, at least about 4×10^5, at least about 5×10^5, at least about 6×10^5, at least about 7×10^5, at least about 8×10^5, at least about 9×10^5, at least about 1×10^6, at least about 2×10^6, at least about 3×10^6, at least about 4×10^6, at least about 5×10^6, at least about 6×10^6, at least about 7×10^6, at least about 8×10^6, at least about 9×10^6, at least about 1×10^7, at least about 2×10^7, at least about 3×10^7, at least about 4×10^7, at least about 5×10^7, at least about 6×10^7, at least about 7×10^7, at least about 8×10^7, at

least about 9 x 10^7, at least about 1 x 10^8, at least about 2 x 10^8, at least about 3 x 10^8, at least about 4 x 10^8, at least about 5 x 10^8, at least about 6 x 10^8, at least about 7 x 10^8, at least about 8 x 10^8, at least about 9 x 10^8, at least about 1 x 10^9, at least about 2 x 10^9, at least about 3 x 10^9, at least about 4 x 10^9, at least about 5 x 10^9, at least about 6 x 10^9, at least about 7 x 10^9, at least about 8 x 10^9, at least about 9 x 10^9, at least about 1 x 10^{10}, at least about 2 x 10^{10}, at least about 3 x 10^{10}, at least about 4 x 10^{10}, at least about 5 x 10^{10}, at least about 6 x 10^{10}, at least about 7 x 10^{10}, at least about 8 x 10^{10}, at least about 9 x 10^{10}, at least about 1 x 10^{11}, at least about 2 x 10^{11}, at least about 3 x 10^{11}, at least about 4 x 10^{11}, or at least about 5 x 10^{11} AAV VP capsid polypeptides.

[0127] In certain embodiments, provided herein is a recombinant adeno-associated virus AAV VP1 capsid polypeptide having at least one mutation in a residue of region 581 to residue 589 in SEQ ID NO: 1, inclusive, wherein the mutation confers at least about 1.1-fold, at least about 1.2-fold, at least about 1.3-fold, at least about 1.4-fold, at least about 1.5-fold, at least about 1.6-fold, at least about 1.7-fold, at least about 1.8-fold, at least about 1.9-fold, at least about 2-fold, at least about 2.2-fold, at least about 2.4-fold, at least about 2.6-fold, at least about 2.8-fold, at least about 3-fold, at least about 3.5-fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 20-fold, at least about 30-fold, at least about 40-fold, at least about 50-fold, at least about 100-fold, at least about 200-fold, at least about 300-fold, at least about 400-fold, or at least about 500-fold increased accumulation of an AAV virion having said AAV VP1 capsid polypeptide in a target tissue (e.g., a retinal tissue), target cell (e.g., retinal pigment epithelial cells, photoreceptor cells, rod photoreceptor cells, cone photoreceptor cells, or combinations thereof), or both as compared to a non-target tissue (e.g., vitreous humor or aqueous humor), as compared to wild type AAV virion having a wild type AAV5 VP1 capsid polypeptide, and wherein the AAVVP1 capsid polypeptide does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8. In some embodiments, a VP1 capsid polypeptide comprises a 581 to 589 region comprising one or more amino acid mutations. For example, a VP1 capsid polypeptide may comprise a sequence of SEQ ID NO: 1 in which residues 581 to residue 589 are replaced with a sequence of $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ (SEQ ID NO: 5014), wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V, and wherein the VP1 capsid polypeptide does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

[0128] In some embodiments, an AAV VP1 capsid polypeptide of the present disclosure may have an amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513. In some embodiments, an AAV VP1 capsid polypeptide of the present disclosure may have an amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

rAAV virions, virion libraries

[0129] In another aspect, recombinant AAV virions (rAAV) are provided. The virion comprises an AAV VP capsid polypeptide as described above. In some embodiments, the rAAV has increased tropism for primate and human ocular tissue (e.g., retinal tissue), or may have increased accumulation in ocular cells (e.g., retinal pigment epithelial cells, photoreceptor cells, rod photoreceptor cells, cone photoreceptor cells, or combinations thereof), or both, as compared to a rAAV having the native AAV5 VP1 capsid polypeptide (SEQ ID NO:1). In some embodiments, the rAAV has increased ability to assemble, or exhibits greater virion stability, as compared to a rAAV having the native AAV5 VP1 capsid polypeptide (SEQ ID NO: 1).

[0130] In certain of these embodiments, the rAAV has increased ability to infect one or more ocular tissues selected from aqueous humor, choroid, retina, optic nerve, vitreous humor, and combinations thereof following intravitreal administration, sub-retinal injection, topical mucosal administration, or systemic administration as compared to a rAAV having the native AAV5 VP1 capsid polypeptide (SEQ ID NO: 1). In some embodiments, the rAAV has increased tissue tropism for retinal tissue compared to a wild type AAV5 capsid. In some embodiments, the rAAV has increased accumulation in photoreceptor cells (e.g., rod photoreceptor cells, cone photoreceptor cells, or a combination thereof), retinal pigment epithelial cells, or both, compared to a wild type AAV5 capsid.

[0131] Additionally, provided are polynucleotide sequences encoding the rAAV capsid VP proteins described herein.

[0132] In a further aspect, libraries are provided that comprise a plurality of rAAV as described above. The plurality of rAAVs comprise a plurality of VP capsid polypeptides having different primary amino acid sequences. An rAAV of the plurality of rAAVs may comprise a polypeptide of SEQ ID NO: 2 comprising one or more amino acid variations in the 581 to 589 region.

[0133] In some embodiments, the library comprises at least 1×10^9 different AAV VP capsid polypeptides, at least 2.5×10^9 different AAV VP capsid polypeptides, at least 5×10^9 different

AAV VP capsid polypeptides, at least 7.5 x 10^9 different AAV VP capsid polypeptides, at least 1 x 10^{10} different AAV VP capsid polypeptides, at least 2.5 x 10^{10} different AAV VP capsid polypeptides, at least 5 x 10^{10} different AAV VP capsid polypeptides, at least 7.5 x 10^{10} different AAV VP capsid polypeptides, at least 1 x 10^{11} different AAV VP capsid polypeptides, at least 2.5 x 10^{11} different AAV VP capsid polypeptides, or at least 5 x 10^{11} different AAV VP capsid polypeptides. The library may comprise AAV VP capsid polypeptides comprising 581 to 589 region variants. For example, a VP1 capsid polypeptide may comprise a sequence of SEQ ID NO: 1 in which residues 581 to residue 589 are replaced with a sequence of $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ (SEQ ID NO: 5014), wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V, and wherein the VP1 capsid polypeptide does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

[0134] In some embodiments, an AAV virion of the present disclosure may comprise an AAV VP1 capsid polypeptide having an amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513. In some embodiments, an AAV virion of the present disclosure may comprise an AAV VP1 capsid polypeptide having an amino acid sequence of SEQ ID NO: 2, wherein $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2 is any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

Pharmaceutical compositions

[0135] In another aspect, pharmaceutical compositions are provided. The pharmaceutical composition comprises a rAAV as described above and a pharmaceutically acceptable carrier.

[0136] A pharmaceutical composition can comprise a first active ingredient. The first active ingredient can comprise a viral vector as described herein and/or any payload as described herein. The pharmaceutical composition can be formulated in unit dose form. The pharmaceutical composition can comprise a pharmaceutically acceptable excipient, diluent, or carrier. The pharmaceutical composition can comprise a second, third, or fourth active ingredient – such as to facilitate enhanced gene replacement, RNA editing, DNA editing, or imaging.

[0137] A pharmaceutical composition described herein can compromise an excipient. An excipient can comprise a cryo-preservative, such as DMSO, glycerol, polyvinylpyrrolidone (PVP), or any combination thereof. An excipient can comprise a cryo-preservative, such as a

sucrose, a trehalose, a starch, a salt of any of these, a derivative of any of these, or any combination thereof. An excipient can comprise a pH agent (to minimize oxidation or degradation of a component of the composition), a stabilizing agent (to prevent modification or degradation of a component of the composition), a buffering agent (to enhance temperature stability), a solubilizing agent (to increase protein solubility), or any combination thereof. An excipient can comprise a surfactant, a sugar, an amino acid, an antioxidant, a salt, a non-ionic surfactant, a solubilizer, a triglyceride, an alcohol, or any combination thereof. An excipient can comprise sodium carbonate, acetate, citrate, phosphate, poly-ethylene glycol (PEG), human serum albumin (HSA), sorbitol, sucrose, trehalose, polysorbate 80, sodium phosphate, sucrose, disodium phosphate, mannitol, polysorbate 20, histidine, citrate, albumin, sodium hydroxide, glycine, sodium citrate, trehalose, arginine, sodium acetate, acetate, HCl, disodium edetate, lecithin, glycerol, xanthan rubber, soy isoflavones, polysorbate 80, ethyl alcohol, water, teprenone, or any combination thereof.

[0138] Compositions and methods provided herein can utilize pharmaceutical compositions. The compositions described throughout can be formulated into a pharmaceutical and be used to treat a human or mammal, in need thereof, diagnosed with a disease. In some cases, pharmaceutical compositions can be used prophylactically.

[0139] The compositions provided herein can be utilized in methods provided herein. Any of the provided compositions provided herein can be utilized in methods provided herein. In some cases, a method comprises at least partially preventing, reducing, ameliorating, and/or treating a disease or condition, or a symptom of a disease or condition. A subject can be a human or non-human. A subject can be a mammal (e.g., rat, mouse, cow, dog, pig, sheep, horse). A subject can be a vertebrate or an invertebrate. A subject can be a laboratory animal. A subject can be a patient. A subject can be suffering from a disease. A subject can display symptoms of a disease. A subject may not display symptoms of a disease, but still have a disease. A subject can be under medical care of a caregiver (e.g., the subject is hospitalized and is treated by a physician).

Methods of treatment or detection

[0140] In some aspects, the present disclosure provides for methods of treatment using an rAAV virion having any one of the engineered AAV VP capsid polypeptide sequences disclosed herein. In some aspects, the present disclosure provides for methods of detection using an rAAV virion having any one of the engineered AAV VP capsid polypeptide sequences disclosed herein. A method of treatment may comprise administering to a subject an effective amount of a pharmaceutical composition comprising rAAV virions assembled from VP polypeptides

comprising a 581 to 589 region that confers tissue tropism or preference (e.g., ocular tissue tropism) to the rAAV. The rAAV virions may encapsidate any payload, including those payloads disclosed herein. For example, a method of treatment may comprise administering an effective amount of a pharmaceutical composition comprising rAAV virions assembled from VP polypeptides comprising a 581 to 589 region having a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513. In another example, a method of treatment may comprise administering an effective amount of a pharmaceutical composition comprising rAAV virions assembled from VP polypeptides comprising a 581 to 589 region having a sequence of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0141] In some embodiments, the effective amount is at least 1 x 10^8 viral genomes per dose. In some embodiments, the effective amount is at least 5 x 10^8 viral genomes/dose, 7.5 x 10^8 viral genomes/dose, at least 1 x 10^9 viral genomes/dose, at least 2.5 x 10^9 viral genomes/dose, at least 5 x 10^9 viral genomes/dose. In some embodiments, an effective amount of an rAAV assembled from VP polypeptides comprising a 581 to 589 region conferring ocular tissue tropism or preference (e.g., retinal tissue tropism) may be lower than an effective amount of an AAV assembled from VP1, VP2, and VP3 polypeptides of SEQ ID NO: 1, SEQ ID NO: 10, and SEQ ID NO: 11, respectively.

[0142] In some embodiments, the effective amount is at least 1 x 10^{11} viral genomes, at least 5 x 10^{11} viral genomes, at least 1 x 10^{12} viral genomes, at least 5 x 10^{12} viral genomes, at least 1 x 10^{13} viral genomes, at least 1 x 10^{14} viral genomes, or at least 5 x 10^{14} viral genomes. In some embodiments, an effective amount of an rAAV assembled from VP polypeptides comprising a 581 to 589 region conferring ocular tissue tropism may be lower than an effective amount of an AAV assembled from VP1, VP2, and VP3 polypeptides of SEQ ID NO: 1, SEQ ID NO: 10, and SEQ ID NO: 11, respectively.

[0143] In some embodiments, the rAAV virion is administered via an ocular administration route, such as intravitreal administration, subconjunctival administration, retrobulbar administration, sub-retinal injection, topical mucosal administration, or intracameral administration. In some embodiments, the rAAV virion is administered via a systemic administration route including enteral routes of administration and parenteral routes of administration. The rAAV virion may be administered intravenously. In some embodiments, the rAAV may be administered intramuscularly. In some embodiments, the rAAV may be administered intraperitoneally. In some embodiments, the rAAV may be administered topically. In some embodiments, the rAAV may be administered orally. In particular embodiments, the

rAAV virion is administered intravenously. In some embodiments, the rAAV is administered intrathecally. In some embodiments, the rAAV is administered by intracerebral ventricular injection. In some embodiments, the rAAV is administered by intracisternal magna administration. In some embodiments, the rAAV is administered by intravitreal injection.

[0144] In various embodiments, the patient suffers from one of the conditions listed in **TABLE 1**, below. In particular embodiments, the patient suffers from one of the conditions listed in **TABLE 1** and the rAAV includes a payload comprising the transgene product associated therewith in **TABLE 1**. In some embodiments, an rAAV may be selected to specifically target the primary gene delivery target (e.g., the eye). For example, an rAAV selected to target the eye may comprise VP capsid polypeptides comprising a 581 to 589 region that confers ocular tissue tropism.

[0145] In some embodiments, an rAAV virion of the present disclosure, having any of the engineered AAV VP capsid polypeptide sequences disclosed herein, comprises a vector genome, the vector genome comprising a therapeutic polynucleotide or payload. In further embodiments, said payload may be under control of regulatory sequences that direct expression in infected human cells. In some embodiments, the payload may be under control of a cell type- or tissue type-specific promoter to direct expression in a target cell type or target tissue type. For example, expression of the payload may be under control of a retinal-specific promoter to promote retinal-specific expression, a retinal pigment epithelium-specific promoter to promote retinal pigment epithelium-specific expression, a choroid-specific promoter to promote choroid-specific expression, a photoreceptor-specific promoter to promote photoreceptor-specific expression, or an optic nerve-specific promoter to promote optic nerve-specific expression. In some embodiments, the payload comprises a therapeutic polynucleotide encoding any genetically encodable payload, such as an RNA (e.g., a guide RNA), a suppressor tRNA, a transgene, or a genome modifying entity.

[0146] In some embodiments, the therapeutic polynucleotide encodes a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, or an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof. In some embodiments, the therapeutic polynucleotide encodes a linear therapeutic polynucleotide or a circular therapeutic polynucleotide.

[0147] In some embodiments, the therapeutic polynucleotide is a transgene, encoding a therapeutic protein. In some embodiments, the therapeutic protein is an antibody that binds a target molecule (e.g., an anti-VEGF antibody that binds VEGF). In particular embodiments, the transgene encodes a protein selected from the targets suitable for modification or transgene

products of **TABLE 1**. In some embodiments, the transgene encodes a protein that binds a target provided in **TABLE 1**. In some embodiments, the payload encodes a polynucleotide that targets a target provided in **TABLE 1**. In some embodiments, an ocular payload or a transgene encoding an ocular target is encapsidated by an rAAV comprising VP capsid polypeptides comprising a 581 to 589 region that confers ocular tissue tropism or preference.

TABLE 1 – Suitable Therapeutic Targets or Payloads

Condition	**Payload or Target**
3-Methylglutaconic Aciduria, Type Iii	AFG3L2, MECR, OPA1
Abetalipoproteinemia	MTTP
Abnormal Threshold of Rods	HBA2, PROC
Aceruloplasminemia	CP
Achromatopsia	ATF6, CABP4, CNGA3, CNGB3, PDE6C
Achromatopsia 3	CNGB3
Achromatopsia 4	GNAT2
ad Retinitis Pigmentosa	NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, AGBL5
Age-related macular degeneration (AMD), e.g., wet AMD, or dry AMD	NOS2A, CFH, CF, C2, C3, C5A, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, VEGFA, VEGFC, CD59, RHO
Aland Island Eye Disease	CACNA1F
Albinism	TYRP1
Albinism, Ocular, Type I	GPR143
Albinism, Oculocutaneous, Type Ia	TYR
Albinism, Oculocutaneous, Type Ii	MC1R, OCA2
Alport Syndrome	COL4A3, COL4A4, COL4A5
Alzheimer Disease, Familial, 1	APP, GRN, PSEN1
Amblyopia	CACNA1F
Amyotrophic Lateral Sclerosis 2, Juvenile	ALS2
Anterior Segment Dysgenesis 2	FOXE3
Auditory Neuropathy and Optic Atrophy	FDXR
Autosomal Dominant Cerebellar Ataxia	KAT6B

Condition	Payload or Target
Autosomal Dominant Congenital Stationary Night Blindness	SNRNP200
Bardet-Biedl Syndrome	ARL6, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, CEP290, IFT172, MKKS, MKS1, SDCCAG8, TRIM32, TTC8, WDPCP
Bardet-Biedl Syndrome 1	BBIP1, BBS1, BBS10, LZTFL1
Bardet-Biedl Syndrome 13	MKS1
Bardet-Biedl Syndrome 17	LZTFL1
Bardet-Biedl Syndrome 2	BBS2, MKKS
Bardet-Biedl Syndrome 3	ARL6
Bardet-Biedl Syndrome 5	BBS5
Bardet-Biedl Syndrome 8	TTC8
Bardet-Biedl Syndrome 9	BBS9
Bartter Syndrome, Type 3	CLCNKB
Basal Laminar Drusen	CFH
Bestrophinopathy, Autosomal Recessive	BEST1
Bietti Crystalline Corneoretinal Dystrophy	CYP4V2
Blau Syndrome	NOD2
Blue Cone Monochromacy	OPN1LW
Bohring-Opitz Syndrome	ASXL1
Bosma Arhinia Microphthalmia Syndrome	SMCHD1
Boucher-Neuhauser Syndrome	PNPLA6
Branchiooculofacial Syndrome	EYA1, TFAP2A
Butterfly-Shaped Pigment Dystrophy	CTNNA1, PRPH2
Cafe-Au-Lait Spots, Multiple	NF1
Cataracts	GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50/GJA3 and 8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, CRYGC
Cerebral Cavernous Malformation, Familial	KRIT1, PDCD10
Cerebral Cavernous Malformations	CCM2, KRIT1
Cerebral Cavernous Malformations 2	CCM2

Condition	Payload or Target
Cerebral Cavernous Malformations 3	KRIT1, PDCD10
Cerebral Creatine Deficiency Syndrome 2	GAMT
Cerebroretinal Microangiopathy with Calcifications and Cysts 1	CTC1
Ceroid Lipofuscinosis, Neuronal, 11	GRN
Ceroid Lipofuscinosis, Neuronal, 3	CLN3
Ceroid Lipofuscinosis, Neuronal, 4	CLN6
Ceroid Lipofuscinosis, Neuronal, 6a	CLN5, CLN6, SMPD1, TPP1
Ceroid Lipofuscinosis, Neuronal, 8, Northern Epilepsy Variant	CLN8
Charge Syndrome	CHD7, PUF60
Chorioretinal Scar	CHD7
Choroidal Dystrophy, Central Areolar 2	PRPH2
Choroidal Dystrophy, Central Areolar, 1	GUCY2D, PRPH2
Choroideraemia	REP1
Choroideremia	CHM, Rab escort protein
Cohen Syndrome	VPS13B
Coloboma of Iris	PRR12, TMEM67
Coloboma of Macula	CDON, YAP1
Coloboma, Ocular, Autosomal Dominant	SERPINA1
Coloboma, Ocular, Autosomal Recessive	SALL2
Colorblindness, Partial, Protan Series	OPN1LW
Cone Dystrophy	UPF1
Cone Dystrophy 4	PDE6C
Cone-Rod Dystrophy 15	CDHR1
Cone-Rod Dystrophy 2	CABP4, CEP290, CERKL, CRB1, CRX, DRAM2, FAM161A, GUCY2D, PROM1, PRPH2, RPGR, TTLL5, USH2A
Cone-Rod Dystrophy 22	TLCD3B
Cone-Rod Dystrophy 3	ABCA4

Condition	Payload or Target
Cone-Rod Dystrophy 6	ABCA4, ABHD12, CABP4, CERKL, CNGA3, GUCY2D, KCNV2, NMNAT1, SAG, SRD5A3, WDR19
Cone-Rod Dystrophy 9	ADAM9
Congenital Dyserythropoietic Anemia	PNPLA1, TGM1
Congenital Ptosis	FBN1
Congenital Retinal Arteriovenous Communication	MITF, MYO15A, USH2A
Congenital Stationary Night Blindness	ABCA4, CABP4, CACNA1F, GRK1, NYX, PDE6B, TRPM1
Contractural Arachnodactyly, Congenital	FBN2
Corpus Callosum, Agenesis of	ARID1B, CDH2, CREBBP, DCC
D-Bifunctional Protein Deficiency	HSD17B4
Deafness, Autosomal Recessive 18a	USH1C
Deafness, Autosomal Recessive 2	MYO7A
Deafness, Autosomal Recessive 31	WHRN
Diabetes and Deafness, Maternally Inherited	MT-TE, MT-TL1
Donnai-Barrow Syndrome	LRP2
Duchenne and Becker Muscular Dystrophy	DMD
Dyskeratosis Congenita	CTC1, RTEL1, TERC, TERT, TINF2
Ectopia Lentis 2, Isolated, Autosomal Recessive	ADAMTSL4
Enhanced S-Cone Syndrome	NR2E3, NRL
Exudative Vitreoretinopathy	FZD4, LRP5, RCBTB1, ZNF408
Exudative Vitreoretinopathy 4	LRP5
Exudative Vitreoretinopathy 5	TSPAN12
Exudative Vitreoretinopathy 7	CTNNB1
Familial Retinoblastoma	RB1
Focal Dermal Hypoplasia	PORCN
Fundus Albipunctatus	PRPH2, RDH5, RHO, RLBP1
Fundus Dystrophy	ABCA4, ABHD12, ADGRV1, AHI1, AIPL1, ALMS1, ARL2BP, BBS1, BBS10, BBS12, BBS2, BBS9, BEST1, C1QTNF5, CABP4, CACNA1F, CC2D2A, CDH23, CDH3, CDHR1, CDKL5;RS1,

Condition	Payload or Target
	CEP290, CEP78, CERKL, CFAP410, CHM, CLN3, CLRN1, CNGA1, CNGA3, CNGB1, CNGB3, COL18A1, COL2A1, CRB1, CRX, CYP4V2, DRAM2, EYS, FAM161A, FLVCR1, FRMD7, GRM6, GUCY2D, HGSNAT, HK1, IFT140, IFT172, IMPG1, IMPG2, INPP5E, IQCB1, KCNV2, KIF11, KIZ, LCA5, LRAT, LRP5, MERTK, MFRP, MYO7A, NMNAT1, NPHP4, NR2E3, NRL, OAT, OPA1, PCARE, PCDH15, PDE6A, PDE6B, PDE6C, PEX1, PRCD, PROM1, PRPF31, PRPF8, PRPH2, RBP3, RDH12, RDH5, RHO, RLBP1, RP1, RP1L1, RP2, RPE65, RPGR, RPGRIP1, RS1, SAG, SLC24A1, SNRNP200, SPATA7, TOPORS, TTLL5, TULP1, USH2A
Glaucoma	CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, CYP1B1, LTBP2
Glaucoma 1, Open Angle, F	ASB10, OPTN
Glaucoma 3, Primary Congenital, a	CYP1B1
Glaucoma, Primary Open Angle	LTBP2, MYOC, OPTN
Glucocorticoid Deficiency 4 with or Without Mineralocorticoid Deficiency	NNT
Glycogen Storage Disease Iv	GBE1
Gm1 Gangliosidosis	GLB1
Gyrate Atrophy of Choroid and Retina	OAT, RIMS1
Hemophagocytic Lymphohistiocytosis, Familial, 3	UNC13D
Hereditary Spastic Paraplegia	ALDH18A1, AP4B1, AP4M1, AP5Z1, ATL1, CYP2U1, CYP7B1, DDHD2, FA2H, GBA2, KIF1C, NIPA1, PNPLA6, POLG, REEP1, SACS, SPAST, SPG11, SPG21, SPG7, ZFYVE26
Hermansky-Pudlak Syndrome	BLOC1S6, HPS1, HPS3, HPS4, HPS5, HPS6, RUNX1
Hermansky-Pudlak Syndrome 8	BLOC1S3
Heterochromia Iridis	MITF
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	SLC25A15
Iminoglycinuria	SLC36A2
Incontinentia Pigmenti	IKBKG
Inherited Retinal Disorder	VPS13B

Condition	Payload or Target
Intraocular Pressure Quantitative Trait Locus	ZEB1
Isolated Ectopia Lentis	FBN1
Jalili Syndrome	CNNM4
Joubert Syndrome 3	AHI1
Juvenile Retinoschisis	ATP1A3
Kearns-Sayre Syndrome	MT-TL1, MT-TY
Keratitis, Neurotrophic	NGF
Keratoconjunctivitis, Atopic	
Keratoconjunctivitis, Vernal	
Keratomalacia	CEP290
Knobloch Syndrome	COL18A1
Kufor-Rakeb Syndrome	ATP13A2
Late-Onset Retinal Degeneration	C1QTNF5
Leber congenital amaurosis (LCA)	RPE65, GUCY2D, KIR7.1
Leber Congenital Amaurosis 1	CRB1, GUCY2D, LCA5, RPGRIP1, TULP1
Leber Congenital Amaurosis 10	CEP290
Leber Congenital Amaurosis 12	RD3
Leber Congenital Amaurosis 13	RDH12
Leber Congenital Amaurosis 14	LRAT
Leber Congenital Amaurosis 15	TULP1
Leber Congenital Amaurosis 16	KCNJ13
Leber Congenital Amaurosis 17	GDF6
Leber Congenital Amaurosis 19	USP45
Leber Congenital Amaurosis 2	RPE65
Leber Congenital Amaurosis 3	SPATA7
Leber Congenital Amaurosis 4	AIPL1
Leber Congenital Amaurosis 5	LCA5
Leber Congenital Amaurosis 6	RPGRIP1
Leber Congenital Amaurosis 7	CRX
Leber Congenital Amaurosis 8	CRB1
Leber Congenital Amaurosis 9	NMNAT1
Leber hereditary optic neuropathy (LHON)	ND4, MT-ND1

Condition	Payload or Target
Leber Hereditary Optic Neuropathy, Modifier of	MT-ATP6, MT-ND1, MT-ND2, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, NDUFS2
Leber Plus Disease	ABCA4, AHI1, AIPL1, ALMS1, CEP290, CRB1, GRM6, GUCY2D, INPP5E, IQCB1, LCA5, LRAT, NDUFAF5, NMNAT1, PDE6B, PEX1, RDH12, RP2, RPE65, RPGRIP1, SLC38A8, SPATA7, TULP1, USH2A
Liberfarb Syndrome	PISD
Long-Chain 3-Hydroxyacyl-Coa Dehydrogenase Deficiency	HADHA, HADHB, HMGCL
Macular Degeneration, Age-Related, 13	CFI
Macular Degeneration, Age-Related, 2	ABCA4, MT-TL1
Macular Degeneration, diabetic	VEGFA, VEGFC
Macular Degeneration, Oedema	VEGFA, VEGFC
Macular Dystrophy, Patterned, 1	PRPH2
Macular Dystrophy, Vitelliform, 2	BEST1, IMPG2, PRPH2
Macular Dystrophy, Vitelliform, 3	PRPH2
Macular Dystrophy, Vitelliform, 4	IMPG1
Macular Dystrophy, Vitelliform, 5	IMPG2
Marfan Syndrome	FBN1, TGFBR2, MTHFR, MTR, MTRR
Maturity-Onset Diabetes of the Young	APPL1, GCK, HNF1A, HNF1B, KCNJ11, MLKL
Melanoma, Uveal	SF3B1
Mental Retardation, Truncal Obesity, Retinal Dystrophy, and Micropenis Syndrome	INPP5E
Methylmalonic Acidemia with Homocystinuria	MMACHC
Microcephaly and Chorioretinopathy, Autosomal Recessive, 1	TUBGCP6
Microcephaly and Chorioretinopathy, Autosomal Recessive, 3	TUBGCP4
Microcephaly with or Without Chorioretinopathy, Lymphedema, or Mental Retardation	KIF11
Microphthalmia	ALDH1A3
Microphthalmia, Isolated 2	VSX2

Condition	Payload or Target
Microphthalmia, Isolated 3	RAX
Microphthalmia, Isolated 5	MFRP
Microphthalmia, Isolated 7	GDF3
Microphthalmia, Isolated, with Coloboma 10	RBP4
Microphthalmia, Isolated, with Coloboma 5	SHH
Microphthalmia, Isolated, with Coloboma 6	GDF6
Microphthalmia, Isolated, with Coloboma 7	ABCB6
Microphthalmia, Isolated, with Coloboma 9	TENM3
Microphthalmia, Syndromic 9	STRA6, WNT7B
Mrcs Syndrome	BEST1
Mucolipidosis Iv	MCOLN1
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 3	PIGT
Muscular Dystrophy, Becker Type	DMD
Muscular Dystrophy-Dystroglycanopathy , Type a, 3	POMGNT1
Muscular Dystrophy-Dystroglycanopathy , Type B, 3	POMGNT1
Muscular Dystrophy-Dystroglycanopathy , Type C, 3	POMGNT1
Myeloperoxidase Deficiency	MPO
Myopia	HGF, C-MET, UMODL1, MMP-1/2, PAX6, CBS, MTHFR, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2
Myopia 2, Autosomal Dominant	CNP
Myopia 21, Autosomal Dominant	ZNF644
Myopia 24, Autosomal Dominant	SLC39A5
Myopia 25, Autosomal Dominant	P4HA2
Myopia 26, X-Linked, Female-Limited	ARR3
Myopia 27, Autosomal Dominant	CPSF1
Myopia 6	NCAPH2;SCO2;TYMP, TYMP;NCAPH2;SCO2

Condition	Payload or Target
Myotonia Congenita, Autosomal Recessive	CLCN1
Neonatal Adrenoleukodystrophy	PEX1
Neurofibromatosis, Type Ii	NF2
Neuronal Ceroid Lipofuscinosis	CLN3, CLN5, CLN6, CLN8, CTSD, PPT1, TPP1
Neuronal Ceroid-Lipofuscinoses	PPT1
Neuroocular Syndrome	PRR12
Neuropathy, Ataxia, and Retinitis Pigmentosa	MT-ATP6
Neuropathy, Ischaemic Optic	
Nevus of Ota	HRAS
Newfoundland Rod-Cone Dystrophy	RLBP1
Night Blindness, Congenital Stationary, Autosomal Dominant 1	RHO
Night Blindness, Congenital Stationary, Type 1e	GPR179
Night Blindness, Congenital Stationary, Type 2a	CACNA1F
Nonsyndromic Hearing Loss	GJB2, GJB3, GJB6, SOHLH1
Noonan Syndrome with Multiple Lentigines	PTPN11, RAF1
Norrie Disease	NDP
Oculocutaneous Albinism	SLC24A5, TYR
Oculocutaneous Albinism, Type Viii	DCT
Oguchi Disease 1	SAG
Oliver-Mcfarlane Syndrome	PNPLA6
Opitz Gbbb Syndrome	MID1, SPECC1L
Optic Atrophy 1	MT-ATP8
Optic Atrophy 10 with or Without Ataxia, Mental Retardation, and Seizures	RTN4IP1
Optic Atrophy 12	AFG3L2
Optic Atrophy 13 with Retinal and Foveal Abnormalities	SSBP1
Optic Atrophy 3, Autosomal Dominant	DNAJC19, MT-ND1, OPA3

Condition	Payload or Target
Optic Atrophy 7 with or Without Auditory Neuropathy	TMEM126A
Optic Atrophy 9	ACO2
Optic Atrophy with or Without Deafness, Ophthalmoplegia, Myopathy, Ataxia, and Neuropathy	OPA1
Optic Nerve Glioma	NF1
Optic Nerve Hypoplasia, Bilateral	ATOH7, COL4A1, PAX6
Optical Neuropathy	Complex I or ND genes, OPA1, RPE65
Osteopetrosis, Autosomal Recessive 3	CA2
Osteoporosis-Pseudoglioma Syndrome	LRP5
Papillorenal Syndrome	PAX2
Pathologic Nystagmus	CEP290
Pendred Syndrome	FOXI1, SLC26A4
Peroxisomal Disease	PEX1
Persistent Hyperplastic Primary Vitreous, Autosomal Recessive	ATOH7
Pigmented Paravenous Chorioretinal Atrophy	CRB1, MT-TH, PRPH2
Polypoidal Choroidal Vasculopathy	C2, C3, CFH, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP
Posterior Column Ataxia with Retinitis Pigmentosa	FLVCR1
Primary Congenital Glaucoma	CYP1B1
Primary Hyperoxaluria	AGXT, GRHPR
Progressive External Ophthalmoplegia with Mitochondrial Dna Deletions, Autosomal Dominant 1	MT-TL1, POLG
Progressive External Ophthalmoplegia with Mitochondrial Dna Deletions, Autosomal Dominant 2	SLC25A4
Progressive External Ophthalmoplegia with Mitochondrial Dna Deletions, Autosomal Dominant 3	TWNK
Progressive External Ophthalmoplegia with Mitochondrial Dna Deletions, Autosomal Dominant 4	POLG2

Condition	Payload or Target
Progressive External Ophthalmoplegia with Mitochondrial Dna Deletions, Autosomal Recessive 1	POLG, TWNK
Progressive Myoclonus Epilepsy	CSTB, EPM2A, GOSR2, SCARB2
Proliferative Vasculopathy and Hydranencephaly-Hydrocephaly Syndrome	FLVCR2
Prolonged Electroretinal Response Suppression	F2, KCNH2
Pseudoxanthoma Elasticum	ABCC2, ABCC6
Pyruvate Carboxylase Deficiency	PC
Rare Genetic Deafness	ACTG1, ADGRV1, ATP6V1B1, CDC14A, CDH23, CLRN1, COL4A5, DIAPH1, EDNRB, ESRRB, EYA1, GIPC3, GJB2, GPSM2, GRXCR1, KCNQ4, LOXHD1, LRTOMT, MARVELD2, MITF, MSRB3, MT-RNR1, MT-TS1, MYO15A, MYO6, MYO7A, OTOA, OTOF, OTOG, OTOGL, PAX3, PCDH15, PJVK, POU3F4, SERPINB6, SLC26A4, SOX10, STRC, SYNE4, TECTA, TMC1, TMPRSS3, USH1C, USH2A, WFS1, WHRN
Refsum Disease, Classic	PEX7, PHYH
Retinal Arterial Macroaneurysm with Supravalvular Pulmonic Stenosis	IGFBP7
Retinal Arteries, Tortuosity of	COL4A1
Retinal Cone Dystrophy 3b	KCNV2
Retinal Dystrophy and Obesity	TUB
Retinal Dystrophy, Iris Coloboma, and Comedogenic Acne Syndrome	RBP4
Retinal Vascular Occlusion	BBS9
Retinitis	RLBP1
Retinitis Pigmentosa	ABCA4, ADGRV1, AHI1, ALMS1, BBS1, BBS1;ZDHHC24, BBS2, BBS7, CACNA1F, CDH3, CDHR1, CEP290, CERKL, CHM, CLRN1, CNGA1, CNGB1, CRB1, EYS, FAM161A, FLVCR1, GUCY2D, HGSNAT, IFT140, IFT172, IMPG2, LCA5, MAK, MERTK, MYO7A, NR2E3, NRL, P3H2, PANK2, PCARE, PDE6A, PDE6B, PPT1, PRCD, PROM1, PRPF31, PRPF8, PRPH2, RCBTB1, RDH12, RHO, RLBP1, RP1, RP1L1, RP2, RPE65, RPGR, RPGRIP1, SLC24A1, SNRNP200, SPATA7, TTLL5, TULP1, USH2A, VPS13B, VSX2

Condition	Payload or Target
Retinitis Pigmentosa (RP, including RLBP1)	RLBP1
Retinitis Pigmentosa 1	RP1
Retinitis Pigmentosa 10	IMPDH1
Retinitis Pigmentosa 11	PRPF31
Retinitis Pigmentosa 12	CRB1
Retinitis Pigmentosa 13	PRPF8
Retinitis Pigmentosa 14	TULP1
Retinitis Pigmentosa 19	ABCA4
Retinitis Pigmentosa 2	RP2
Retinitis Pigmentosa 20	RPE65
Retinitis Pigmentosa 23	OFD1
Retinitis Pigmentosa 25	EYS
Retinitis Pigmentosa 26	CERKL
Retinitis Pigmentosa 27	NRL
Retinitis Pigmentosa 28	FAM161A
Retinitis Pigmentosa 3	RP2, RPGR
Retinitis Pigmentosa 33	SNRNP200
Retinitis Pigmentosa 36	CYGB;PRCD, PRCD
Retinitis Pigmentosa 37	NR2E3
Retinitis Pigmentosa 38	MERTK
Retinitis Pigmentosa 39	USH2A
Retinitis Pigmentosa 4	CFAP418, RHO
Retinitis Pigmentosa 40	PDE6B, PDE6B;PDE6B-AS1
Retinitis Pigmentosa 41	PROM1
Retinitis Pigmentosa 42	KLHL7
Retinitis Pigmentosa 43	PDE6A
Retinitis Pigmentosa 45	CNGB1
Retinitis Pigmentosa 47	SAG
Retinitis Pigmentosa 49	CNGA1
Retinitis Pigmentosa 54	PCARE
Retinitis Pigmentosa 55	ARL6
Retinitis Pigmentosa 56	IMPG2
Retinitis Pigmentosa 59	DHDDS

Condition	Payload or Target
Retinitis Pigmentosa 6	RPGR
Retinitis Pigmentosa 62	MAK
Retinitis Pigmentosa 66	RBP3
Retinitis Pigmentosa 69	KIZ
Retinitis Pigmentosa 7	PRPH2
Retinitis Pigmentosa 76	POMGNT1
Retinitis Pigmentosa 77	REEP6
Retinitis Pigmentosa 85	AHR
Retinitis Pigmentosa 88	RP1L1
Retinitis Pigmentosa 90	IDH3A
Retinitis Pigmentosa 91	ABCA4, CRX, IMPG1
Retinitis Pigmentosa-Deafness Syndrome	MT-TS2
Retinopathy (e.g., diabetic)	
Retinoschisis 1, X-Linked, Juvenile	CDKL5;RS1, RS1
Revesz Syndrome	TINF2
Rhizomelic Chondrodysplasia Punctata, Type 2	GNPAT
Saul-Wilson Syndrome	COG4
Senior-Loken Syndrome 1	IQCB1, NPHP1, SDCCAG8, TRAF3IP1, WDR19
Severe Early-Childhood-Onset Retinal Dystrophy	ABCA4, ALMS1
Short Stature, Optic Nerve Atrophy, and Pelger-Huet Anomaly	NBAS
Short-Rib Thoracic Dysplasia 5 with or Without Polydactyly	WDR19
Short-Rib Thoracic Dysplasia 9 with or Without Polydactyly	IFT140
Sjogren-Larsson Syndrome	ALDH3A2
Spastic Ataxia, Charlevoix-Saguenay Type	SACS
Spastic Paraplegia 15, Autosomal Recessive	ZFYVE26
Spondylometaphyseal Dysplasia, Axial	CFAP410
Stargardt disease	ABCA1, ABCA4, CRB1

Condition	Payload or Target
Stargardt Disease	ABCA4, BEST1, COL2A1, CRB1, CRX, PRPH2, TULP1
Stargardt Disease 3	ELOVL4
Stickler Syndrome	COL9A2
Stickler Syndrome, Type I, Nonsyndromic Ocular	COL2A1
Sveinsson Chorioretinal Atrophy	SEMA4A
Syndromic Rod-Cone Dystrophy	EPG5, KIF11
Tay-Sachs Disease	HEXA
Temtamy Syndrome	C12orf57
Tetrahydrobiopterin Deficiency	ATP1A3
Tietz Albinism-Deafness Syndrome	MITF
Tumoral Calcinosis, Hyperphosphatemic, Familial, 1	FGF23
Usher Syndrome	ADGRV1, CEP250, CLRN1, MYO7A, PROM1, USH1C, USH1G, USH2A
Usher Syndrome 2A	USH2A
Usher Syndrome Type 2	ADGRV1, CDH23, USH2A
Usher Syndrome, Type I	CDH23, MYO7A, PCDH15, USH1C
Usher Syndrome, Type I (USH1)	MYO7A
Usher Syndrome, Type Ic	USH1C
Usher Syndrome, Type Id	CDH23, PCDH15
Usher Syndrome, Type if	PCDH15
Usher Syndrome, Type Ig	PCDH15, USH1G
Usher Syndrome, Type Iia	USH2A
Usher Syndrome, Type Iic	ADGRV1
Usher Syndrome, Type Iid	WHRN
Usher Syndrome, Type Iiia	CLRN1
Usher Syndrome, Type Iv	ARSG
Uveal Melanoma	PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2
Uveitis	
Vascular Dementia	HTRA1, NOTCH3

Condition	Payload or Target
Vasculopathy, Retinal, with Cerebral Leukoencephalopathy and Systemic Manifestations	TREX1
Von Hippel-Lindau Syndrome	VHL
Wagner Vitreoretinopathy	VCAN
Walker-Warburg Syndrome	FKRP, FKTN, POMT1
Weaver Syndrome	EZH2
Wet AMD	Anti-VEGF antibody
Wet AMD, Dry AMD	NRP1
X-linked retinitis pigmentosa (X-linked RP)	RPGR
X-linked Retinoschisis	RS1

[0148] In some embodiments, the therapeutic polynucleotide encodes a therapeutic RNA. In some embodiments the therapeutic polynucleotide encodes an RNA, such as a guide RNA (including an engineered or synthetic guide RNA) for genome editing or for RNA editing. The guide RNA may target a gene, such as those provided in **TABLE 1** or encoding a protein nucleotide provided in **TABLE 1**, to promote editing of the target gene. In some embodiments, editing of the target gene may treat a condition in a subject, such as a condition provided in **TABLE 1**.

[0149] In some embodiments, the therapeutic polynucleotide encodes a tRNA or a modified tRNA (engineered or synthetic tRNA). For example, the tRNA or modified tRNA can be a suppressor tRNA. The suppressor tRNA can be engineered to have an anticodon region that recognizes a stop codon, such as any premature stop codon (opal, ochre, or amber stop codons). A suppressor tRNA may target a premature stop codon in a gene, such as those provided in **TABLE 1** or encoding a protein nucleotide provided in **TABLE 1**, to promote readthrough of the gene. In some embodiments, suppressing the premature stop codon may treat a condition in a subject, such as a condition provided in **TABLE 1**.

[0150] In some embodiments, the therapeutic polynucleotide (e.g., a therapeutic RNA, a tRNA, or a genome modifying entity) can target a gene listed in **TABLE 1** or any gene associated with an ocular disease, such as achromatopsia, macular degeneration (e.g., wet AMD or dry AMD), cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked

retinoschisis, or any genetic disease affecting an ocular tissue. In some embodiments, the targeted gene may be CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50/GJA3 and 8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I or ND genes, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, RS1, a fragment any of these, or any combination thereof. In some embodiments, the therapeutic polynucleotide is a gene therapy payload (e.g., a transgene) and, thus, may itself be one of the genes listed in **TABLE 1** or any gene associated with an ocular disease, such as achromatopsia, macular degeneration (e.g., wet AMD or dry AMD), cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis, or any genetic disease. In some embodiments, the transgene may be CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50/GJA3 and 8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I or ND genes, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, RS1, a fragment any of these, or any combination thereof. In some embodiments, the transgene may encode a protein that targets a gene, a protein, or a protein encoded by a gene provided in **TABLE 1**, a fragment any of these, or any combination thereof.

[0151] An engineered AAV comprising a VP capsid polypeptide comprising an ocular tissue-tropic 581 to 589 region may be used to deliver a payload to treat an ocular condition, or a condition of the eye. For example, an engineered AAV comprising a VP capsid polypeptide

comprising a 581 to 589 region conferring ocular tissue tropism may be used to treat an ocular condition (e.g., achromatopsia, macular degeneration (e.g., wet AMD or dry AMD), cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis). The 581 to 589 region of the VP capsid polypeptide may have a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, the engineered AAV comprising a VP capsid polypeptide comprising an ocular tissue-tropic 581 to 589 region may be used to deliver a transgene encoding a protein associated with an ocular condition or that targets a protein associated with an ocular condition (e.g., a protein encoded by CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50/GJA3 and 8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I or ND genes, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, RS1). For example, an engineered AAV comprising a VP capsid polypeptide comprising a retina tissue-tropic 581 to 589 region (e.g., any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513) may be used to deliver a payload encoding a therapeutic protein associated with retinitis pigmentosa (e.g., NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, or AGBL5) to retina tissue to treat retinitis pigmentosa. In another example, an engineered AAV comprising a VP capsid polypeptide comprising an RPE tissue-tropic 581 to 589 region (e.g., any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013) may be used to deliver a payload encoding a therapeutic protein associated with dry age-related macular degeneration to RPE tissue to treat dry age-related macular degeneration.

[0152] In some embodiments, the therapeutic polynucleotide encodes genome modifying entities. For example, a genome modifying entity may be a DNA editing enzyme, an RNA editing enzyme, a transcriptional activator, or a transcriptional repressor. The DNA editing

enzyme may be any DNA editing enzyme, including any CRISPR/Cas systems, meganucleases, zinc-finger nucleases, (ZFNs), TALE Nucleases (TALENs and megaTALENS). The CRISPR/Cas system can be a Cas3, Cas8, Cas10, Cas9, Cas4, Cas12, or Cas13. The RNA editing enzyme may be ADAR. In some embodiments, the ADAR is a human ADAR1 or human ADAR2. The transcriptional activator may be VP64. A transcriptional repressor may be KRAB. Such genome modifying entities may target any gene listed in **TABLE 1** for editing.

[0153] In some embodiments, the present disclosure provides for rAAV virions having an engineered AAV VP capsid polypeptide (e.g., comprising a 581 to 589 region variant), where the virion encapsidates any one of or any combination of the therapeutic payloads disclosed herein. In some embodiments, multiple copies of the therapeutic payload are encapsidated. The 581 to 589 region of the engineered AAV VP capsid polypeptide may have a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013.

[0154] In some embodiments, the therapeutic polynucleotide is a polynucleotide capable of serving as a homology template for homology-directed repair. In some embodiments, the therapeutic polynucleotide may be a guide polynucleotide for a CRISPR/Cas system or an ADAR enzyme. For example, the therapeutic polynucleotide may be a CRISPR/Cas guide RNA or an ADAR guide RNA.

[0155] In some embodiments, an rAAV virion of the present disclosure, having any of the engineered AAV VP capsid polypeptide sequences disclosed herein, comprises a vector genome, the vector genome comprising a detectable polynucleotide or payload. In further embodiments, said payload may be under control of regulatory sequences that direct expression in infected human cells. In some embodiments, the payload may be under control of a cell type- or tissue type-specific promoter to direct expression in a target cell type or target tissue type. For example, expression of the payload may be under control of a retinal-specific promoter to promote retinal-specific expression, a retinal pigment epithelium-specific promoter to promote retinal pigment epithelium-specific expression, a choroid-specific promoter to promote choroid-specific expression, a photoreceptor-specific promoter to promote photoreceptor-specific expression, or an optic nerve-specific promoter to promote optic nerve-specific expression. Examples of detectable polynucleotides include, but are not limited to, any genetically encodable detectable moiety. For example, a genetically encodable detectable moiety may be a fluorescent protein such as EGFP, GFP, YFP, RFP, CFP, or any variants thereof. In some embodiments, the present disclosure provides for rAAV virions having an engineered AAV VP capsid polypeptide, where the virion encapsidates any one of or any combination of the

detectable payloads disclosed herein. In some embodiments, multiple copies of the detectable payload are encapsidated.

[0156] In some embodiments, the present disclosure provides for rAAV virions having an engineered AAV VP capsid polypeptide, where the virion encapsidates any one of or any combination of the therapeutic payloads and detectable payloads disclosed herein. For example, an rAAV of the present disclosure having an engineered AAV VP capsid polypeptide may encapsidate a transgene and a fluorescent protein. As another example, an rAAV of the present disclosure having an engineered AAV VP capsid polypeptide may encapsidate a therapeutic RNA (e.g., a guide RNA) and a fluorescent protein.

[0157] Delivering a payload (e.g., a payload encoding a therapeutic polypeptide or a therapeutic polynucleotide) using the ocular tissue specific AAVs described herein may produce lower toxicity in a subject compared to non-specific AAVs (e.g., AAVs comprising a VP1 polypeptide of SEQ ID NO: 1). Tissue specific AAVs (e.g., ocular tissue specific AAVs) may be effective at lower doses compared to non-specific AAVs since a larger fraction of the administered AAVs infect the relevant tissue (e.g., ocular tissue). As a result, a therapeutically effective dose of tissue specific AAVs may be lower than a therapeutically effective dose of non-specific AAVs, leading to lower toxicity due administering a lower dose. For example, administration of a therapeutically effective dose of tissue specific AAVs may result in lower liver toxicity than administration of a therapeutically effective dose of non-specific AAVs. Administration of a lower dose may also lead to lower production of neutralizing antibodies in the subject. Neutralizing antibodies may decrease the efficacy of the AAV therapy by inhibiting infection of the target tissue or may cause severe side effects in the subject due to the immune response. Additionally, tissue specific AAVs (e.g., ocular tissue specific) may produce fewer off-target effects compared to non-specific AAVs when administered at the same dose since fewer of the AAVs infect off target tissues (e.g., non-targeted ocular tissues such as aqueous humor or vitreous humor). Off-target effects may include increased gene expression in an off-target tissue, decreased gene expression in an off-target tissue, gene editing in an off-target tissue, immune response, or liver toxicity.

In Vivo Selected VP Polypeptides

[0158] In a further aspect, engineered (synonymously, recombinant) adeno-associated virus (AAV) VP capsid polypeptides identified using the methods described herein are provided.

[0159] In some embodiments, the engineered adeno-associated virus (AAV) viral protein (VP) capsid polypeptide has an amino acid sequence at least 70% identical to SEQ ID NO: 1, wherein

the engineered AAV VP capsid polypeptide has at least one substitution as compared to SEQ ID NO: 1 in the 581 to 589 region, corresponding to residue 581 to residue 589 of SEQ ID NO: 1, inclusive, wherein the capsid polypeptide is capable of assembling into a recombinant AAV virion (rAAV), and wherein the VP capsid polypeptide does not have the sequence of any of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8. In some embodiments, the VP capsid polypeptide comprises one or more amino acid substitutions relative to SEQ ID NO: 1 in the region from residue 581 to residue 589, inclusive. The VP capsid polypeptide may comprise a sequence of SEQ ID NO: 2, wherein the 581 to 589 region has a sequence conferring ocular tissue tropism or preference.

[0160] In some embodiments, the engineered adeno-associated virus (AAV) viral protein (VP) capsid polypeptide is ocular tissue-tropic and has an amino acid sequence at least 70% identical to SEQ ID NO: 1, wherein the engineered AAV VP capsid polypeptide has at least one substitution as compared to SEQ ID NO: 1 in the 581 to 589 region, corresponding to residue 581 to residue 589 of SEQ ID NO: 1, inclusive, wherein the capsid polypeptide is capable of assembling into a recombinant AAV virion (rAAV), wherein the at least one substitution confers higher tropism for an ocular tissue on the rAAV as compared to an rAAV virion having an AAV5 VP capsid polypeptide of SEQ ID NO: 1, and wherein the VP capsid polypeptide does not have the sequence of any of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8. In some embodiments, the ocular tissue-tropic VP capsid polypeptide comprises one or more amino acid substitutions relative to SEQ ID NO: 1 in the region from residue 581 to residue 589, inclusive.

[0161] In particular embodiments, the engineered adeno-associated virus (AAV) viral protein (VP) capsid polypeptide (e.g., an ocular tissue-tropic VP capsid polypeptide) has an amino acid sequence at least 75%, 77.7%, 80%, 85%, 88.8%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% identical to the sequence of SEQ ID NO: 1.

[0162] In some embodiments, the AAV VP capsid polypeptide is an ocular tissue-tropic capsid polypeptide and has an amino acid sequence of SEQ ID NO: 2, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from any amino acid, wherein the capsid polypeptide is capable of assembling into a recombinant AAV virion (rAAV), wherein the at least one substitution confers higher tropism for an ocular tissue on the rAAV as compared to an rAAV virion having an AAV5 VP capsid polypeptide of SEQ ID NO: 1, and wherein the VP capsid polypeptide does not have the sequence of any of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8, optionally with further mutations elsewhere in the VP capsid polypeptide. In some embodiments, $X^1X^2X^3X^4X^5X^6X^7X^8X^9$ (SEQ

ID NO: 5014) of the ocular tissue-tropic VP capsid polypeptide correspond to a 581 to 589 region conferring ocular tissue tropism or preference.

[0163] In some embodiments, the engineered adeno-associated virus (AAV) viral protein (VP) capsid polypeptide (e.g., an ocular tissue-tropic VP capsid polypeptide) has an amino acid sequence of SEQ ID NO: 2, wherein amino acid residues X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V; wherein the engineered AAV VP capsid polypeptide is capable of assembling into a recombinant AAV virion (rAAV); and wherein the rAAV VP capsid polypeptide does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

[0164] In some embodiments, the 581 to 589 region of the engineered VP capsid polypeptide, corresponding to residues 581 to 589, inclusive, with reference to SEQ ID NO: 1, has a sequence that is at least 70%, at least 75%, at least 77.7%, at least 80%, at least 85%, at least 88.8%,at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a 581 to 589 region described herein. In some embodiments, the 581 to 589 region of the engineered VP capsid polypeptide comprises 1 amino acid substitution relative to a 581 to 589 region described herein. In some embodiments, the 581 to 589 region of the engineered VP capsid polypeptide comprises 2 amino acid substitutions relative to a 581 to 589 region described herein. In particular embodiments, the 581 to 589 region of the engineered VP capsid polypeptide has a sequence that is identical to a 581 to 589 region described herein.

[0165] In some embodiments, the engineered adeno-associated virus (AAV) viral protein (VP) capsid polypeptide is an engineered AAV5 viral capsid protein, wherein the engineered AAV VP5 capsid polypeptide has at least one substitution as compared to SEQ ID NO: 1 in the 581 to 589 region, corresponding to residues 581 to 589, inclusive, of SEQ ID NO: 1, inclusive; wherein the capsid polypeptide is capable of assembling into a recombinant AAV virion (rAAV); wherein the at least one substitution confers higher tropism for an ocular tissue on the rAAV as compared to an rAAV virion having an AAV5 VP capsid polypeptide of SEQ ID NO: 1, and wherein the VP capsid polypeptide does not have the sequence of any of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8, optionally with further mutations elsewhere in the VP protein.

[0166] In some embodiments, the AAV VP capsid polypeptides have an amino acid sequence of SEQ ID NO: 2, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V; and wherein the polypeptide

does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8.

[0167] In some embodiments, the engineered AAV VP capsid polypeptide comprises a polypeptide sequence represented by the formula: **(A)-(X)-(B)** wherein: (A) is the polypeptide sequence of SEQ ID NO: 12 (VAYNVGGQMATNNQSSTTAP, corresponding to residues 561 to 580 of SEQ ID NO: 2); (X) is a 581 to 589 region that confers ocular tissue tropism on a recombinant AAV virion (rAAV); and (B) is the polypeptide sequence of SEQ ID NO: 13 (IVPGSVWMERDVYLQGPIWA, corresponding to residues 590 to 609 of SEQ ID NO: 2); and wherein the capsid polypeptide is capable of assembling into the rAAV and, the capsid does not have the sequence of any of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or SEQ ID NO: 8. Also encompassed herein are rAAVs composed of engineered AAV5 VP2 capsid polypeptides and engineered AAV5 VP3 capsid polypeptides comprising a 581 to 589 region that confers ocular tissue tropism at the region corresponding to amino acid residues 445 to 453 in AAV5 VP2 or the region corresponding to amino acid residues 389 to 397 in AAV5 VP3.

[0168] In some embodiments, the engineered AAV VP capsid polypeptide confers ocular tissue tropism or preference, wherein the ocular tissue is selected from the group consisting of aqueous humor, choroid, retina, optic nerve, vitreous humor, remaining eye tissue, and any combination thereof.

[0169] Described below are engineered mutated AAV5 VP1 polypeptide sequences that confer stable or improved virion assembly, tissue tropism, or both. In some embodiments, the present disclosure provides an AAV5 VP1 capsid polypeptide having a sequence homology of no more than 98.7% to SEQ ID NO: 1, wherein the AAV5 capsid polypeptide sequence has at least one mutation in a region from a position corresponding to 581 to a position corresponding to 589 of SEQ ID NO: 1. In some embodiments, an engineered AAV5 polypeptide comprises at least one amino acid substitution relative to residues 561 to 580 of SEQ ID NO: 1.

[0170] Also encompassed herein are rAAVs composed of engineered AAV5 VP2 capsid polypeptides and engineered AAV5 VP3 capsid polypeptides comprising a 581 to 589 region that confers ocular tissue tropism at the region corresponding to amino acid residues 445 to 453 in AAV5 VP2 or the region corresponding to amino acid residues 389 to 397 in AAV5 VP3.

Engineered VP Polypeptides Competent for rAAV Assembly

[0171] In various preferred embodiments, the mutated (engineered, recombinant) VP capsid polypeptides of the present disclosure are capable of forming an assembled virion, and in some

instances that exhibit similar or improved stability when compared to a virion that comprises the AAV5 VP1 capsid polypeptide of SEQ ID NO: 1.

[0172] The frequency of a given amino acid residue occurring in assembled, purified viruses at a specified position within the 581 to 589 region, corresponding to position 581 to position 589 of SEQ ID NO: 1, or corresponding to X^1 to X^9 as generalized in SEQ ID NO: 2, over the frequency of that given amino acid residue occurring at the specified position in the entire plasmid library was analyzed to identify sequence rules for capsid polypeptide sequences that favor viral capsid assembly. Based on the determined amino acid residue frequency, the contribution of each amino acid at each position of the 581 to 589 region to capsid assembly was determined, and sequences of the 581 to 589 region ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$ of SEQ ID NO: 2) that favor capsid assembly, and rules for selecting sequences that favor capsid assembly, were identified.

[0173] Disclosed herein are engineered AAV5 VP capsid polypeptides capable of forming an assembled viral capsid that may exhibit similar or improved stability as compared to wild type AAV5 VP capsid polypeptide, wherein the engineered variant AAV5 VP capsid polypeptide sequence has one or more mutations, wherein the VP1 polypeptide sequence has said one or more mutations in a 581 to 589 region (corresponding to position 581 to position 589 in SEQ ID NO: 2), and wherein X^1 is selected from A, D, E, G, L, M, N, Q, S, T, or V, or X^1 is selected from A, D, E, M, or T. In some embodiments, X^1 is E; or X^2 is selected from A, C, D, E, G, H, I, N, P, Q, S, T, or V, or X^2 is selected from A, S, T, or V, or X^2 is A; or wherein X^3 is selected from A, D, E, G, H, M, N, Q, S, T, or V, or X^3 is selected from D, E, N, Q or T, or X^3 is D or T; or wherein X^4 is selected from A, D, E, G, H, N, P, Q, S, or T, or X^4 is selected from D, E, P, or Q, or X^4 is E; or wherein X^5 is selected from A, C, D, E, G, H, N, Q, S, T, or Y, or X^5 is selected from D, E, N, Q or T, or X^5 is N; or wherein X^6 is selected from A, D, E, G, H, N, P, Q, S, or T, or X^6 is selected from D, N, or Q, or X^6 is D; or wherein X^7 is selected from A, C, D, E, G, H, N, Q, S, or T, or X^7 is selected from A, D, E or G, or X^7 is A; or wherein X^8 is selected from A, C, D, E, G, H, N, Q, S, or T, or X^8 comprises A, D, G, or S, or X^8 is G; or wherein X^9 is selected from A, D, E, G, H, N, P, Q, S, or T, or X^9 is selected from A, D, G, or P, or X^9 is G.

[0174] In various embodiments, the VP polypeptide is capable of forming an assembled viral capsid, and in some instances exhibits similar or improved stability when compared to a virion that comprises the AAV5 VP1 capsid polypeptide of SEQ ID NO:1.

[0175] Examples of amino acid substitutions within a 581 to 589 region that may favor viral capsid assembly are provided in **TABLE 2**. In some embodiments, the following amino acids can be independently mutated, in any combination, at any one or more positions X^1- X^9, with

reference to SEQ ID NO: 2, to provide an AAV VP1 capsid that is capable of assembling. Additionally, one or more mutations outside of the X^1- X^9 region can be allowed, as long as the capsid is still capable of assembling.

TABLE 2 – 581 to 589 Region Amino Acid Variations for Viral Assembly

Viral Assembly Options
X^1 is A, D, E, G, L, M, N, Q, S, T, or V
X^1 is A, D, E, M, or T
X^1 is E
X^2 is A, C, D, E, G, H, I, N, P, Q, S, T, or V
X^2 is A, S, T, or V
X^2 is A
X^3 is A, D, E, G, H, M, N, Q, S, T, or V
X^3 is D, E, N, Q or T
X^3 is D or T
X^4 is A, D, E, G, H, N, P, Q, S, or T
X^4 is D, E, P, or Q
X^4 is E
X^5 is A, C, D, E, G, H, N, Q, S, T, or Y
X^5 is D, E, N, Q or T
X^5 is N.
X^6 is A, D, E, G, H, N, P, Q, S, or T;
X^6 is D, N, or Q; or
X^6 is D.
X^7 is s A, C, D, E, G, H, N, Q, S, or T;
X^7 is A, D, E or G; or
X^7 is A.
X^8 is A, C, D, E, G, H, N, Q, S, or T;
X^8 is A, D, G, or S; or
X^8 is G.

Viral Assembly Options
X^9 is A, D, E, G, H, N, P, Q, S, or T;
X^9 is A, D, G, or P; or
X^9 is G.

581 to 589 Regions for Ocular Tissue Tropism

[0176] The present disclosure provides AAV5 virions with a VP capsid polypeptide having at least one mutation in a region with residues that interact with target cells (e.g., a target eye cell in a target ocular tissue of interest), where the at least one mutation confers increased ocular tissue tropism or preference as compared to a wild type VP capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1). In some embodiments, provided herein are AAV5 VP1 capsid polypeptide having a sequence homology of at least 80% to SEQ ID NO: 1, wherein the AAV5 VP1 capsid polypeptide has at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 of SEQ ID NO: 1, and wherein said at least one mutation drives increased ocular tissue tropism as compared to the wild type VP capsid polypeptide (SEQ ID NO: 1). The following sequences rules and sequences also apply to the 581 to 589 region in AAV5 VP2 (amino acid residues 445 to 453; VP2 sequence shown in SEQ ID NO: 10) and in AAV5 VP3 (amino acid residues 389 to 397; VP3 sequences shown in SEQ ID NO: 11). Thus, the present disclosure encompasses AAV5 VP2 capsid polypeptides and AAV5 VP3 capsid polypeptides having one or more amino acid substitutions in the 581 to 589 regions of VP2 and VP3, corresponding to the AAV5 VP1 amino acid residues of the 581 to 589, where the one or more mutations comport to the rules or sequences in the following section.

[0177] VP capsid polypeptides (e.g., V1, VP2, or VP3 capsid polypeptides, or combinations thereof) comprising an ocular tissue-tropic 581 to 589 region, or any 581 to 589 region adhering to the rules identified herein) may assemble to form an rAAV with altered surface properties compared to a wild type AAV (e.g., comprising a VP1 polypeptide of SEQ ID NO: 1). The surface may form an interface that forms interactions with a target tissue, and the altered surface properties of the rAAV may promote tissue specific interactions (e.g., ocular tissue-specific interactions) between the rAAV and the target tissue. In some embodiments, the altered surface properties may be an altered charge distribution, increased or decreased hydrophobicity, altered availability or distribution of hydrogen bond donors or acceptors, or formation or reshaping of binding pockets. Such altered surface properties may favor interactions between the rAAV and ocular tissue while disfavoring interactions between the rAAV and non-ocular tissue. In some

embodiments, the altered surface properties may favor interactions between the rAAV and a specific ocular tissue or ocular cells (e.g., retina, optic nerve, choroid, photoreceptor cells, aqueous humor, or vitreous humor) while disfavoring interactions between the rAAV and other ocular tissues or cells or non-ocular tissues.

[0178] An ocular tissue-tropic rAAV assembled from VP capsid polypeptides (e.g., V1, VP2, or VP3 capsid polypeptides, or combinations thereof) comprising a 581 to 589 region, or any 581 to 589 region adhering to the rules identified herein) may preferentially infect an ocular tissue (e.g., retinal tissue), ocular cells (e.g., retinal pigment epithelial cells, photoreceptor cells, rod photoreceptor cells, cone photoreceptor cells, or combinations thereof), or both, as compared to other ocular tissue (e.g., choroid, aqueous humor, or vitreous humor) or other ocular cells (e.g., photoreceptor cells) at a higher level as compared to wild type AAV5. The ocular tissue-tropic AAV may infect the ocular tissue at a rate that is at least about 1.1-fold, at least about 1.2-fold, at least about 1.3-fold, at least about 1.4-fold, at least about 1.5-fold, at least about 1.6-fold, at least about 1.7-fold, at least about 1.8-fold, at least about 1.9-fold, at least about 2-fold, at least about 2.2-fold, at least about 2.4-fold, at least about 2.6-fold, at least about 2.8-fold, at least about 3-fold, at least about 3.5-fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 20-fold, at least about 30-fold, at least about 40-fold, at least about 50-fold, at least about 100-fold, at least about 200-fold, at least about 300-fold, at least about 400-fold, or at least about 500-fold an infection rate for the other ocular tissue, as compared to wild type AAV5.

[0179] In some embodiments, the ocular tissue-tropic rAAV assembled from VP capsid polypeptides (e.g., V1, VP2, or VP3 capsid polypeptides, or combinations thereof) comprising a 581 to 589 region (e.g., any 581 to 589 region adhering to the rules identified herein) may deliver a payload to the tissue infected by the rAAV. The payload (e.g., a payload encoding a therapeutic peptide or a therapeutic polynucleotide) may be expressed in the tissue. In some embodiments, an expression level of the payload in an ocular tissue (e.g., retinal tissue), ocular cell (e.g., retinal pigment epithelial cell, photoreceptor cell, rod photoreceptor cell, cone photoreceptor cell, or combinations thereof), or both may have at least about 2.5-fold, at least about 2.8-fold, at least about 3-fold, at least about 3.2-fold, at least about 3.5-fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 20-fold, at least about 50-fold, at least about 75-fold, at least about 100-fold, at least about 200-fold, at least about 500-fold higher, or at least about 1000-fold an expression level in a different ocular tissue

(e.g., choroid, vitreous humor, or aqueous humor) or ocular cell (e.g., photoreceptor cells). In some embodiments, the payload may be under control of a cell type- or tissue type-specific promoter to direct expression in a target cell type or target tissue type. For example, expression of the payload may be under control of a retinal-specific promoter to promote retinal-specific expression, a retinal pigment epithelium-specific promoter to promote retinal pigment epithelium-specific expression, a choroid-specific promoter to promote choroid-specific expression, a photoreceptor-specific promoter to promote photoreceptor-specific expression, or an optic nerve-specific promoter to promote optic nerve-specific expression.

[0180] In some embodiments, payload delivery to the ocular tissue using an ocular tissue-tropic AAV may have at least about 1.1-fold, at least about 1.2-fold, at least about 1.3-fold, at least about 1.4-fold, at least about 1.5-fold, at least about 1.6-fold, at least about 1.7-fold, at least about 1.8-fold, at least about 1.9-fold, at least about 2-fold, at least about 2.2-fold, at least about 2.4-fold, at least about 2.6-fold, at least about 2.8-fold, at least about 3-fold, at least about 3.5-fold, at least about 4-fold, at least about 4.5-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 20-fold, at least about 30-fold, at least about 40-fold, at least about 50-fold, at least about 100-fold, at least about 200-fold, at least about 300-fold, at least about 400-fold, or at least about 500-fold higher specificity for the ocular tissue as compared to a wild type AAV (e.g., a wild type AAV5).

Ocular Tissue-Tropic Sequences

[0181] Recombinant AAV viral capsids with specificity for ocular tissues (ocular tissue-tropic rAAVs) may be identified by screening rAAV libraries comprising VP capsid polypeptides with 581 to 589 regions, as described herein. The libraries may be screened in non-human primates (NHPs) by intravitreally administering the rAAV library and identifying sequences of 581 to 589 regions in VP capsid polypeptides that conferred tissue-tropic accumulation in or infection of ocular tissues (e.g., retina) to the rAAVs.

[0182] Disclosed herein are engineered AAV5 VP capsid polypeptides capable of forming an assembled virion that exhibits increased ocular tissue tropism or preference as compared to a wild type AAV VP capsid polypeptide (e.g., a VP1 of SEQ ID NO: 1, a VP2 of SEQ ID NO: 10, or aVP3 of SEQ ID NO: 11), wherein the engineered variant AAV5 VP capsid polypeptide sequence has one or more amino acid substitutions in a 581 to 589 region of the VP capsid polypeptide, corresponding to positions 581 to 589 in SEQ ID NO: 2 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$). In some embodiments, X^1 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W,

Y, or V. In some embodiments, X^2 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^3 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^4 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^5 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^6 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^7 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^8 is selected A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^9 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V.

[0183] An ocular tissue-tropic 581 to 589 region may comprise one or more positively charged or basic amino acid residues. The positively charged or basic amino acid residues may be independently selected from K, R, or H. In some embodiments, at least one of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of the 581 to 589 region is K, R, or H. In some embodiments at least two of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of the 581 to 589 region are independently selected from K, R, or H. In some embodiments, at least three of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of the 581 to 589 region are independently selected from K, R, or H.

[0184] An ocular tissue-tropic 581 to 589 region may comprise fewer negatively charged or acidic amino acid residues than the 581 to 589 region of a wild type VP polypeptide (e.g., SEQ ID NO: 1). The negatively charged or acidic amino acid residues may be D or E. In some embodiments, no more than one of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of the 581 to 589 region is E or E. In some embodiments, none of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of the 581 to 589 region are D or E.

[0185] In some embodiments, provided herein are AAV5 VP capsid polypeptide having at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 of AAV5 VP1 (e.g., SEQ ID NO: 1), wherein said at least one mutation drives increased ocular tissue tropism.

[0186] Retina Tissue-Tropic AAV VP Capsid Polypeptides. Described herein are engineered AAV VP capsid polypeptides comprising a variant 581 to 589 region predicted to confer increased retina tissue tropism, and predicted to confer increased retina tissue tropism compared to a wild type AAV VP capsid polypeptide (e.g., an AAV5 VP capsid polypeptide), based on a primary screen of a recombinant AAV5 capsid library. **TABLE 3** provides 581 to 589 region sequences predicted to confer retina tissue tropism or preference.

TABLE 3 – Exemplary 581 to 589 Region Sequences for Retinal Targeting

SEQ ID NO	581 to 589 Region
14	AALHSRMYQ
15	AAMRWQRES
16	AAVLKYWQQ
17	ACCQKRRSQ
18	ACKGKQKWA
19	ACVSLRQGC
20	ADCPLYCQP
21	AEKGCRKYG
22	AFISTRRAG
23	AFKFKSDWG
24	AFLTIRRHY
25	AFMRPQQFP
26	AFVDNLMDP
27	AGALARKMM
28	AGVSKRTGS
29	AHKYSRTMQ
30	AHVKPVQTM
31	AHWPKQYDP
32	AICRKDRHQ
33	AIKATRFRN
34	AIKCREQMR
35	AIKELRLWP
36	AIKMSRRYE
37	AIKTRGCSY
38	AIRLAGPIG
39	AIYHDLRAM
40	ALKITRLME
41	ALKNVPLYG
42	ALKSRGKGD
43	ALKTTSKWP
44	AMCAKKKWC
45	AMKLHKSAG
46	AMKQKQAYQ
47	ANIQYRHGM
48	ANKASKRAC
49	APKPATKHP
50	AQYPMHRHQ
51	ARSRLKNQT
52	ASHGMGRQA
53	ASRQKYKCV
54	ATHMLGRHG
55	ATKQKTCLG
56	ATRGCCHSW
57	ATWKEELSE

SEQ ID NO	581 to 589 Region
58	AVAGWLRAE
59	AVGQSKHVP
60	AVHFKKCHL
61	AVKMKSTPP
62	AVRTSRHCF
63	AWKLKKSYM
64	AYKQKQKYN
65	CAKPKVAIC
66	CAKVHRNWD
67	CARFERHMY
68	CCKCRKYMS
69	CCQPKPWKW
70	CDYKRVKKY
71	CEMFWARVI
72	CFGTIRRGC
73	CFILLKARS
74	CFKEYRHHS
75	CIHPKSKYL
76	CIKQKKSSN
77	CIRSLFHAG
78	CKHTCNQCI
79	CKKHQGYMP
80	CKMPISKTD
81	CLNCKERRT
82	CMKIRQAMR
83	CMKTKGHMP
84	CMQRKCRMV
85	CQGAIRRHC
86	CQYHPRKWP
87	CRCKRTREQ
88	CSHGYSRVG
89	CSKMIRSLE
90	CSKTKNNVR
91	CSKVANVMH
92	CSRLRRWQF
93	CTFLYDEQY
94	CTKQKKRGN
95	CTRDGRKWG
96	CVLTSRMGS
97	CVRNVKNCM
98	DAFKYKRNA
99	DAHSYRTHF
100	DAKCRWKYC
101	DAKKLHKIE

SEQ ID NO	581 to 589 Region
102	DALVYRRNQ
103	DARINRTCY
104	DARQKKCYQ
105	DARQLRQYH
106	DARWRSITG
107	DAVRARYMQ
108	DCRQVRKVA
109	DFDGTFDFV
110	DFKSRHKTC
111	DFNRFRYHG
112	DGNKARVKN
113	DGRKYMRGC
114	DIARQRKFQ
115	DIIRMRRTT
116	DIKLKKKCD
117	DIKNIRSHH
118	DIRTSRVHV
119	DITKAKRAH
120	DKAKRGHSS
121	DKKDKKGWY
122	DKKRSQWSC
123	DKVRRERCH
124	DMKKRHGSC
125	DMRKAGQTY
126	DMSRQRAQF
127	DPKKKGTWS
128	DQAKFRRSY
129	DQYRMRQQQ
130	DRCKKQSGA
131	DRIGFKKQQ
132	DRKLKANWY
133	DSKYGRKGL
134	DSNKRTRYS
135	DSRHSRVME
136	DSRIMRSAE
137	DSRIVRTSS
138	DSRLIRCFH
139	DSSRKGQMN
140	DTKAWRNPS
141	DTKSRKEMD
142	DTKVKRHVA
143	DTKWSRMRA
144	DTRRCVHRS
145	DTRSKGRFT

SEQ ID NO	581 to 589 Region
146	DVKNRSMAW
147	DVKPSRGGY
148	DVKQRRAPH
149	DVKTRRIFS
150	DVNRKREYS
151	DVRAVRFWP
152	DVRRMAKAA
153	DVRSKALMC
154	DVRTERRIS
155	DVRTNRIEH
156	DVTSRKWLN
157	DWKPKRCMP
158	DYQPPRKSA
159	DYRQNDVAE
160	DYRRSLKAM
161	DYTRFRSHQ
162	EAGKGRKYW
163	EAKAKQMPG
164	EAKGRVIGP
165	EAKGTRCPF
166	EAKIRNFTM
167	EAKMFVRHH
168	EAKNIRCKA
169	EAKTKRFCR
170	EAKVQRGYN
171	EAKWSGRKN
172	EAMWWRHGG
173	EARLTRCCL
174	EARSCRCGL
175	EARTRAHIG
176	EARVIRSNV
177	EARYKGTQY
178	EASIKKQAM
179	EASKRMIVK
180	ECHKIKKGY
181	ECRFNRKKG
182	EERPRIITR
183	EFHRKTRAS
184	EFKPRKSGA
185	EFKRKHIQQ
186	EFRAQRTLA
187	EFRKSGSCY
188	EFRMVRAQE

SEQ ID NO	581 to 589 Region
189	EFRYQRAHC
190	EFSSRWSVF
191	EGKPRSRLG
192	EGKSRRHHD
193	EGKYGKKHG
194	EGRGMRRQC
195	EHKQKMRER
196	EHRPVRSQM
197	EHRTRHGWT
198	EHVRLKHLA
199	EIAKYRWVQ
200	EIKPCRHRC
201	EIKPRRIAS
202	EIKSKKKFD
203	EIKWQRGYY
204	EIRKSGHKQ
205	EIRMNKSNA
206	EIRTSKEAR
207	EIWKCRRQV
208	EKAIMKLRS
209	EKAPSKKGI
210	EKGYNKHRG
211	EKKLLNRWW
212	EKKPKNRYN
213	EKKTKQRMQ
214	EKKWRGIMP
215	EKREKHRQT
216	EKVRTCWRG
217	ELKGKKAIQ
218	ELRRYGFQH
219	EMKAKKCHT
220	EMKLMKKVW
221	EMKMGRQWA
222	EMKQMRKFP
223	EMRVKRTER
224	ENKSAKRGC
225	ENTRRKFTS
226	EPKLKVYKS
227	EPKSRPFKC
228	EQARSRKVG
229	EQGRTKKMY
230	EQKLRKAMP
231	EQKNSRAQF

SEQ ID NO	581 to 589 Region
232	EQRQFRAKD
233	EQRSSRYAA
234	ERCRFKNGN
235	ERHTMHKAP
236	ERKGTVKMT
237	ERKQKGTCG
238	ERVQARKYC
239	ESFKRKVGH
240	ESKSYKCLN
241	ESMRGRKMP
242	ESRDVRAMN
243	ESRFNRSQG
244	ESRFRKDSN
245	ESRIKREWH
246	ESRKAHHDR
247	ESRPFRRFH
248	ETARKGRWY
249	ETKKHSSFW
250	ETKLFKWQD
251	ETKLKKADK
252	ETKRHQMAQ
253	ETKRRQCGY
254	ETKVHKVIG
255	ETKYRKRAE
256	ETRAGRTKG
257	ETRHRMVGC
258	ETRLGKHTY
259	ETRLMRSVD
260	ETRPQRMGH
261	ETRRIQRWD
262	ETRYRANIG
263	ETVRQKHNQ
264	EVKIKKRTI
265	EVKNKGRGQ
266	EVKPARSTF
267	EVKSRQCWQ
268	EVLRMRHEQ
269	EVNRNKMRT
270	EVQRSKRIS
271	EVRPFRQGQ
272	EVRSSRLQN
273	EWKKRTTWN
274	EYARFKGHQ

SEQ ID NO	581 to 589 Region
275	EYKHKKTGW
276	EYKLQRSAQ
277	FAKDRRNPG
278	FAKEMRVYE
279	FAKMSGRYA
280	FAMDIRFAQ
281	FAVARSQQC
282	FMKNKRNYG
283	FPRNVTMLS
284	FQAPSRISP
285	FRDCKIRRY
286	FSQATRRQV
287	FTKAWAKRE
288	FVWSYMFGP
289	GAFCRLSAD
290	GAIRSTHSC
291	GAKTFQKLQ
292	GERLGRKVP
293	GFRMKEKMS
294	GFVKTNKSA
295	GFWPYLYMG
296	GIGQKKSWY
297	GIKSHKREP
298	GIVRRNTAN
299	GKGTMCCEC
300	GKNRCKFQC
301	GLGTKQFRN
302	GMAVKRREP
303	GMFKLNQSC
304	GMKVHRKAP
305	GMLQNRSHQ
306	GNKATNIML
307	GQGLFRRQC
308	GQKGSGRQA
309	GQKLRTSSG
310	GRSQKDWGI
311	GSAWQIWSD
312	GSKFTRQCY
313	GSKQQKGGV
314	GSKQTTGYT
315	GSKSHSHWM
316	GSKSNYHSG
317	GSSSKTTCC

SEQ ID NO	581 to 589 Region
318	GTAGCKKAA
319	GTAMFRVSA
320	GTIKRMTAY
321	GTKVKNCRN
322	GTKWSKKWQ
323	GVFDIRKNP
324	GVHWKKTAY
325	GVKFRNKTN
326	GVKLHTPFS
327	GVTGRFCCQ
328	GVVLIRQDD
329	GYKQQRNRD
330	GYKQTHWLG
331	GYWWLFADR
332	HASRKGTFP
333	HAWPMPATW
334	HKQWNYCPS
335	HKRTAPWTN
336	HQKYKKLTG
337	HRRPFQTKT
338	HVRSNLPIC
339	IAFQYQNRL
340	IAKMKSRYP
341	IARSGWMSG
342	IAYHYWKDV
343	ICLKRHAKA
344	IEKQRRVYA
345	IGAKRSWTS
346	IGIPKNHKP
347	IGRWMINSM
348	IGVKAHRSA
349	IHHTNFHSP
350	IHMKRAAYS
351	IIKPRSKVD
352	IKQKGELKC
353	ILLKHMKYP
354	IMKDRKSGS
355	IMPRCWDMC
356	IPQPSRKMP
357	IPRTINRCT
358	IQHRFLTYQ
359	IQKCMTRQA
360	ISTQPRQQS

SEQ ID NO	581 to 589 Region
361	ISWIQRTCM
362	ITFGTRKDA
363	ITFWKMRDG
364	ITKDIRWKG
365	ITRDSRWGM
366	ITTTARKVP
367	IVKEVRTNH
368	IVKPRGQCI
369	IVKQLKRTA
370	IVKYRVGTS
371	IVVESENRH
372	IVVRRFYDP
373	IVYSSRQNP
374	KAGTPGIQN
375	KEARHTRRE
376	KEFLYLSRE
377	KEKEYKKYF
378	KFRDAQNMS
379	KIKVANAAS
380	KKPANMFPW
381	KNRAVQGFN
382	KPGMVMNPN
383	KPRPKLNST
384	KQRHWGAKW
385	KQRSGWCCH
386	KSCKGRANG
387	KSFYGEHYF
388	KSNQMGKSP
389	KVKVRACSD
390	LAKDCRACN
391	LAKFKNKIL
392	LANTYHWEQ
393	LANVKGRVA
394	LAPRKQVQW
395	LARAKTSSV
396	LARYLGSQN
397	LCKEGRKAG
398	LCKWSKKQC
399	LFRMNMRTH
400	LGKSRKQMA
401	LIECRRRCP
402	LIKCKDRFT
403	LIKWNRKAM

SEQ ID NO	581 to 589 Region
404	LIRLYTNKE
405	LLCKVKDYQ
406	LLIKKNRGV
407	LLRLAQQGP
408	LLRMTTYAW
409	LMKICKSFP
410	LMWSRFEVP
411	LNMHYRSHK
412	LNRQRGHAS
413	LPERCRKQS
414	LPKPTKKGP
415	LPKSTKRWG
416	LQKMSRFMN
417	LQKTRSIIQ
418	LQTKKNRHY
419	LRVPRYGQS
420	LSKKRERCN
421	LSKTKSYVE
422	LTRFHGGMY
423	LVKDRCSGY
424	LVRMHRSDQ
425	LVSRLPSMR
426	LVVQRNVRQ
427	LWKTSRQCN
428	LYIHRWVSG
429	MAEHQIVTT
430	MAIRGTKAN
431	MAKLCQRKC
432	MALDFRNGK
433	MCAGYHREQ
434	MCKAHMRKD
435	MCTATSRYK
436	MEKQLKLHN
437	MFVTYYTLY
438	MGAPKKTLG
439	MHWSVHYNS
440	MHYLAMSAR
441	MIAEDEYWA
442	MIDSRKRSA
443	MISLKKKMS
444	MKILKYSQE
445	MKKDKTNST
446	MKLNRNHDC

SEQ ID NO	581 to 589 Region
447	MKSRPFMGS
448	MMAGMRISS
449	MMAKPLWAY
450	MMHQVTHDF
451	MMKGRSYCT
452	MMKPKGHYP
453	MNIKKNHWA
454	MPKRACNKW
455	MPWKIDTGG
456	MQKTSKKYQ
457	MQQRVFRSN
458	MQSLKSRWH
459	MSFKDLKNG
460	MSGSRRNAE
461	MSKQKKAGS
462	MSKSRSLNN
463	MSPFVRKAS
464	MSRESRSVS
465	MSWLERKAN
466	MTEGKKRIP
467	MTGKSPRGA
468	MTGVRWRSQ
469	MTIYQRGAA
470	MTMCLKKYY
471	MTMTMLPWY
472	MTRGHSIWG
473	MTRMRLSGP
474	MTTSRQRCW
475	MTWYHDIHQ
476	MVKHHRESF
477	MVKWSWHKC
478	MVMKRVMVP
479	MVVPAKYKW
480	MVWSADSYE
481	MWKDIRQWH
482	MWKSRLDSY
483	MYKCGIKCH
484	MYRAKLTAQ
485	NAMWLRHYD
486	NCAQYYGTG
487	NFKDMRSQE
488	NIGLKKKYF
489	NIRQPNQCA

SEQ ID NO	581 to 589 Region
490	NKHSQRREA
491	NKRDHKYWG
492	NKTKSHYGN
493	NMNHVAFAY
494	NMYMYRAQH
495	NNKGLSQNT
496	NQRLYAKSE
497	NRMRYSCYS
498	NSKTWGTLS
499	NTFISYRDQ
500	NTGKRSRQA
501	NTHALGRHG
502	NTKLSRYGM
503	NTKSAVKQP
504	NTLPSRYGN
505	NTNFRNMSW
506	NTNPSGKNF
507	NTYCKKHCS
508	NVAPKSHKW
509	NVAWRTRDL
510	NVKGIAHYC
511	NVKTLHHMW
512	NVSMLGRWN
513	NVTNQKKTW
514	NWNPCRKNA
515	NYWWMLSGP
516	PCGGKVIKA
517	PKRKGNEWC
518	PMKPTKYAH
519	PSSVKQTKA
520	PTKVLNRYN
521	PWAGTRWKQ
522	QAGCKGTWR
523	QAHMFFKHE
524	QAKWRNLWN
525	QAMHYWRYP
526	QARDRTAQF
527	QAVARGNLK
528	QCCKRKTGL
529	QCKLKGNLM
530	QCKTKKSAS
531	QCKYRYTKG
532	QCQPRKHTP

SEQ ID NO	581 to 589 Region
533	QCVCKKMKG
534	QCWPTMKCD
535	QDYQEDGKK
536	QEKKKANLT
537	QFKLKTRES
538	QGAGGRKDQ
539	QGALYKKQF
540	QIAKVQKTR
541	QIFRLPQAG
542	QIRDKSRHH
543	QLTRYMKST
544	QMHHKKNWM
545	QMHPESYSA
546	QMKSKTKWL
547	QMWFRYASE
548	QNSQIKKVG
549	QPEQRRKVP
550	QPKLRSQVM
551	QPKTRSMYQ
552	QPKVNRHTG
553	QPLYFRSQG
554	QQMTKKNFG
555	QSAGRKTVA
556	QSFLSLTPG
557	QSHMYGRIS
558	QSIYFRHGI
559	QSQNLRRQC
560	QSYWNLSYQ
561	QTKTYREGG
562	QTRGGCKRA
563	QTTQPRQWP
564	QVFATLTSW
565	QVFLNLREG
566	QVHGILRAH
567	QVKWKNRFP
568	QVSKCQIRK
569	QVSMRGHYR
570	QVVRNHHKE
571	RCGYHHSQT
572	RCRVAIVWT
573	RFAYWKNQG
574	RHQKRNWAN
575	RMFSVPMWD

SEQ ID NO	581 to 589 Region
576	RNKPIKHGP
577	RPNRVMARM
578	RTCYWSANE
579	RVHPWSQRQ
580	RWKDKNKLM
581	RWKHLKGVC
582	SAGWRSHCV
583	SALYHGAGF
584	SASWKGKTP
585	SCKPKSKST
586	SCMRKGRFQ
587	SDVRKPRQH
588	SECNNPFVM
589	SGCQMKRAF
590	SHKCKTSMT
591	SHKEIKGQA
592	SHPNTRQGD
593	SIGMRSHMG
594	SIKVQKRAG
595	SIQRLKWVN
596	SKDSFRRCC
597	SKHPRMQQA
598	SKHQYHQDA
599	SKKTGGIQT
600	SLKQQSYRG
601	SLRQNHMHQ
602	SNTTVRKQY
603	SQLSFRSAT
604	SQPRNKFSG
605	SRHRYPKCS
606	SRRVSSRMF
607	SRVKMSRQH
608	SSMPMFSGA
609	STAQKCKFM
610	STFYRFRDP
611	STGPKKNST
612	STKISRLHN
613	STKSRSHYH
614	STSSAKKYP
615	SVGYGKPWQ
616	SVHMNLRAH
617	SVKLRSWSK
618	SVKPCCRNR

SEQ ID NO	581 to 589 Region
619	SVRDIRYGP
620	SWWPLMTWG
621	SYVKPIQRP
622	SYWGYSRAH
623	TAKYRGLWQ
624	TARQFKSPR
625	TASSRLCCH
626	TCKGVSYRT
627	TCKPHGKCT
628	TCKYRSHLA
629	TCRGYNDSY
630	TFTRPLCMS
631	TGAFRRSGA
632	TGKLRGGWH
633	TGRFSSHMH
634	TGVKRNHAG
635	THHKARYTG
636	THKEKRTAI
637	THSSFKKMQ
638	TIIRRNTTT
639	TIIWARSMA
640	TIKTSRTDD
641	TIKYKSGNG
642	TIRDLRTQN
643	TMAQSWRSI
644	TMKSKQRWV
645	TMRSKSCSM
646	TMRWRNHSE
647	TNKFTRKGW
648	TNWLIKWMG
649	TNWPHVKAY
650	TPKSRGVYA
651	TPKVKSSFN
652	TPRPSTRAP
653	TQCQKKTAR
654	TQFQKLADR
655	TQKPKKSGS
656	TQNASRHMQ
657	TQPKLKRES
658	TQRDRMRAN
659	TQRPTTKTR
660	TSAFKKGFT
661	TSHAIIRLQ

SEQ ID NO	581 to 589 Region
662	TSKFFGMFA
663	TSKMPGRAS
664	TSKPNRKKT
665	TSSYKSRFH
666	TSWWLPSMT
667	TTARNQGTG
668	TTKGQVQCM
669	TTKGTGSHN
670	TTKPGRHSY
671	TTKTVREYG
672	TTRYSTAPS
673	TTVKRLNSF
674	TTWTPEQHP
675	TVKNNVLCG
676	TVKPQMVGR
677	TVKWGNKLW
678	TVNIKTRSH
679	TVREKGHDR
680	TVSSRQRTR
681	TWKTRTCAP
682	TWRYVMKEC
683	TYAKYNRMC
684	TYGFPVSVA
685	TYKYKNNYC
686	VAALNLRHP
687	VACKCKNRP
688	VAHNALKMM
689	VAKVMTTAP
690	VAKWRSKHQ
691	VARIKQDMF
692	VASRGGRGC
693	VASSQKRAI
694	VCKVNRKML
695	VCRHRQQMY
696	VCVKKYRCN
697	VGAGYKHCY
698	VHRFVNRDF
699	VIKGQATER
700	VIKSSWFKG
701	VIMRPISQQ
702	VKHKDQWGP
703	VKHRAKFCD
704	VKQFRKCFC

SEQ ID NO	581 to 589 Region
705	VLDRHWAAY
706	VLKQIGRNS
707	VMKDVKKVW
708	VMKDWKGKH
709	VMMLARQSQ
710	VNPYKLWKT
711	VPFNYWRME
712	VPIRVMRHG
713	VPIYTKWKN
714	VQKTSRRGE
715	VQVRRHAHG
716	VSDIANEAF
717	VSKAKSNFR
718	VSPTIRKSP
719	VSSLKKSQF
720	VSTRDKWRN
721	VTCRCKMKH
722	VTDRKQLRG
723	VTKQKCKMN
724	VTQMKHKGW
725	VTRQKCKMN
726	VVGKVMRDC
727	VVKQVGKQA
728	VVNYTALQD
729	VWGLTRHAG
730	WAKPTKKIM
731	WEPGIITGC
732	WVFSIQKQA
733	YIATKLRDQ
734	YIRDRGHYP
735	YIYPITYSQ
736	YMFEAPWIE
737	YSGAKGHMM
738	AAGASKNAK
739	AAHRPMFTS
740	AAKSFRRAA
741	AARSTQGIA
742	AATHKYRCN
743	AATKEKRHM
744	AAYTSRQLG
745	ACKIKTGQA
746	ACTKERSIR
747	ADKTKKHFA

SEQ ID NO	581 to 589 Region
748	AFKTMRWSM
749	AFPPYKYRK
750	AHRSKKTSM
751	AIYSAMTAF
752	AKAKMSRTY
753	AKKASKRGC
754	AKPIPQTKN
755	ALRLKNSLT
756	AMKMKKTHF
757	AMSKAIRNS
758	ANRFKNTEG
759	AQKSLHYTC
760	ASKPRKRYN
761	ATFRDSDYQ
762	ATHERRKSP
763	ATTKRKGCC
764	ATTRFPDAA
765	AVRFGAAQK
766	AVRLRSKVD
767	AWIRCIQMP
768	AYKQVKREL
769	AYMVRLNHH
770	AYMYRPATE
771	CAKGKTQTS
772	CASRKQRSH
773	CGSSYKKVQ
774	CIVQKTAQK
775	CKCGLKRFS
776	CKCLKTMKQ
777	CKTRACKYC
778	CRCKCAIKC
779	CSKYTAKAW
780	CSQGTKKSY
781	CSTQGRKAM
782	CSTSKKRTF
783	CSTSQRRWG
784	CTGPCCRPQ
785	CTKHLARQH
786	CTKKTRCQG
787	CVDILLVHR
788	CVGLDRRGY
789	DAKFSRGMQ
790	DAKFVRHQH

SEQ ID NO	581 to 589 Region
791	DAKPSRCCL
792	DAKSKKKWY
793	DANIEWHGN
794	DARKWSNCI
795	DARMKGISS
796	DASMWSGIE
797	DDGKEVWHH
798	DGFPKRKAC
799	DGSSIRRYP
800	DHFHPRQSP
801	DIARGKGKP
802	DIKMHRGAC
803	DKKDRKMIY
804	DKKGYALAY
805	DKKQRQWTA
806	DMQRKKREG
807	DQKFMKTYF
808	DRLPSRQCQ
809	DRRGKTSMP
810	DRRGYGVSN
811	DSQKPKKAP
812	DSRCFRRGY
813	DSRNRAHWC
814	DSSRARYKS
815	DTKQKGSPK
816	DTSRVKAAQ
817	DVKLKKRYY
818	DVKPRRSGF
819	DVRTSRGVT
820	DVRWIRHHH
821	DYHRLGRQE
822	EAKLAKSYS
823	EAKYKKNYS
824	EARGRAHSG
825	EARTSRWLA
826	ECKPKAKWM
827	ECKPRRMQA
828	ECRPTRINE
829	EFKHRWQGR
830	EGKLTKRCM
831	EIFKALRAE
832	EIRPCRFRN
833	EIRRQGQAI

SEQ ID NO	581 to 589 Region
834	EIRVIKSHS
835	EKHTFKKWA
836	EKKEAKKFN
837	EKKHKGEFW
838	EKRSISVHT
839	EMKVTKMRG
840	ENKLVKKTP
841	EQQCFLHGN
842	EQRIMRSQA
843	ERFHKMSAD
844	ERKARSTYC
845	ERQQRCRFS
846	ERVPMWRNA
847	ERYPQRSAF
848	ESGCNQPQD
849	ESGRKSRAE
850	ESIRAKRVA
851	ESKGYRSGC
852	ESKIKSAAS
853	ESKNVKDWK
854	ESKYRNRMC
855	ETHRKNQHN
856	ETIPFLDLG
857	ETKYVRKEW
858	ETRMRANFQ
859	ETRPFRGNE
860	ETRSRCHCA
861	ETRVSRNMP
862	ETRYFKNAY
863	ETVERCNFI
864	ETVRQKGHN
865	EVGNRKWQS
866	EVKRAPSTL
867	EVKWRKCLQ
868	EVLRPRAIA
869	EVRALRTQH
870	EVRMSRTIN
871	EVRQSRQVC
872	EVRSARQQS
873	EVTRHRLWS
874	EWHRFGRNS
875	EWWPIRHSW
876	EYKPCRRAV

SEQ ID NO	581 to 589 Region
877	EYKTARHAM
878	FAYKEWLPG
879	FFHSRMSQE
880	FHRALFHAG
881	FICMKKTDQ
882	FIGWMHRAN
883	FIWPIDHTS
884	FLNEYGYYQ
885	FSFQYLKKG
886	FTATSLRFP
887	GAGMKKRMS
888	GAKLKSRLD
889	GDKSRKSKM
890	GFSMMMIPW
891	GHKETRAMG
892	GILRKVNDH
893	GNVKIMRFA
894	GQKTTSTNY
895	GSKMYAHTP
896	GSRDTRQYP
897	GTHLELMNA
898	GTKQKAVIE
899	GTREHGKTP
900	GTWSAMRAT
901	GVKCQKSAK
902	GVKGHSHDR
903	GVWPCYYLQ
904	GYMECDHMQ
905	GYRFVGTTP
906	HAMIFQRAS
907	HAPMYKSAG
908	HNKDLKCQE
909	HRRMRDAIY
910	HSQRCKVIA
911	IAKGQQQMC
912	IAKQKCNCC
913	IAMRKWNCE
914	IANQLTMTT
915	IASILWSSA
916	IAVRYYHQW
917	ICKPKGKWL
918	IERKNNASQ
919	IFRLWNAKE

SEQ ID NO	581 to 589 Region
920	IGGPYRTIN
921	IGKYTKKMT
922	IGRFNNIAE
923	IIRPSSHAC
924	IIRSGTKYP
925	IMRGGTKYG
926	INKTVQRCG
927	INRPTRWPH
928	INVRSQHQH
929	ISNISKWRT
930	ISQSMKFSG
931	ISRDQKHVC
932	ITFPRIRAD
933	KAHAITDHS
934	KGMRCKAME
935	KHLMVPGKM
936	KKMGRMCDR
937	KMHRCKDDR
938	KNEVDTNGE
939	KSAVHQGGH
940	KSDTFRRVF
941	KTHKFSSCL
942	KVRSNREQM
943	KWQGSTHKT
944	KWTYNNTDL
945	LAGKMAHWQ
946	LAYMKILQQ
947	LCNIRCRSG
948	LDAQIVCYG
949	LFKAAVKAP
950	LFKPKKTSQ
951	LGKFSGAGS
952	LHKQYYHGM
953	LHWLIKESG
954	LKERKEVRA
955	LKGSSKSSF
956	LLWINTMIW
957	LMFYTLSRD
958	LMRNVNVEP
959	LNRQHGHAP
960	LNRYVSMGV
961	LPKVARKMF
962	LQGRYMGAQ

SEQ ID NO	581 to 589 Region
963	LQKNGRYSG
964	LSIRRNCCG
965	LSRHTKQLA
966	LSRPTMTIS
967	LTAKPFKCQ
968	LTGKYVGYS
969	LTKSRGQCS
970	LTRAHRSHE
971	LVIGRHQNW
972	LVRDIREFS
973	LVRYKSGGD
974	LVYTSLKDA
975	MAKQKKQAM
976	MAMEQRRFG
977	MAMREMKVC
978	MAMYYRMDD
979	MCRDRGKMV
980	MDGRFKATS
981	MEGCFMYVF
982	MGWPKHQDP
983	MHKVKSGNA
984	MIKNSGKEL
985	MIRGQRGGG
986	MIWPMSVQH
987	MLKMGFRYA
988	MLKYRQGGG
989	MLTYWTSRN
990	MMKCKRWDY
991	MMKSHKAGN
992	MNKDKRIMP
993	MNVQKRNYF
994	MPKLNRKAQ
995	MPKNYGHAP
996	MPMIKLSYS
997	MQAQPRKQG
998	MQHYLHHAT
999	MQRYKSKCC
1000	MQYMQRNAY
1001	MSKESRSQP
1002	MSLGQRTSW
1003	MSMVRKDQQ
1004	MTAGKKAWN
1005	MTTLQRQFM

SEQ ID NO	581 to 589 Region
1006	MVIPVEIMI
1007	MVKMKCTCT
1008	MVWPITRTD
1009	MVWPKQTEA
1010	MVWWEEKMC
1011	MVYRPLTSS
1012	MWAGKSRWC
1013	MWAPFRHWN
1014	MWAQTRQQW
1015	MYWHQTLSE
1016	NAKLNKRQM
1017	NHKSYPVAP
1018	NKHSTRAMD
1019	NRHKCGSWS
1020	NSGLKKYYG
1021	NSRNMLQNE
1022	NTKIRSVQH
1023	NTKSKSQLA
1024	NTVRTFHGW
1025	NVHAKLSAE
1026	NVKPTAWKW
1027	NYRSHRKIA
1028	PAVKKVERQ
1029	PCKLAGTWD
1030	PIGKHAFKC
1031	PLVKSGFGT
1032	PQEKRKNVA
1033	PQFTYRKYP
1034	QAAFHLKNA
1035	QATTKRTIF
1036	QCNVRTKMF
1037	QDFRLSSGM
1038	QEKCNRRGC
1039	QFAKQVKWF
1040	QGFMVMKAV
1041	QGKVKERTM
1042	QGRQVLGRE
1043	QILIKDCFS
1044	QKQKRTRAQ
1045	QMSGRCTCR
1046	QNRAIRSYT
1047	QPKFFYRSA
1048	QQLDATHER

SEQ ID NO	581 to 589 Region
1049	QQTKRSCMA
1050	QRKDKQTQH
1051	QSFRFWKHH
1052	QSKFKIPYC
1053	QSKLRLTEP
1054	QSQSTKAVW
1055	QSRQTGKFW
1056	QTCRKDRHF
1057	QTMKQIRAT
1058	QTRISRWDG
1059	QVFLKIRQE
1060	QVHNRLTQL
1061	QVHPSRWIR
1062	QVKMGKPNH
1063	QVMRQNTIT
1064	QYTRFNHVP
1065	RFKVWTCSC
1066	RFYDAMQMH
1067	RHDKQANGS
1068	RKNPTTCYS
1069	RKPHSGWRC
1070	RKRFTSMDP
1071	RLEDVHGNK
1072	RNKEWTGKG
1073	RQLPMNCCE
1074	RVNPELHMG
1075	SAKMQQISL
1076	SARDYREIA
1077	SARISAIGP
1078	SCKFKKSFF
1079	SCKHVVKVP
1080	SFIRTHRSW
1081	SFKMMTRQA
1082	SFKQKAREY
1083	SFRPTTWKQ
1084	SGSHYRRFP
1085	SHKFTGRCG
1086	SLNQFVMHE
1087	SQKHHTRSH
1088	SQKIVHYTN
1089	SSAQWLACD
1090	SSKFMACAS
1091	SSKLVSKTW

SEQ ID NO	581 to 589 Region
1092	SSRFLCHNE
1093	STKAWRYTG
1094	STKQAKRTA
1095	STTHLLRYP
1096	SVKLIGSEW
1097	SVVWPAQVE
1098	SWGYCMLDQ
1099	SWHMKMIAG
1100	SWKGMGKAD
1101	TAKITGSGS
1102	TAVRWMNGR
1103	TEYTRKKVP
1104	TGKSKSRMV
1105	TGKSKTWMP
1106	TGMRMPHGG
1107	TGTLTRWGP
1108	THFRKNWES
1109	TIANSRSHM
1110	TIKLSRFEP
1111	TIKVGHSRC
1112	TIWQRSGVD
1113	TKAIHNQSI
1114	TLKAYNHQI
1115	TMGFKTRYQ
1116	TMRGQPFGV
1117	TPDKRKWAQ
1118	TPILAGLVY
1119	TPKCIKWQQ
1120	TPRFHNKVP
1121	TPRSTRFCA
1122	TQHSLKAMM
1123	TSGWYKKSY
1124	TSKVKMWEY
1125	TSKVRSKCP
1126	TSVPHKWKR
1127	TTHLKLAAA
1128	TTKDGRAFE
1129	TTKEKKKDW
1130	TTKMGKWAA
1131	TTKPYQSIR
1132	TTKSRGFIP
1133	TTLRRHCCC
1134	TTLRTIKQA

SEQ ID NO	581 to 589 Region
1135	TTRTNSICS
1136	TVFYRHHHL
1137	TVGLGRRGA
1138	TVKSHTPMA
1139	TVKSREHSM
1140	TVLNYRRGF
1141	TVNVNKKAY
1142	TVRLQSYAQ
1143	TVRTLFKGN
1144	TVVAKTLRA
1145	TWRFNNHLC
1146	TYFKVMKDS
1147	VARPNVHQE
1148	VASSPRVCP
1149	VCVGRRAER
1150	VFKQFGKRE
1151	VGTSARKIG
1152	VLAPYRNCE
1153	VMVKRLATG
1154	VRQRPKFRP
1155	VSRTRIDSH
1156	VTKPKTVAD
1157	VTKWKNSGG
1158	VTMSRRSVW
1159	VTRSCCSFG
1160	VVKGMVCPC
1161	VVMQNNVAE
1162	WIEYISWWG
1163	YNFPKSAAE
1164	YNKSYRETG
1165	YPKPTRRDC
1166	YQKPSQTWS
1167	YSNLKSKAQ
1168	YTRGCHGCS
1169	YVSYARQSV

[0187] In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 14 – SEQ ID NO: 1169. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 14 – SEQ ID NO: 1169.

[0188] **TABLE 4** provides additional 581 to 589 region sequences predicted to confer retina tissue tropism or preference, based on a primary screen of a recombinant AAV5 capsid library.

TABLE 4 – Additional Exemplary 581 to 589 Region Sequences for Retinal Targeting

SEQ ID NO	581 to 589 Region
1170	KSRKVKCLK
1171	KKKYKGHIP
1172	KKRKKILFM
1173	KTKCTKTKN
1174	KRKKAKVIE
1175	KQKIKKTAF
1176	KKCGKKRHY
1177	LCKNKKMKN
1178	KKKRKGQCP
1179	KQKTKHWMK
1180	CSRKAKFKK
1181	KAKNKACKK
1182	AKKKTLITK
1183	RKKKGKPSA
1184	HRRRAQYRS
1185	KGKKIKLMM
1186	TKKPCKYKS
1187	KKKTKTQIP
1188	KKTKGKSGT
1189	CRRRRKIHE
1190	IKTRKKWKY
1191	KAKFKKWAS
1192	KCRKKVKVA
1193	KKSVKKALV
1194	KSRKKQVKH
1195	YMKKHKKGQ
1196	KKTLKKWLP
1197	RRRRASCAE
1198	KGKKRKTAM
1199	KQKKKQNHQ
1200	KKYNKKGMW
1201	VVKHKKKVC
1202	KKKCKNIFA
1203	KLNKWKSKQ
1204	KKKQKCVRG
1205	AKKAKRWHK
1206	KKRKLFVKN
1207	KRKKKNHCR
1208	KIKKKFDTI
1209	KVKIKQIKQ
1210	KKKIKMFCT
1211	IYKWKKKGT
1212	KRKGKKFCS
1213	KKKTCKFEG

SEQ ID NO	581 to 589 Region
1214	KTRMKRIQV
1215	QAKKKKQWD
1216	MKKKQKNVA
1217	KKRKAHLQW
1218	IKTKKKWGY
1219	KCKAFKGYT
1220	KVHKKKGWH
1221	RFRKFRRCT
1222	KSKKTKCLD
1223	KKKQKQCYF
1224	KQKKKPAIW
1225	AKKRRKGSM
1226	KVGKHLKKG
1227	TRRRRWCGN
1228	KKKKKRIFR
1229	KPKMGKYTK
1230	ARKKKAGKC
1231	MTKMKKKMC
1232	KRARLKHSQ
1233	KGKKRAKTG
1234	KQKFFKHAM
1235	KKKRNRDGL
1236	RSKQFRVHD
1237	KRRKPCWRQ
1238	QTKQKKWKN
1239	KQRKHKVDT
1240	KAKSKKGLM
1241	EVKKKKFMP
1242	KVKSHKLGQ
1243	KKKRVQSRD
1244	KAKRCKASC
1245	VQKKGWQKK
1246	KRKWKRDCF
1247	KAKKSKHDR
1248	KCKMMKIKC
1249	KKKKFPECG
1250	RYKHHRFLP
1251	KKHRKGQMT
1252	EWKKKKCFF
1253	VKKRSKVQA
1254	RRRRILHCP
1255	MKKRQRGAS
1256	KKHKKQLEN
1257	QTKPKKTKC

SEQ ID NO	581 to 589 Region
1258	KKKMQCIKC
1259	QQKEKKWKE
1260	KTKLYKYCY
1261	PKKFKVHKC
1262	YARRAKSTE
1263	KPVKKQFKE
1264	RCRSRRYPE
1265	KRRYRKHNY
1266	HKRTLKHWF
1267	RTRRLSPRE
1268	SKRKKGCVG
1269	TKPKKKWWA
1270	QSRKAKRIQ
1271	RFKSRRSRA
1272	LVGKKKTGK
1273	MVKLKKKHH
1274	KAKYWKHRF
1275	RPKKVKNCE
1276	HCRKRRHFH
1277	VKKMKIWKH
1278	KVRSKKMWS
1279	ITKSKKKWT
1280	KARKKMWSC
1281	KVKPKSNKS
1282	KIKRIIVAH
1283	KKAHAKKVM
1284	KKKQKRVGH
1285	RKKGGKLVC
1286	TKRKHKPVN
1287	RRKSCRFHR
1288	KKKYHPKWT
1289	AAKRQKIQW
1290	FVRKLKTTT
1291	YCKLYKKKG
1292	RRVRKHQRE
1293	PKLKKKGFS
1294	CPKNKKKVP
1295	FKKCKGTKS
1296	RQRKFKCMQ
1297	KKHRFKLPV
1298	DAKKDRYKK
1299	KKHRSHPSQ
1300	KMRKTKLWG
1301	EKKKYCHKT

SEQ ID NO	581 to 589 Region
1302	DVKKKKWPP
1303	QVKSKKKQI
1304	KIRKTKVYN
1305	KIIKIKKFW
1306	MKRKLKYAN
1307	KAKSRQFCQ
1308	ARARRRYCN
1309	KKRGYHFQH
1310	NKKQKCQKV
1311	VTCKKKSKS
1312	CIKKCKQWY
1313	KAQKHLKKC
1314	VRRKVRRTP
1315	KSRQKKGPH
1316	KRKTAKYFQ
1317	KYKSRKVNS
1318	YFRARRRYS
1319	TRRKKKSWN
1320	KKKPKSHLG
1321	KRKKSGHFY
1322	NRRVSRWRK
1323	QRQKIRRRT
1324	KMPKQKFKN
1325	KKNKKCKKP
1326	DTKRKKSCA
1327	SKKRHRSHV
1328	KYKQGGKQY
1329	KSARKKWSC
1330	HKKHFKKPL
1331	GRRKYRADR
1332	SVKHYKKHQ
1333	NTKRLKCKQ
1334	EKKFKKCGG
1335	KKRYYHRPC
1336	KGRKIRTQT
1337	VKKRPKWSK
1338	QIRRKKAYY
1339	TCKRKKLNA
1340	KARSLSRWL
1341	KLKYIKRSA
1342	KQRYRKHGQ
1343	RWRRRQKLQ
1344	DIKFKKKIF

SEQ ID NO	581 to 589 Region
1345	HKKKCQNCN
1346	RMKRYHYTG
1347	KVKCIKQLG
1348	RAKRYKHTW
1349	KGKCMKNAQ
1350	KNKKRVRGV
1351	KLKKQPFKG
1352	LKRKHRRTG
1353	MKTKTHCKS
1354	FYKRMRMHN
1355	HRKFKKQAY
1356	CKSRKRRGQ
1357	HKKRTVAWM
1358	KAKFCRKPQ
1359	KHRKFRCMT
1360	RRGRRWVPQ
1361	CFRKYKNKG
1362	KWKSKGKNC
1363	HKHRKQRYV
1364	RTRRYRHWL
1365	KTRKGRSNH
1366	PCRRRRLWG
1367	KMRKAHVTG
1368	SRKKCKVCY
1369	KSKSKYWGV
1370	KKKSKLFWN
1371	KKMKCKEAR
1372	VGKLKKKWQ
1373	SVKSKKSGL
1374	FSRKKKLYY
1375	VNYKKKGKC
1376	KWRKMKGCY
1377	KMKSKADKG
1378	ARKLKRTRF
1379	KYRKTNVFW
1380	KNKKEHKSD
1381	KGKHRKFYA
1382	KRKLGKFNG
1383	KKARKGQPW
1384	TAKRQRIKH
1385	KRKRTNYWW
1386	MQRKKKCTG
1387	KKEKKIWTC

SEQ ID NO	581 to 589 Region
1388	KQRKRFNSW
1389	KKKALGFRS
1390	KVRPKRAGP
1391	EHRRRRIVG
1392	KKKKCQAAP
1393	VKKIKHVKG
1394	RVRPTRKQC
1395	KERKQKEMM
1396	KRKKFMNAR
1397	RIRKMTRTQ
1398	KKKPNRIAA
1399	KKKTIRHNP
1400	VKKPRGRHP
1401	RCRKFKSDM
1402	KSKYAKNQA
1403	KTCKTKTMF
1404	HKKCKSQKS
1405	KGRKYWCGG
1406	KHKRRTFYP
1407	KKSKEKAPF
1408	KTCKKSKIV
1409	RKKRWHVQY
1410	KRSRLKRSH
1411	SKKRYMYKS
1412	SKVRKRFRV
1413	CKAKRKSGY
1414	VCRRIKGRW
1415	HKTHKKKMT
1416	KQKKYVMTA
1417	KRRKQYHCK
1418	KKATFKQAK
1419	RIKCKKTTL
1420	FKKRYLLWT
1421	KKDRHKHKS
1422	LARKFKLWH
1423	TCCKKKKWM
1424	RRRKIMGHS
1425	KIKPCKKNH
1426	KCKQYKMSV
1427	KQKLQKQAP
1428	KIKQCKRAW
1429	KRKKQSVYN
1430	HCKYHKKGF

SEQ ID NO	581 to 589 Region
1431	GRRCCRRGF
1432	TKRLKTRRD
1433	QRPRKRKGG
1434	KAKCSKSYC
1435	RRRKGLMIQ
1436	GKKKSKLGE
1437	RKKALKRHG
1438	SSKRRKQCF
1439	KMKFQKYAC
1440	KIRKWSAFE
1441	KKRRTVHPN
1442	KAGWLKKEK
1443	KHKTKHNWE
1444	DHKRQKRQP
1445	KYKHRGGYT
1446	EKKVKKEQW
1447	MSKRFKTMG
1448	PMKKKEYKC
1449	QKKWKFKTC
1450	EKKPQKKQY
1451	RGKARRSYA
1452	KIKRNRSNM
1453	SKKCGKKDF
1454	YWKKIKRWN
1455	KYKQVKKLA
1456	KQRKCYYKT
1457	HRRKTRYFR
1458	NCKGKCVKK
1459	KTKFRGSKS
1460	FKRKTRIDG
1461	KTKCFKGGF
1462	RVKHYRHYQ
1463	DKKPKKQYW
1464	HRKSKKWQP
1465	RKGKKDCKG
1466	KSRKHIRTW
1467	AKQRQRHQP
1468	MTKSKKRWN
1469	RRRRYMLIA
1470	CKKTKTHKF
1471	KQVKKKKES
1472	HTKRKGAWM
1473	KRMKRSRND

SEQ ID NO	581 to 589 Region
1474	KQRRKCVCY
1475	KKKCQSFGS
1476	KKKASGWTT
1477	EVKSKKRQP
1478	CRRRLKCGE
1479	KAKSRGGYN
1480	LAKYKKSYH
1481	KCKKCYKCD
1482	LKKKTKPCG
1483	EARRKKGWH
1484	CPRKSKFCM
1485	MNARVKRVG
1486	KCKFVKAHT
1487	KKRNKAQYV
1488	MVKRNKHYG
1489	KARWKGRVQ
1490	CSKKRKAGT
1491	GVRKTKWCN
1492	KQKFRGMRY
1493	VKRKHKFEN
1494	KGRKWGGTG
1495	IVKRLKQGA
1496	SKRKLGQVN
1497	KYKSQKWTV
1498	KRTRKKRMV
1499	MYKLKKTAV
1500	HRRKWLYPA
1501	KKKTYSCLS
1502	KRKRLPYGM
1503	KRRKNVWCP
1504	HKRKRYVAV
1505	KVRVHKMVC
1506	KWRKEKMHY
1507	KQKQKKVGP
1508	KRKAKQGCN
1509	TNKSKKSQN
1510	VKRRKIYGA
1511	KIRLRKGVS
1512	KCKIVKQMG
1513	KCRKQHHTM
1514	RAKIHRYYT
1515	GKRKHMPCP
1516	KCKKDRKQC

SEQ ID NO	581 to 589 Region
1517	QKHRTKKWS
1518	IKKKFGRCC
1519	LKRKDKFGE
1520	KSRKAWLCM
1521	RFRGHRCWR
1522	EKRKSKCCP
1523	KRRKQMHRV
1524	KQKWWKYGC
1525	KQKYGKFYN
1526	NGKLFKKHV
1527	TTKSFKWRQ
1528	KKRIHRHEY
1529	HTKSKKFFS
1530	KSRSKQRQC
1531	NVRRYKTHI
1532	VKKRYHRQQ
1533	HIRKAKKQC
1534	KRRRIRHLM
1535	KKKIGTKCF
1536	ESKRKRSMN
1537	YCKLKKIHQ
1538	NKMSKKKVC
1539	FFKKRRVCC
1540	RKKVCRFSN
1541	SVKMMKTLP
1542	KVRWKHGGA
1543	ITRKNKLWQ
1544	VIRRMRNFF
1545	RRRRLTPSA
1546	KNRRKKYAC
1547	KIRQKCMKF
1548	ACKNKKKDG
1549	CFKRRKYMV
1550	KAKKRANDY
1551	RRKHMRSKS
1552	GSRRRKHTH
1553	KVKMRGFWD
1554	KGRKRHQYM
1555	RYKSCKAKG
1556	RRQRSRYWF
1557	HIRKQKNNN
1558	GSRKRKMCT
1559	RYKCYREYP

SEQ ID NO	581 to 589 Region
1560	CKKFAKKHD
1561	KDKMCKAKG
1562	KRRKTHTKV
1563	SGKKGKSDN
1564	HKRKPYSWM
1565	RHRKKVTHD
1566	IVKSKKSYI
1567	QSKTTKKVC
1568	TKTAKKCKG
1569	RKGKCKFVY
1570	KTKRSWCSG
1571	SSKKPKHCA
1572	RLRRMWYSG
1573	HKRRNNWWP
1574	KCKLQKNNV
1575	KAKSRRYVE
1576	KRKFYKCNM
1577	KKKYCIGHM
1578	KKKANRATY
1579	DFKKCKMWQ
1580	KRKALKVDS
1581	KKQRFRAAY
1582	YHRKGKHRN
1583	HVRSKRHMM
1584	KFGKQKTLC
1585	TKRRYHHHC
1586	KKHRGSFHN
1587	RMKTRKTCS
1588	KMKCSKHKD
1589	GNRRRKYWG
1590	CYRRYKSYC
1591	EWKRYRVQS
1592	LKKTHKKSH
1593	KLKNKHWFC
1594	ICHRRRRCH
1595	PKRKQKWAS
1596	KHKRSYQAH
1597	KLKSNKQCC
1598	KRKKNTFVV
1599	KRRSYKWIN
1600	TARKTKQMI
1601	VARRKRHYT
1602	HKHRYRYLW

SEQ ID NO	581 to 589 Region
1603	STRRMTRGM
1604	MVRRYRSAA
1605	KAKVRQFSK
1606	MCKRVRTPP
1607	HRRKKVTCA
1608	HQKKQKWPH
1609	TRKRYVVYA
1610	KFRKANWPE
1611	KSRQYKRTW
1612	EMKKYKKWP
1613	KLKKKLSEE
1614	TFKKTKFIP
1615	CKKKTLAQV
1616	QKAKYKWCF
1617	GKRRMRSGW
1618	KKHKAGGQL
1619	MAKNKKCGL
1620	FVKSRRFPN
1621	KCRKIAHNC
1622	HRKPRRVHS
1623	TRRRTKISQ
1624	RVRHKRRHW
1625	KVRNWKSMA
1626	FRRTRRYWS
1627	VTKYKKKAF
1628	YKRKQQCAQ
1629	KRKYHKLCN
1630	KKRHRVSHT
1631	LMKAKKKDT
1632	KYKNKKIVG
1633	IVKKHKKAE
1634	DVKFCRYYR
1635	GYPRRGRRT
1636	VKKGPRTEK
1637	TNKSKKCMW
1638	AFKRFRSDC
1639	KAKQKGFMN
1640	AIKAKKVGF
1641	KTKRRMLRQ
1642	KGKKHQFSP
1643	KKKSHKLSM
1644	KSKIQKIHM
1645	MSRKKMWRS

SEQ ID NO	581 to 589 Region
1646	KKYRFNWNH
1647	KKKCQQCCH
1648	KIKAFRWQG
1649	QLKKFKYKA
1650	RTRKANHGT
1651	EARKAKMYA
1652	SVKKWKQRE
1653	AKGKPKVMC
1654	RGRKRWVNH
1655	KSKCFKLQS
1656	KRQSRKCRG
1657	KGRGTKYKY
1658	KIKRMKARC
1659	MVKSKKKNF
1660	AVKYYRRQQ
1661	KHKWKRTSF
1662	KKKSCICVY
1663	KGRKCGPMM
1664	MIRKAKINC
1665	KAKTKQQWS
1666	KKSKCHQRC
1667	TAKRQGLKQ
1668	KYRQKRCVQ
1669	KQKVQCSHK
1670	KWKRHFKGS
1671	HKKYWKNSA
1672	KVRSKQWVW
1673	QKRKYVHKG
1674	RKKFIKMQC
1675	PRRRTRLTH
1676	KIRPKRLEM
1677	KQKVTKIGS
1678	FKRKTAVKP
1679	KVKSGKRAQ
1680	KLRAARYRG
1681	KVKPRGMHR
1682	KVRRHKGVL
1683	KYKAMKTCG
1684	LMKFKKQFC
1685	KKKQKTAHH
1686	KAKSKWHNF
1687	KIKRYGSCD
1688	DAKKWKKCH

SEQ ID NO	581 to 589 Region
1689	KRRRSKYET
1690	RIRFIKYAH
1691	RVKWTRQNQ
1692	MGRKLKSKE
1693	KTRKVHIWT
1694	TKKITKHSS
1695	VGKRSKISW
1696	MPKRKRCAS
1697	NHKSYKRQH
1698	LKNKTKKQA
1699	NYKKFKCFQ
1700	RHRHDRFRH
1701	KLKIVKWAH
1702	SYKVKKSAY
1703	AGKKFKCSI
1704	SARKKGQVI
1705	RRRLQKSNS
1706	MAKTKKYWQ
1707	KRRKYWRFE
1708	LWKYKKKFD
1709	KWKCGKFYS
1710	KKRSVKSKG
1711	IAKKHKSGM
1712	RVNKMKTYP
1713	RRKSTKNHK
1714	LARKCKWVC
1715	SVKKAKWYN
1716	KWRAIKGQS
1717	KKTVKRRTG
1718	KIKMLKGVM
1719	VHKLNKMKW
1720	KGKVYKDKQ
1721	KYKLRKTLF
1722	IVKLKKCIM
1723	RKRASKVCN
1724	KKTRRKKEF
1725	KKRKLDFCS
1726	KAARKKSMC
1727	KARKCTPSH
1728	MNKKTKYHH
1729	RKKSRYCHP
1730	QAKQKKHYH
1731	TVKKHKDSN

SEQ ID NO	581 to 589 Region
1732	NVKSKKKFW
1733	SVKRCKAYT
1734	KHRKSIWVQ
1735	NKRKKSQDV
1736	RRRGWKERC
1737	KRKYRQNGN
1738	KFKTPKGWT
1739	KKKFGGAHW
1740	AVKRRKCPG
1741	KRIRKKISS
1742	IKKSPKKRM
1743	KARNSRYSI
1744	MVKPRRSIA
1745	YTKSKKSAL
1746	HRKRWHAMH
1747	KRKNAGRGV
1748	KAHKRKQAN
1749	KKARSHWRC
1750	KMRPSKFHS
1751	RVRKARSFP
1752	KARKYGRYL
1753	RKKRQACWF
1754	SQKAYRGHS
1755	HIRKARYDH
1756	HAKQKHQKQ
1757	RTKSCKWKH
1758	KSRKQYAQW
1759	KGGKKRCKV
1760	DKPKKKYAA
1761	KLKSCKQCS
1762	HTKAYRRES
1763	KKRLKPTSG
1764	HKKYRKQWA
1765	KTKFRKNCT
1766	TLKCKRKGM
1767	KSRKHANSG
1768	KRKRCMIDH
1769	HKRRITYWM
1770	ISKAKKTNM
1771	KFRNRRCAY
1772	TTKYHKKCW
1773	RTRKWKWWP
1774	KTKQLKCTK

SEQ ID NO	581 to 589 Region
1775	NFRKYKMHN
1776	KRRRSPYMS
1777	NAKWIKKWY
1778	KYRIRRHMC
1779	GSKNKKQMC
1780	MLKKGKHHP
1781	YWKRTRFQF
1782	IMRKFKRES
1783	KRKRVAAKD
1784	KARKQWMHS
1785	RSKIYRTWE
1786	SCKKKRMIF
1787	KTRLKKITR
1788	TARKRKHTT
1789	HFKCQKWRF
1790	KGQRKKSGL
1791	KSKGKQWYT
1792	KRRPIRDCF
1793	TVKKSRLRN
1794	SMRKFKWKE
1795	VGKGKKQMC
1796	QKGLKKHKP
1797	PSRKLKRLC
1798	SVRRNKHVY
1799	FMKRCKMQT
1800	NKKKFHHAQ
1801	TNKKFKSVS
1802	TRRKRPCYP
1803	NRKRQRNWE
1804	RAKTSRTEV
1805	YKPRKRNAT
1806	CKKKLSRHQ
1807	KVRKSRGQS
1808	HQKGKKRGL
1809	SKKPMKKCC
1810	KQKKSHSHG
1811	RIKLQRAMH
1812	KQKKQLDTT
1813	THKCKKTGV
1814	RLKMHRAMC
1815	KHKCSKFYQ
1816	NVRNKRAHP
1817	NKHKPKYHL

SEQ ID NO	581 to 589 Region
1818	SAKLKKRCN
1819	KGKNKIGDN
1820	KLKSKTFAS
1821	QCKRTKHYK
1822	YAKPKKYCL
1823	KRSRMRCFW
1824	QKKQLKAAA
1825	LKLRKKHGQ
1826	KTKKAYVVS
1827	RSMRIRRDY
1828	KKKTNTHLG
1829	KRKYNRSWC
1830	RRRKQDHVC
1831	CVKSKKTGY
1832	SCKSKKSQH
1833	LRKQKKWTG
1834	KRRKCPQYE
1835	KIKNRKSWE
1836	AGRKAKRVW
1837	KRRHGHIHS
1838	KMKNMTMWM
1839	KRRHNKNYD
1840	IRMRKKVGG
1841	VRKHIKRQY
1842	KKKTSWMGM
1843	HKRFYKVMW
1844	HKKRVCRMG
1845	KVCKFKQSA
1846	WFKIKRRRS
1847	KRRNKHPYW
1848	KTKCNRKAT
1849	DCKKKGALS
1850	KGSFKKKMP
1851	KGRYKQRSS
1852	HKQRKQQWV
1853	HKKRENYVF
1854	VKRKPPRGM
1855	KAKLYRQFP
1856	KCRRARSMD
1857	KATKKFAAT
1858	SKCNKKKWF
1859	KSSRKRIYQ
1860	KKRAGGMCH

SEQ ID NO	581 to 589 Region
1861	RRRMRKIAF
1862	KNKKASIIG
1863	RKRMAKQPG
1864	NVRKHKCIH
1865	KWKRTKIVW
1866	VGRFGRVGT
1867	CVKTKKTAP
1868	KKRSFNCIF
1869	MQKKTKGCY
1870	SVKYKKQTN
1871	KKHKHQINC
1872	KCKPVRRAE
1873	IYRRYMRAH
1874	QCRRGRHQQ
1875	HKRKWFDKP
1876	KQRKLGLGE
1877	KNKIYREIQ
1878	KQKQTKFGN
1879	RVKIPIQIR
1880	NKHRYKCKY
1881	RKRYSKLNS
1882	NKHKMRHHN
1883	KRQRKIWRQ
1884	KVRRCKLKY
1885	CSKKSKRQS
1886	HRKTVKWNA
1887	KGKSPKLTG
1888	HIRKHWGSR
1889	KSKSKSVHD
1890	NTRKLKNCW
1891	RNKRRAWNN
1892	FCKSKRINC
1893	KRKGQGRTC
1894	NKCGKKKQP
1895	RCRRQKVPY
1896	EKRKKGIHA
1897	LTRKYKYCT
1898	KTRRPHQTV
1899	QVKHFKWTS
1900	KVKFSKWYK
1901	QKCKVKYAY
1902	VKRLKKAVC
1903	SEKRMKRKG

SEQ ID NO	581 to 589 Region
1904	KCGRKPINK
1905	LQKAKKHWQ
1906	DFKVRKKYP
1907	KVRHWKCSM
1908	KSRKQANAE
1909	KNRLKKRSP
1910	KHRMFQRSW
1911	HMRKAKQFT
1912	RERKLKFQD
1913	KYKSGKHHW
1914	KRRHIRRPG
1915	KWKFKPFSQ
1916	KRKKQQGYH
1917	LKRRSPHQY
1918	IQRKSKCGC
1919	KGKMKRLET
1920	VIKFKKCYS
1921	SVKPRKKAS
1922	KGGKNKVMV
1923	MAKSCKCKQ
1924	KKDKKHLTF
1925	KSKPRGRGT
1926	CSKLMKKKP
1927	KSRKQGISC
1928	KTKEKKLCY
1929	QGKSKKWNF
1930	FKKRMHRKC
1931	KTKKHGNQQ
1932	KKKLYWSQP
1933	TVKKAKRFS
1934	HKHRSIVKC
1935	HNKKMRLSG
1936	CYKSKKLCN
1937	KVKWRVKPE
1938	KARFIRHSA
1939	KKRVGPNVA
1940	KKNRKAKDY
1941	KKKWKEWLH
1942	CHRKVKIVC
1943	KKKFWTIGN
1944	MAKRPRLGT
1945	KLRTMKGLG
1946	QYKAYKKVQ

SEQ ID NO	581 to 589 Region
1947	TFRKCKGYW
1948	NKRKKAFDN
1949	KKKWTQHMS
1950	RQKAIKSFH
1951	KYRGWKSPG
1952	ANKKRRRAY
1953	VVKAKKNIM
1954	KKIKYRKTF
1955	KKKWQGQAP
1956	GAKWYKKGM
1957	RSRPSKQVV
1958	GTRRNRVQQ
1959	IRKKSRSKS
1960	KKKHLHGHS
1961	GLKKHKMAS
1962	SKRRTNRAV
1963	RQKKKMANE
1964	WRKRCKNTS
1965	LGRKQKLWH
1966	AVRYKRRQE
1967	KQRKSVGRQ
1968	KWKKQTCFL
1969	KGKRRWCKC
1970	CVRRTRWRN
1971	KRRKTPLHT
1972	MKKHHRQHW
1973	YTKSSRKGP
1974	KQRFFKTGS
1975	KLKHRGRWH
1976	HVKGHRRLV
1977	LKRKQRCQH
1978	DSKYRRSAR
1979	KQRKATICS
1980	EYKKKHKCG
1981	KIRPKKQVY
1982	CRKVHRNYC
1983	KARMKRQKR
1984	KLKKPRNCY
1985	KRKWWLMHS
1986	KIKMHGWRH
1987	KNKKAKYCS
1988	KIKKKQLDD
1989	KRARQKWQA

SEQ ID NO	581 to 589 Region
1990	RTKNRYWRV
1991	YKPRHLHKE
1992	KRPGKRKRN
1993	KIKLFKQGY
1994	IKKRMNSSL
1995	RRRHYKVNS
1996	KSKMSKHGA
1997	KLKEHKRMF
1998	AKKMLKRRG
1999	QAKIIKKGM
2000	NHRRKKCQF
2001	CRRKSKGQC
2002	KGRGMKWMH
2003	RWRLKKFQG
2004	RTRKWQKIW
2005	WKKRYSLQM
2006	CKKRYSHGQ
2007	DAKSKKRAA
2008	SKKRNQLIQ
2009	SPRPRKQAM
2010	VKKKAGLTQ
2011	HHRKPKYDT
2012	NRKARRCTD
2013	IAKWKKCTM

[0189] In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 1170 – SEQ ID NO: 2013.

[0190] Retinal Pigment Epithelium Tissue-Tropic AAV VP Capsid Polypeptides. Described herein are engineered AAV VP capsid polypeptides comprising a variant 581 to 589 region predicted to confer increased retinal pigment epithelium (RPE) tissue tropism, and predicted to confer increased retina tissue tropism compared to a wild type AAV VP capsid polypeptide (e.g., an AAV5 VP capsid polypeptide), based on a primary screen of a recombinant AAV5 capsid library. In some embodiments, an RPE tissue-tropic engineered AAV VP capsid polypeptide may also have tropism for choroid tissue. **TABLE 5** provides 581 to 589 region sequences predicted to confer RPE tissue tropism or preference.

TABLE 5 – Exemplary 581 to 589 Region Sequences for RPE Targeting

SEQ ID NO	581 to 589 Region
2014	DCTFHDAEI
2015	TDEHVKMGP
2016	GTVWKNWPD
2017	NIEPTANCQ
2018	DEMAHYASS
2019	WINYTVKDR
2020	EFDQCTHGI
2021	QIYVTHQGP
2022	GTVNEYSWN
2023	VRYACLYEN
2024	WFDHNYCFG
2025	EYCPCGEVQ
2026	DRPCAVHEA
2027	VCVNRLECP
2028	TEQKQYESI
2029	TDNCKGECQ
2030	CNTQFMKRE
2031	MMIQNHCLS
2032	AVTAPTFRG
2033	FYTNAGCYC
2034	AQQSWEQIQ
2035	MHMNQCVID
2036	IHTIEQKCS
2037	IKLDVEMAG
2038	AHCTKTMQV
2039	MPQQNVAVP
2040	MQYFWHYAH
2041	AYESKIHTG
2042	MSLWCSEER
2043	LATAHSMRF
2044	VWYFYNEAP
2045	VQMAVLAYW
2046	VVLTQLEDS
2047	NQMFNNEYP
2048	HTYGSLAQY
2049	NTFMECVGG
2050	VKQMGCDIA
2051	HGQCALHTV
2052	MIGTFAYHQ
2053	VNPTKAEYA
2054	LMLGAYKEC
2055	MGEPTCEYR
2056	LTVMWGCCY
2057	PNHCYSTWN

SEQ ID NO	581 to 589 Region
2058	DLHAYICFI
2059	WVTMHNQLC
2060	GMEYYAHNW
2061	PPNVTVDQE
2062	QPDTVWHYA
2063	VSWVERACP
2064	CPPDHCYTA
2065	NTQSQACYI
2066	EYWFTHAEN
2067	PLEVWQTYT
2068	LVTMADHHA
2069	STENHHFEN
2070	DALTDFEGC
2071	EHCDGWRIS
2072	AQQAVEEVQ
2073	MITNLFMAG
2074	NKTDGHYQC
2075	DGLNEEMWK
2076	TQLRDMISS
2077	SEQRTNHYA
2078	HVTDHQGGI
2079	HQCCGLVMQ
2080	AQNGFDKDL
2081	VFQAFMRSM
2082	FSCPKDGYA
2083	NGGMFELTL
2084	QNDTLEHFY
2085	DQLQKDFYF
2086	TSDATCQWI
2087	ATNENIMAW
2088	EPAQKAGIS
2089	QTALRWNWD
2090	ELEPVVCQW
2091	NACTHNTFT
2092	HADANTKTY
2093	PEYSTDHPN
2094	YAVTDQEGH
2095	AIFMHPLTE
2096	AWQGATHEA
2097	QTYFMHTSA
2098	TASHVAEFK
2099	IHPVQFCKC
2100	QHMISHDKA
2101	IYTHCWHEY

SEQ ID NO	581 to 589 Region
2102	IAEPHYTAA
2103	TDMIVKEQC
2104	NNQPPDGAC
2105	QIEPTPEHT
2106	EILVYMYFH
2107	MMCNKIHDE
2108	MVFTRFDHN
2109	LWECATCNP
2110	NVEMGPRAM
2111	CANMEDTDY
2112	PDKACQMID
2113	SHGEKCMSV
2114	EFTLFDSDR
2115	ETLFYNAFA
2116	VTLISHCKC
2117	LNCCYKEMT
2118	TCTSCVHDY
2119	FTCIWFRWA
2120	MHPSTSVTC
2121	QKNHFEMQQ
2122	NDLYKANYN
2123	TVFQMQMCN
2124	PEHCEAWPV
2125	DVEMFFMVG
2126	MLYWCLQNG
2127	YTGWLMSDM
2128	HCVVMQRMY
2129	LHDVAAENR
2130	EEEHCAKLG
2131	HTMYVDTAN
2132	CLDWLHREY
2133	PPCETAHTY
2134	GVHTKMIAW
2135	HDVCMSYKS
2136	NLPQPVLMM
2137	IPGDYVNLS
2138	TSTVFHNWC
2139	DKLDINMTL
2140	CHYQGEHIP
2141	TYEVNCENA
2142	NFDTQPKAI
2143	MCMPADQTL
2144	AKETWDCVG
2145	PGPAHVDHI

SEQ ID NO	581 to 589 Region
2146	ATIVTQHGC
2147	GMYIMKEHQ
2148	PTHATTMVQ
2149	DVYAMVRPC
2150	ESHPLWHDL
2151	QSVMASTAN
2152	NEGVCSYVQ
2153	HIYSCDQSN
2154	STTKHENGH
2155	GQQPYNRME
2156	ITVTKCSDV
2157	VADTCCDMM
2158	DKHLTCQQA
2159	VEAVLFTAI
2160	VEPCRWYTD
2161	CSQSTCKMT
2162	YIAQPVDMA
2163	HICDMPKGR
2164	TIYPRLPLT
2165	QHSNLTRPC
2166	EKACCFTHL
2167	ASEENLMVK
2168	MKYTAWMDG
2169	VQYACLYEN
2170	EATLNDNHC
2171	ACNLVYADS
2172	NALNIHNLT
2173	CWILHMRSA
2174	GLDVWPWET
2175	QTAEVKACN
2176	VHTCMYGMT
2177	WVMAHNLPS
2178	PEAGYQSEC
2179	HAQMMLSGN
2180	IHFACMVMH
2181	AWQMQVNGP
2182	NFQITEAGQ
2183	CEDSFYKFD
2184	IMTSQMYPA
2185	RSELYGMTL
2186	QTLMVLRNM
2187	EHLYGDIVY
2188	MEQQMKMMF

SEQ ID NO	581 to 589 Region
2189	EFELDTKLC
2190	TINVQNFPT
2191	TQVLEEMAW
2192	TSFSASHWG
2193	QTIYRFNAA
2194	VIDPRHDGY
2195	NEWNQCQAH
2196	TTVNNHDGW
2197	CAYQKHGYV
2198	QTHWQYCRV
2199	SQARICSYC
2200	TNNFRMIAS
2201	TRMQADNMH
2202	NLDNKNEGP
2203	RWVGLWCAD
2204	DRQAMVKTD
2205	NAQHRSQAP
2206	EKLMLHQSV
2207	LVICMQSST
2208	TVHHGFADP
2209	KSTCETDIQ
2210	NQCFHCAWN
2211	NMPMTQNGH
2212	LFGMMPQMK
2213	TIHPFSASR
2214	FGMQDHCVC
2215	FGPLLGTIP
2216	AQGRYASQC
2217	VIHQEWPCT
2218	ETPNNEQTH
2219	QRMYLDHCL
2220	SSGCWYQLG
2221	TNEHQMVPW
2222	RSYVQDFEQ
2223	EIHVKFRYD
2224	GIHAMIVSE
2225	QNEICECYL
2226	IGVCWNYAD
2227	DENGYSAPF
2228	PMIMHQLAG
2229	DASMWGFHT
2230	DLSTFNHWY
2231	QVHQLTESV

SEQ ID NO	581 to 589 Region
2232	EIVNWLERE
2233	IFDWANWHY
2234	CEDILTTAA
2235	NSYPPGQGA
2236	TTSPRMMYQ
2237	TFSFVLDQD
2238	PLDRINMPF
2239	TAHSTMWGW
2240	EIGPDQDTC
2241	ELHITCLYS
2242	MNFLFEVSY
2243	MHGNQHAHK
2244	EFMNHSNAA
2245	ETDPTNRID
2246	GQLVECAAS
2247	NQHDFIRHF
2248	WAETGFCME
2249	VTHQIQRGF
2250	YRDPWVQCS
2251	LCNATWADP
2252	HLWPDTCFQ
2253	TVPEEYLRP
2254	GIGCAETAH
2255	SHDICCKFE
2256	SHNTCESIE
2257	ASDPFQMSM
2258	VFYMGHCCY
2259	YQAQCAMSG
2260	FQWCTQLGC
2261	IMTSWTKIC
2262	MQNAIARHA
2263	SVIHFGSYT
2264	GWQDMMQMP
2265	LCHADGRCS
2266	WLMDNTFPW
2267	LMGYCQKNM
2268	HQNWDNGAP
2269	ERFCELHKA
2270	CSLRTCFGG
2271	PTCAHNYRT
2272	LMDHTCKCD
2273	YTSDAAHQV
2274	SIQKEDNQH

SEQ ID NO	581 to 589 Region
2275	YQFPRESVI
2276	MINGPKCYY
2277	IANQKGLTV
2278	SFISWAELC
2279	RSGYQDWMH
2280	VHLPDTRNV
2281	DSGWHHACQ
2282	FVTTITTHY
2283	YGDANWAVM
2284	PVTILADEY
2285	LNYAGYCRP
2286	MNIYHENLS
2287	VTLTCNTNA
2288	FANASGFWR
2289	ITNDHNHLW
2290	DKLHGQREY
2291	SNTLLCKMV
2292	QISNVTANN
2293	GNQWYQCTA
2294	EIWACYTHG
2295	DWLQEHNGN
2296	ETYKSAEWG
2297	GICMPQEHA
2298	IHFFNLDHC
2299	CQELYGIHD
2300	QHQHVFKDS
2301	AHCVDMDTW
2302	NTADKWRLG
2303	YWHEMLSWP
2304	SACPSENRE
2305	PNWQCLEHD
2306	FLHAVWARP
2307	TNHWDHRSG
2308	SHVCRLSAE
2309	LVCVASSAC
2310	YVGMIPVHP
2311	PQSSHIGDT
2312	GSTIQNRHA
2313	DHLCFPINE
2314	TTLALGDYG
2315	PVHEWKSHQ
2316	KCASYTEPP
2317	EWELCNTTT

SEQ ID NO	581 to 589 Region
2318	EVACNKMMQ
2319	HTMSTTLVY
2320	STEACNYGS
2321	SLMCMEHTY
2322	TTGIYMCDQ
2323	FAMVMHDQP
2324	SRHCCLEFS
2325	TWNIACGRH
2326	EVHFSRITC
2327	FHTNYFWEG
2328	MTEYKVGFY
2329	DICDFCRQF
2330	VTMTVFHPF
2331	HTELDGCYV
2332	AWGMACTTW
2333	WISMTVGAP
2334	FANYCVAMP
2335	NILALCEGT
2336	DRLTHCCEP
2337	HCDYHVCKG
2338	HSVIKESCE
2339	MSMQKMLDN
2340	VLHQCAIEV
2341	ANVTMQHQY
2342	GPVDKAGAN
2343	KEDSKASNP
2344	DTPSYKCNW
2345	LHHFHMKHA
2346	ATNQVIRHM
2347	WSASDPYSM
2348	KEEFVHQQW
2349	CYQDIQHMV
2350	DHMEMCSSA
2351	YPVWVKVQN
2352	LPQQKNEWY
2353	TNAEFYMMR
2354	FWQLIDSAL
2355	YPVGLYQGI
2356	CTFPMHGVG
2357	GDNVCCYPQ
2358	TVGTMINAY
2359	DGSERQNAY
2360	ENFCIYKDS

SEQ ID NO	581 to 589 Region
2361	EHGMKYQHP
2362	GATPFEKMN
2363	HNIWLETGW
2364	TSHQKFMGS
2365	LTGSDGQSS
2366	CEVQCPFDC
2367	QVWACYLPS
2368	WFTFFMAGA
2369	TPKMEICQA
2370	DNNWMYQAD
2371	THALSMKGT
2372	IACLEQATF
2373	GVNWYINSF
2374	TIVDWVHMG
2375	TRLDMAMDA
2376	PEHPVGYTT
2377	TEGLFEWGW
2378	NNPTKTCTT
2379	CLIQQDVVC
2380	LWECYYCNS
2381	PVGIWPSIE
2382	LREFLTVQT
2383	LADGQFMGN
2384	AYQLKVFFN
2385	WVDNLMRHS
2386	NAEFEGCVT
2387	SVTVFWHPG
2388	MHAPANTQD
2389	ASYCIHRSY
2390	TKSEPCLDC
2391	GEVRMSANY
2392	EVYSHDSQY
2393	EQMSNDASY
2394	YPHAYMVTG
2395	SAIPFIRHG
2396	HGGPQVMRS
2397	NVRECHALV
2398	TAGMMQYCD
2399	CEHEMSSYY
2400	HDNGTNKKM
2401	MIPAWNVTQ
2402	AYVSAPRID
2403	IANQNESSW

SEQ ID NO	581 to 589 Region
2404	NTFMLELDS
2405	MITQWMHHR
2406	ADNVQWSEC
2407	SITCPSQTC
2408	FVDPWEWTR
2409	PCLQIGMQQ
2410	APCNKTHSW
2411	DGPSDFKTC
2412	VNAPPSHVE
2413	CPNEMVHYK
2414	VSNEWEASD
2415	TWNPRCWQP
2416	FCEQFGSLC
2417	LQCFLANRE
2418	RMDMHNNST
2419	YCNFIVNAM
2420	PTHTKGNEN
2421	NNFEQRVGH
2422	IMGYLWTQN
2423	YSAWMREFN
2424	DLFNIIQMD
2425	FVSNQTKWE
2426	QCLPLHNHC
2427	GVGFIPTPY
2428	DFVSNWDKF
2429	PQIICMMTV
2430	RPDHEQEST
2431	THLFHKEHA
2432	TGNMAYNCG
2433	MHDQRMYTW
2434	VVGWLTHQA
2435	MILQKNMER
2436	QVEQCLKED
2437	LKISPVNER
2438	AYEFCKNED
2439	IFEHHNRYP
2440	DAYTFINGC
2441	EACLHGFSE
2442	VMGQMAYQY
2443	LNSLVVQGK
2444	HLDPCGWAG
2445	TYSDKIVNT
2446	SFGACYQFA

SEQ ID NO	581 to 589 Region
2447	TQQAFFCVR
2448	EQMWNHHET
2449	VKPADANAG
2450	AIPTFHRAG
2451	NWIVSAKQQ
2452	GMYACQMEW
2453	CGHMSHRSQ
2454	GVCCNHNQI
2455	SLGPVNMTS
2456	TVAGEQMEP
2457	SLLWAVWLD
2458	CAVIGVENP
2459	GVQLIWAGL
2460	HNYASGWVT
2461	DHIWRHEAG
2462	PKLQDVERC
2463	GWPNQSYIC
2464	ENENTWHSG
2465	DKQHTVSAM
2466	PTGFWPYVH
2467	GCTMCYMYC
2468	FTIPQVRYS
2469	AEEIVYESW
2470	TTNAPCEIN
2471	ISDQFGSWI
2472	IVHGTATAE
2473	TATIVKQHW
2474	MICQNMSHT
2475	LIKPANGEC
2476	KDFNSELTN
2477	TPEEPVRGG
2478	NQMFDQNEY
2479	YLQVSMQGY
2480	NHVRNVEQC
2481	TIMHTQRGA
2482	FVSQPGYAV
2483	SMYVMPFWL
2484	VMILSNHGC
2485	VWGPFHLTR
2486	YGYHEDMMC
2487	TSTAESARD
2488	NTAHLYGFD
2489	PFSPKAQVA

SEQ ID NO	581 to 589 Region
2490	INCYSYNEF
2491	MKHMPMTDN
2492	HTHCVLAEH
2493	MVTTLAGND
2494	IYVQKHSDW
2495	PAFLDGVEG
2496	MTPGRHVLS
2497	CDQWLQCYQ
2498	AADSRGVPN
2499	AWCSFQHIK
2500	MQMAYYQSH
2501	QKVCHMTAI
2502	TNWRTDVNG
2503	EINEWTIAN
2504	FTEFYQAHD
2505	SEKCWPDYQ
2506	GYTGNDESS
2507	WFSQNGWAH
2508	QCALETPIP
2509	DEILRYSFQ
2510	KAVITESAC
2511	ALSAWGMPS
2512	VIWSVEHAE
2513	NAHLKMTAS

[0191] In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513.

Ocular Tissue-Tropic Sequences Generated by Machine Learning

[0192] Additional 581 to 589 regions that confer ocular tissue tropism may be generated using machine learning algorithms trained with sequences identified in ocular tissue in *in vivo* screens. The machine learning algorithms may be employed to identify patterns in amino acid sequences that favor accumulation in ocular tissue (e.g., retina, RPE, or both) as compared to other tissues (e.g., non-ocular tissues). Alternatively or in addition, the machine learning algorithms may be employed to identify patterns in amino acid sequences that favor accumulation in ocular tissue as compared to a wild type AAV capsid (e.g., comprising a VP capsid polypeptide of SEQ ID NO: 1). These patterns may be used to generate new sequences of 581 to 589 regions that confer ocular tissue tropism to VP capsid polypeptides and rAAVs assembled from the VP capsid polypeptides. In some embodiments, new sequences of 581 to 589 regions may be generated by randomly sampling amino acid residues at each position of 581 to 589 regions that favored ocular tissue tropism in an *in vivo* screen. The generated sequences may be tested using classifiers (e.g., gradient boosting classifiers or random forests classifiers) to predict ocular tissue-specificity for each 581 to 589 region. The 581 to 589 regions with the highest predicted ocular tissue-specificity may be identified as ocular tissue-tropic sequences.

[0193] Disclosed herein are engineered AAV5 VP capsid polypeptides capable of forming an assembled virion that exhibits increased ocular tissue tropism as compared to a wild type AAV

VP capsid polypeptide (e.g., a VP1 of SEQ ID NO: 1, a VP2 of SEQ ID NO: 10, or aVP3 of SEQ ID NO: 11), wherein the engineered variant AAV5 VP capsid polypeptide sequence has one or more amino acid substitutions in a 581 to 589 region of the VP capsid polypeptide, corresponding to positions 581 to 589 in SEQ ID NO: 2 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$). In some embodiments, X^1 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^2 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^3 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^4 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^5 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^6 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^7 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^8 is selected A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V. In some embodiments, X^9 is selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, or V.

[0194] In some embodiments, provided herein are AAV5 VP capsid polypeptide having at least one mutation in a 581 to 589 region, wherein said at least one mutation drives increased ocular tissue tropism.

[0195] Retina Tissue-Tropic AAV VP Capsid Polypeptides. Described herein are engineered AAV VP capsid polypeptides comprising a variant 581 to 589 region predicted to confer increased retina tissue tropism compared to a wild type AAV VP capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1), generated and selected using machine learning. **TABLE 6** provides 581 to 589 region sequences predicted to confer retina tissue tropism or preference.

TABLE 6 – Additional Exemplary 581 to 589 Region Sequences for Retinal Targeting

SEQ ID NO	581 to 589 Region
2514	HKKRARQRP
2515	HKKKKKQEP
2516	HKKKARTRP
2517	HKKRKRVRP
2518	HKRRARVQP
2519	AKRRKKRRN
2520	HKRKKKRRT
2521	HKRRARYRP
2522	HKKKGRMRP
2523	HKRKKKRRP
2524	HKKRKKQRV
2525	TKKRKRICP
2526	HRKRGRVKP
2527	HKKKARQKT
2528	HKKRKRLRS
2529	AKKKKRMRP
2530	HKKRYKQRP
2531	HKKRGREQP
2532	HRRRKKQRP
2533	HKKKKKQKP
2534	HDRKKKFRP
2535	HKKRKRKRP
2536	HKRKKKLET
2537	HKKRGRTRW
2538	HCRRARSYP
2539	HKKKAKQRP
2540	HKKRARHKD
2541	HCKRKKVRS
2542	HSRRARVQP
2543	TKKRKRTQW
2544	HKKRKRMKS
2545	HKKRKRQKW
2546	HDKKARSKP
2547	HKKRKRQRP
2548	HCRRARMRC
2549	HKKKKRVAS
2550	HKRKKRQAY
2551	APKRKKFRP
2552	HLRKAKTAP
2553	AKKKKKFRP
2554	HKKKGRMKP
2555	HDRRGKQRP
2556	HLPRQRVKP
2557	TDKKKKQCW

SEQ ID NO	581 to 589 Region
2558	TKKKKKHCP
2559	SKKKGRERP
2560	HDKRGKMKP
2561	KLKRARTQP
2562	MKKRKRQAW
2563	HLKRAKFRT
2564	HKKRKREKP
2565	MKKRKKQRN
2566	HDKKKRQRE
2567	HRRRKKQKC
2568	HRRRKRLQP
2569	HGRRAKVRP
2570	HKKKKRANP
2571	HKRKKKTRP
2572	AKRRARTKP
2573	HKKRLRMRP
2574	AKKRKRSRP
2575	HPKRAKAKP
2576	HKKRKRHKP
2577	HRRRKKLKN
2578	HDKKKRVKP
2579	HQKKKRLQP
2580	HKKRARFQS
2581	HKRKKKIKP
2582	HKKRKRQEP
2583	HKKRARHRP
2584	HKKRLKHIW
2585	HKKKKRMRP
2586	HCKKKRVRY
2587	HKKRKRSGN
2588	HKKKKKARP
2589	ARKRKKLKP
2590	SKKKGRQKP
2591	HKKRDKQRP
2592	HKKRKRMRY
2593	HKKRKRHRT
2594	HPKRKKLAP
2595	HKRRARQRP
2596	HKRKKRTRC
2597	HDKRKRHRW
2598	QPKRKRVAP
2599	CDKKKKTRP
2600	HKRRKKLRP
2601	HKRKARTRP

SEQ ID NO	581 to 589 Region
2602	HRKKLKSKP
2603	HKKKLRVRP
2604	MDKKGKTCW
2605	HKKRARVEP
2606	MKKRGRTPP
2607	HKRRKRTRN
2608	AKKKKREKL
2609	HCRRAKQRE
2610	HKKKLRMRW
2611	HPKRKRTRD
2612	HKKKSKQKP
2613	HQRRKKKKP
2614	TKKRKRVKA
2615	HKKRLRVKP
2616	HKKKKKVRP
2617	TKKRKRVRS
2618	HCRRGKVRC
2619	HKRRKRMRP
2620	HKKKKRQAW
2621	HKKKKRLRP
2622	HKKKKKRCS
2623	HDRKKKTKP
2624	HKKRKRHGP
2625	HKRRARKRP
2626	HKKKKKVRC
2627	HKRKKRQRP
2628	HKKRKRDRP
2629	HKKKAKFQP
2630	HDKRKRTRN
2631	HKKKKRFNP
2632	TKKKKRQKW
2633	ALKKKRQKP
2634	HKKRLRFKP
2635	AKKKKRQRP
2636	HRKRAKVAP
2637	HCKKKKQIP
2638	AKKRKRQKW
2639	HKKKGKHRV
2640	HKKRDRMCS
2641	HKKRARLKP
2642	AKRRKKAKP
2643	TLKRKRTKP
2644	HKKRARLAY
2645	HKKRKRRRW

SEQ ID NO	581 to 589 Region
2646	HLKKKRKQN
2647	HKKRKKLRP
2648	HKRKKKFGP
2649	EKKKSKMQP
2650	HCKRAKTRP
2651	TKKKKRHKN
2652	HKRRKKERW
2653	HKRRGKQRP
2654	HKKRKRTKP
2655	AKKRAKQRP
2656	HKKKGRTRP
2657	HCRRKKVRW
2658	HKKRKRFKP
2659	HKKKKRHKP
2660	HEKRKRFKP
2661	HKKKKRTRV
2662	HPRKAKCRD
2663	HKKRAKQRT
2664	HKKRARHQT
2665	HKKRKRHRL
2666	HRRKAKTRT
2667	HKKKKRTYW
2668	HKKRKRLRC
2669	HKKRKKQRP
2670	TKKRKRLRP
2671	HDKRKRVKP
2672	HDRRKKTAP
2673	HKRKKKVRP
2674	AKKKKRQKP
2675	HLRKKRLRP
2676	HKKRKRQKP
2677	HKRKKRQRW
2678	KDKKKRVRP
2679	HDRRKKFKH
2680	TKKKKRMRP
2681	HKRRKRRGW
2682	HKRKSRTRP
2683	HRKRKRVCP
2684	MKKRKRQRP
2685	HKKKKKQRP
2686	HRKKKRVKS
2687	TKKRARQRA
2688	MKKKGRVRP

SEQ ID NO	581 to 589 Region
2689	HRKRGRMRA
2690	MKKRKRVVP
2691	HKKRKRLRY
2692	HCKKKRQRP
2693	HDRKKKVQP
2694	HCKRAKTGP
2695	TPKRKRLRS
2696	HKKRGRVRP
2697	TKKRKRQRY
2698	MRRRGRSRP
2699	HKKKKKQCP
2700	HKRKKKDQT
2701	HCKKARFRP
2702	HDKRLKQRW
2703	HLKRKRTRE
2704	HKKRKRTRW
2705	HKRKKRFNV
2706	CDKKLRFFP
2707	KKRRARQGP
2708	TKKRSKVRS
2709	HDKRLRHKE
2710	AKKKKKVWW
2711	HKKKKRLRW
2712	HKKRLKQKN
2713	HKKRKRLRV
2714	HKKKKKERP
2715	HKKRKRSQP
2716	HKKRARVRP
2717	HKKKKKFRT
2718	AKKKGKLRQ
2719	QKKKGRDRS
2720	HERKKKLRP
2721	HKRKKKTKE
2722	HKKRKKVKP
2723	HKKRARLRW
2724	MKKKKRVRP
2725	HKKRARLRS
2726	HQRRAKTRP
2727	HRKKLRQKP
2728	HDKKKKMMP
2729	HKRRKRICP
2730	HRRKKKQKM
2731	TRKRSRVIN

SEQ ID NO	581 to 589 Region
2732	HKKRKKRRW
2733	HKKRKRRVP
2734	HKKRKRMRP
2735	TKRRARVRT
2736	HKKRKRVAP
2737	HPKRKRHRP
2738	SKKKKRFAP
2739	TLRKKRQRP
2740	KKRKKRKGN
2741	HKKRKRTRP
2742	HKKRKRHNP
2743	HKKKGRHQC
2744	HKKKKRSRP
2745	HDKRKKQKP
2746	HKKRKKQRE
2747	HKKKGKVKP
2748	HLKKKKKQP
2749	HPKKKKLRP
2750	HRKRAKVRC
2751	HDKKKRLRP
2752	TKKRKKDKE
2753	HKKRARQRY
2754	MKKRARLRC
2755	HKKRARFRL
2756	HKKRGRIRP
2757	HQKKCKTCP
2758	HPKRARTRP
2759	MKKKKRQCN
2760	HLKKKRWRW
2761	HKKKKRLKN
2762	HKKRKRART
2763	HKKRKKMRP
2764	HKRRKRRRS
2765	HQRRKKLRN
2766	HKRKKRLRN
2767	HKKRKRMKP
2768	HKKKKRVPY
2769	KDKKKKLKP
2770	AKKKARMKW
2771	TCKKAKMCP
2772	HKKKLKMWP
2773	HDRKKKQIW
2774	HKKKKRMCP

SEQ ID NO	581 to 589 Region
2775	HKKKLRQRP
2776	TKKRKRQRP
2777	AKKRKRQAP
2778	KQKKKREWP
2779	AKKRARQKP
2780	HCRKKKTRY
2781	AKKRLKVQP
2782	HCKKKKQRP
2783	KKKRKKRRP
2784	ADRRAKVRP
2785	HGKKGRVRP
2786	HKRKAKVRN
2787	HLKKKRRKT
2788	HEKRKRERP
2789	HCRRKKERP
2790	TKKRKRTAP
2791	HLRRARLKN
2792	HKRRKRHRW
2793	HKRKKRQQQ
2794	HDRRGKTQP
2795	TDKRGKQKP
2796	AKKKKRHKM
2797	HKRKKKMRP
2798	HKKRKRLRH
2799	HCKKARRKP
2800	HRKRLRQRP
2801	HKKRGRVKP
2802	HKKRKKDKS
2803	MKKRKRHQH
2804	HKKRKKVKD
2805	HDKRARQRP
2806	HDKRKRVWP
2807	AKKRKKHRP
2808	TRKKKRVKP
2809	HKRRKRHRP
2810	HKKRLRLRP
2811	HKKKKKLRI
2812	HRKRLRSRP
2813	HKRRKKERP
2814	HKRRKRLRT
2815	HKKRKRHRN
2816	HKRRKKLRW
2817	HKKRSKQRP

SEQ ID NO	581 to 589 Region
2818	HDKRKRVRP
2819	HKKKKRVKP
2820	IKRKKRHYP
2821	HRKRAKQQP
2822	HDKRKKMRD
2823	HDKKLRFRW
2824	AKKRSRWRC
2825	HKRRKRQKP
2826	HERKKRVRP
2827	HKKRKRTRV
2828	HKKRLRVRP
2829	HKRKKKHRP
2830	HKKRARHRS
2831	HRKRKRLRP
2832	HKKRKRTYY
2833	YKKKKKVCS
2834	KKKRKRQRW
2835	HKKRKRVKP
2836	HKKRKKVRS
2837	HDKRKKMQP
2838	TKKKAKQKP
2839	HKRKKRWRW
2840	HKKRKRFRP
2841	QQRKARHRP
2842	HCRKDKQQP
2843	HKRKLKWKP
2844	HKKKKRQKP
2845	HKKRKRTCP
2846	TKKKSKTRP
2847	HKKRGRMRP
2848	HKRKKKLKC
2849	HKKKKRFKP
2850	HRKRARLKP
2851	HRKKGKQRP
2852	TRKRKRMRD
2853	HQKKKRQLP
2854	CKRKKRFCP
2855	HPKRKRQYP
2856	HEKRAKHCP
2857	HKRRKRQQP
2858	HKKRKRLND
2859	HKKRGRQQH
2860	HKKKSRHRP

SEQ ID NO	581 to 589 Region
2861	HKKRKRMYP
2862	HKKRARSRW
2863	HDKKAKFRP
2864	HKRRAKQRP
2865	HKRLLKDRP
2866	HKKRARQRL
2867	HKKKKRMKP
2868	HKRKKRVRW
2869	HKKKLRMRP
2870	IKKRARMRP
2871	HKKRKKLCP
2872	HKKRKRFCP
2873	HKKRKKTLA
2874	TKKRKRVCP
2875	HPRKKKLRP
2876	HKKRAKFQP
2877	ACRKGKQAW
2878	HPRRKRTKP
2879	HQRRARLRP
2880	IKKRKRTRP
2881	HRKKKKDKS
2882	HKKRKRQRW
2883	HKKRKRRRM
2884	HPKRKKQRP
2885	HQKRGRCRP
2886	HPKRARFRP
2887	HKKKKRQRY
2888	AKRRAKARP
2889	HKRKKRQKN
2890	HKKRAKSQT
2891	SDKRKRMKT
2892	HKRKKRKRP
2893	HKKRKRMRW
2894	HDKRARTRP
2895	MDKKKRQKP
2896	HKKKKRTAD
2897	HKRKKRLKP
2898	HKKRKRLKP
2899	HKKRARTRP
2900	TKKRARVKP
2901	HDKRKKLNT
2902	HKKKGRHRP
2903	TKKRARFRP

SEQ ID NO	581 to 589 Region
2904	HKKRKRFNP
2905	HDKRKRTRP
2906	TDKRKRFRP
2907	HKKRKKFQP
2908	HKKRKRVQC
2909	HKKKKRQRP
2910	TRKKKKMKN
2911	TKKRKRMRS
2912	HKRRKRTKP
2913	TRKRARVKP
2914	TKKKKRMGY
2915	HKKRGKVRP
2916	KKKRKRQCV
2917	HRKRKRTRP
2918	HDRRAKRAY
2919	HKKKKRERY
2920	HKKKKRHRW
2921	HKRKKKVRY
2922	HKKKLKTQS
2923	HPKRKRMCP
2924	HRKRKRMRP
2925	HRKRARVKP
2926	HDKRKRMRP
2927	HRKKKKVRP
2928	HCRRAKFLP
2929	HDRRKRLRP
2930	HKKRKRFKS
2931	HCRKKRFRP
2932	HKKRARQRS
2933	HKRKKRQKP
2934	HRRRKRFHW
2935	HKKKKRVRP
2936	HKRRKKTRT
2937	HPKRKRTRP
2938	HKKKARSRP
2939	HKKKKKTNN
2940	HKRRARARP
2941	HCRKAKQQP
2942	HPKRAKQIP
2943	HKKRKRLQP
2944	HKKKKKGKP
2945	HKKRKKMCP
2946	HDKKGRVKP

SEQ ID NO	581 to 589 Region
2947	HKKRKRVRC
2948	HKKRKRMDS
2949	HKRKKRFRS
2950	HRKKKRHKW
2951	HQKKKRFRP
2952	HKRRDRTKP
2953	HDKKKRMNP
2954	HKKRSRDRE
2955	HDKKKKQRC
2956	TKKKKRFCS
2957	HEKRGKHRP
2958	HKKRKRFRW
2959	PKKRKRMRW
2960	AKKRSKQQY
2961	AKKKKRMKW
2962	AKKKARVIP
2963	HKKKARQRP
2964	HKKRKKVNP
2965	TPKKKRLQN
2966	HKKRKRLAN
2967	YKKRKRQRL
2968	HRRKTRMRS
2969	HKKRKRQAW
2970	KKKKKRHRP
2971	HKKRGKEKP
2972	AKKRKRQRP
2973	HKKSAKDRP
2974	HKKRQRQAP
2975	HDKKKKFQW
2976	HKKKKKQRW
2977	AKKRKRQKP
2978	HKRRARVKP
2979	HSRRARMRT
2980	HKTRARFKP
2981	AKKRKRLCQ
2982	ACKRKRMKP
2983	HCKRARVKP
2984	HRRRKRGRS
2985	HKKRARVQP
2986	HSKRARQGW
2987	HKKRAKHRC
2988	HDKKKRHKP
2989	HKKRARVKD

SEQ ID NO	581 to 589 Region
2990	HKKRKKVRP
2991	AKRKKRVKP
2992	HKRRKKTAY
2993	HKKKARHRP
2994	ARKRARQQP
2995	IKKRGRVRY
2996	HEKKARVKP
2997	HKRRKKRRT
2998	HKRRKRQRP
2999	TKKRDRHYP
3000	HDKRAKQRP
3001	HKKRKRLRW
3002	HSKKKKFCP
3003	HKKRKKQRW
3004	HCKRAKARC
3005	HKKKKKQQP
3006	AKRKKKQRP
3007	HQKRKKDQP
3008	HKKRKRSKY
3009	HKRRKKTQP
3010	HKRRKRTKW
3011	HDKRARERP
3012	HKKKKKHKT
3013	AKKRKRFRP
3014	KKKRARMRP
3015	HKKRARHEP
3016	HKKRAKERP
3017	HKKRCKSNP
3018	HKKRARFMP
3019	HKRSKRQRW
3020	HLKKKKAKP
3021	HKKRKKHRP
3022	HRKRKKQRP
3023	HKKKKKQKN
3024	HKRRDRKQP
3025	HCKKKKQKW
3026	HKKRKRVRS
3027	HDKKKKTGN
3028	EKKRKRHRT
3029	TKKKKKVRP
3030	HKRKKKVKP
3031	HKKRKREQP
3032	HKKRKKLKW

SEQ ID NO	581 to 589 Region
3033	HKKRDRTKP
3034	HKKRKKQNY
3035	HKRRKRRRH
3036	ADKKAKVAP
3037	HCRKKKQRP
3038	HKKKAKLQP
3039	HKKKGRFRY
3040	HDKRKRFKP
3041	HKRRLRQRP
3042	HPKRKRERP
3043	HKKKLKTCP
3044	HKKKGKQAP
3045	HKKRKKMRN
3046	HKKRKKSRN
3047	TKKRKKVRP
3048	HDKKARTKP
3049	HCKRAKQRP
3050	HRKRARTRP
3051	ACKRGRLRP
3052	HKKRKRHRP
3053	AKKKKRVRP
3054	TKKRKRVRP
3055	HKRKARHKN
3056	HKKKGRLRP
3057	HQKKGKVKP
3058	HKKKKKQRT
3059	AKKRKRRRY
3060	HKKRGRHKY
3061	HKKRKKVCP
3062	HRKKKRQRP
3063	HDKKSKQRP
3064	HKRRKRQWP
3065	AKKRKRLRP
3066	HKRRKRQPP
3067	HDKKKKMKV
3068	HCRRAKTRW
3069	HCKKKKMRP
3070	TCRKGKQRP
3071	HKKRARFKS
3072	SPKRKRFRS
3073	ADKKKRHKP
3074	HDKRARSRP
3075	HKKKKKQQM

SEQ ID NO	581 to 589 Region
3076	HKKRGRVQP
3077	HKRKKKDCQ
3078	HKKKKKFKP
3079	HKKKARLQP
3080	ARKRARVRP
3081	HQKRGRVYP
3082	HKKRKRVRY
3083	HKKKKKLRP
3084	TKKKKRVRP
3085	HLKRARQRP
3086	TKKKKKQRP
3087	QKKRKKQEW
3088	HKKRKRRRH
3089	HKRKKRVRP
3090	HCKRKRMQS
3091	HKKRKRTRY
3092	HKKRKHQKP
3093	HEKKAKTQT
3094	HDKKKKTRP
3095	TKRKGRDKS
3096	HKKRARVKP
3097	HCKRKRVRE
3098	HKKRKRFVL
3099	TRKRAKVQP
3100	TKKKKRRIP
3101	HRKRKRRRP
3102	HEKKKRQKP
3103	HKKKGRMRY
3104	HCRKGRQKY
3105	HDKRKRTKE
3106	HQRSAKQCC
3107	HRKRKRFRP
3108	HKKKLRVQW
3109	HKRRARFRP
3110	HDRRKKQRP
3111	HKRRKRVAP
3112	KKKRKRQKP
3113	HKKKARVKP
3114	HKRRARMRT
3115	HKKKAKVKP
3116	MQKKKRHRP
3117	HKKKKKVKT
3118	TDRRLKTIP

SEQ ID NO	581 to 589 Region
3119	HKRKKRTKW
3120	HKRKLKQRP
3121	TKKKKRQRP
3122	APKRGRFIP
3123	HRKKLRFKP
3124	HKKRARVKT
3125	KKRKKRQRP
3126	HKKKKRQQP
3127	HKRRKRSYS
3128	HCRRAKVKC
3129	QKKRGRRKW
3130	HRRKGRQRT
3131	HKRRKRFRN
3132	HQRRAKLQY
3133	HLKRARVRP
3134	HKKKKRLKP
3135	HKKKKRTCP
3136	HDRKKKTRP
3137	HKKKKKFRA
3138	HDKRARFQP
3139	HRKRGRTKS
3140	HRKRKRHRP
3141	HEKKGREAP
3142	HKRKGRVCP
3143	HKKKGKKRP
3144	HKKRKKCRN
3145	HKKRARVRT
3146	KQKRKRFRS
3147	HKRKKKDRP
3148	HRKRSRVRP
3149	HDKRARVRP
3150	HKKRLRFRN
3151	HKKRKRRNW
3152	HQKRKRTRP
3153	HKKRGKMKW
3154	HKKKGKYRN
3155	HKKKKRMRS
3156	HKKKKRQCE
3157	HKKKKRFEP
3158	HLKRKKSKP
3159	HCKKCRHRP
3160	HKKKKRQRE
3161	HDKRKRLRP

SEQ ID NO	581 to 589 Region
3162	HPKSARQRP
3163	HCKRKKLRP
3164	HDRKKRQRP
3165	HKRRKREKP
3166	HKKRKKRSW
3167	AKKRKRVQT
3168	HKRRAKQGW
3169	ADKRKKMRP
3170	HLKRKRFRP
3171	TKKRGRTNP
3172	HKRKKRTRP
3173	HKKRKRALP
3174	HKRKKRMRN
3175	KKKKKKQRW
3176	HKKRKRVQP
3177	HKKRKRVCP
3178	AKRKKKDIP
3179	HKRKGKMRP
3180	HKRRKKDQW
3181	HDKRAKTKP
3182	HKKKKRVRW
3183	HKKRKRTKA
3184	HDRRKRQRW
3185	HKRKAKERP
3186	HKKKKRHRP
3187	HKKKSRVRP
3188	HKRRKKQKP
3189	HCRRKRLRP
3190	HQRRGRLRT
3191	HKKRKRVRN
3192	AEKKARTQW
3193	TKKRKRAKE
3194	AKKRARQRP
3195	HRKKKRTAP
3196	HKKRKRLRP
3197	PKRKKRQRN
3198	HKRKKKTRW
3199	HRKRKRQRW
3200	TKKRKRRGT
3201	HKRRKKQGP
3202	HKKKKKHRW
3203	HDKKKRERP
3204	HEKRLKFKW

SEQ ID NO	581 to 589 Region
3205	IKKRKRMCY
3206	HKKKKHQRP
3207	HKKRKRHKC
3208	HRKKKRQKP
3209	HDKRKRSRP
3210	HKKKGRQIP
3211	HKRRKRTRP
3212	HRKKKRARP
3213	HKKRLKRRW
3214	HCKRKKLAP
3215	HKKRKKTRW
3216	HKKRGHQRP
3217	HKKRKRFQS
3218	HKKKKRSKP
3219	HKRKKKVKA
3220	HKKKKKHRP
3221	TLKRARVKP
3222	HKKKKKFQP
3223	HPRRKRKRP
3224	AKKRARVRP
3225	HKKKKRQRT
3226	HKRKKRTRM
3227	HRKRSRKRT
3228	HCRRKKQKP
3229	HKKRKRQGP
3230	HKKKLKQRN
3231	MKKKKRLKW
3232	HRKKKKQKW
3233	HKKRKRTKY
3234	MKKRKKHRC
3235	TKKRAKMRP
3236	HRRKKKLRW
3237	TKKRARSNP
3238	HKKKTRHRP
3239	HKRKKRFPP
3240	HKKKKRAKW
3241	HKRKKKARP
3242	HKKRKRHVW
3243	HDRKKKTRE
3244	HKKRKRFPP
3245	HLRKARIEP
3246	HRRKARQRN
3247	HCKKKKQRS

SEQ ID NO	581 to 589 Region
3248	HKKRSRCKP
3249	HGKKKKQQW
3250	AKKKLRQRP
3251	HKKRGRQRP
3252	AKRKKRKRE
3253	HKKRKKTRP
3254	QKRRKRVRP
3255	HKKRKRQRH
3256	HKKRGKFCP
3257	HKKRKRQRS
3258	HKKKKRIRP
3259	HKKRAKQRP
3260	SKKRKRHRP
3261	IKKRKRVEP
3262	TKKRKKMRN
3263	AKKKKKFGS
3264	TQKKGRVKP
3265	HDKRGRQRC
3266	HKRRKRMRW
3267	HKKRKRTQP
3268	HKKKKKVKP
3269	HKKKKKMCW
3270	HKRRKKQND
3271	HKKRKRVGP
3272	YKKRGRMRP
3273	KPKKKRFRG
3274	AKKRKKQKS
3275	HKRRKKWRP
3276	HRKRKRLGY
3277	HKRKDKVRT
3278	HKRKKKHRW
3279	HKRRKRRRP
3280	HKKKGRART
3281	AKKRARWIP
3282	MKRRKKLRP
3283	HKRKKKFKW
3284	TRKRKRVCP
3285	HQKKAKTEP
3286	HKRKLKVRP
3287	IKRRKRMHW
3288	HKKKKKQKV
3289	QCKRGRMRP
3290	HQRKKKHKC

SEQ ID NO	581 to 589 Region
3291	HKKKAKTRT
3292	HKKRKRVRE
3293	TPKRLRMAP
3294	HCKKARVKP
3295	TKRRKRFRP
3296	KDRKKKQRT
3297	HKRKKRMRP
3298	HKKKLRQKA
3299	TDPRGRQKP
3300	HDKKARQRP
3301	HKRKKRAWW
3302	HKKRKRMRC
3303	HKKRLRLRT
3304	TKKKNKMGP
3305	HKRRKRFRY
3306	HKKRKKTKW
3307	HDKKARLVP
3308	HKRRAKTAP
3309	HQRRKKFNN
3310	HKKKKRLCW
3311	HKKRKRFRC
3312	EKKKKRVKP
3313	HKKRKKQKP
3314	TKKKKKQKP
3315	HKKRKKQQN
3316	HKKRGKAKW
3317	AKKKGRHRP
3318	HKKRKRRRP
3319	AKKRARTRW
3320	AKKKKRQCN
3321	HRKRKRTAY
3322	HKRKKRFIP
3323	TKKRKRTKP
3324	KDKKAKTQP
3325	HKKKKRHRC
3326	HRKKKKTWT
3327	AKRKGRLFP
3328	HKKKKHTNP
3329	HKKRLRVRW
3330	HKKRKRQRL
3331	HKRRARQRY
3332	HCKKARSKP
3333	HKKKKKRNH

SEQ ID NO	581 to 589 Region
3334	HKKRSRLKP
3335	HDKRAKQQP
3336	HRKRGRLNP
3337	HKKKAKARP
3338	HKKRARMKP
3339	HKKRGKVEY
3340	HRKRQRARP
3341	HPKKKKQKP
3342	TVKRARVAT
3343	HDRKLRQRP
3344	HEKRKRMAP
3345	HKKRSRMRP
3346	HDKKKKLRP
3347	HKRKGRGRP
3348	HKKKAKVAS
3349	TKKRGRQCP
3350	HCKKKRQKS
3351	AKKRAKQKS
3352	HGKRKKVHT
3353	HRKKKKVPP
3354	SCKRGRTRP
3355	HPKKKRVRP
3356	HKKRKRFWH
3357	HKKKKKFRP
3358	HQKRKRVRA
3359	HKKKARARP
3360	HKKRKRFGP
3361	HRKRKKMRP
3362	ADRKKRMRN
3363	AKRRKRHAP
3364	HKKRKKTNC
3365	HQKRDKQRT
3366	HRKRKRQRC
3367	HQKRKRVKP
3368	AKKRKRVRP
3369	HKRKKRHKC
3370	AKKRSRVHP
3371	HRKRKRHRW
3372	HKKRKRFRT
3373	TKKRKRVQP
3374	AKKRKKVKP
3375	HKKRGRHRS
3376	HRKKKRLRW

SEQ ID NO	581 to 589 Region
3377	SKRKKRFKD
3378	HDKRGRTKP
3379	HERKKRERP
3380	AKKRKRVAP
3381	HKKRLHVRE
3382	HKKRGRLRP
3383	HPKRKRVKP
3384	HKKRSRQRP
3385	HRKKKRTRP
3386	AKKRLRHRS
3387	HQKKKRTRW
3388	HKKRKRGKY
3389	HDKRARFRY
3390	TKCRKRVRP
3391	TRKKKRVCP
3392	HKKRKRVWY
3393	HQKKLRSKP
3394	HKKRLRVRN
3395	HLRKAKTKP
3396	HKRKKRHKP
3397	HKRKARQRE
3398	HKKRARHKP
3399	HKRKAKQAV
3400	HDKRKRTQP
3401	HQKKKRVKP
3402	HPKRLRSRA
3403	HCKRGRVRP
3404	HLRKKRLKP
3405	MKKRKRVRP
3406	KKKKLKFQY
3407	HKRKGKQRP
3408	HDKKKKQRP
3409	TKKRARQRP
3410	HKRKKKLQL
3411	MKKRKRRRP
3412	HKKRGKDCW
3413	PKRRGRTAP
3414	HECRGRFRP
3415	HRRRKRARP
3416	AKKRKRHRP
3417	HDKRGRHRN
3418	AKRRARVKP
3419	HCRKKKQRY

SEQ ID NO	581 to 589 Region
3420	HKKKKRFRH
3421	HKKRKRHRS
3422	HKKRSRVRP
3423	HKKRGRSRT
3424	HKKKKRTKW
3425	MKKKKRFRP
3426	ADKKKKMRP
3427	HRKRKRFKS
3428	HKTRSRQKY
3429	IKKKKRMRP
3430	TKKRKRFKW
3431	TKKKAKLKC
3432	SDKRGRMCP
3433	HKKRAKVKP
3434	HKKKGRQRI
3435	HLKKGKLRP
3436	HKKRAKFKH
3437	KKKKKRTRI
3438	HKKRAKQKP
3439	YKKKKKMKN
3440	HKKKKRKRP
3441	HKKRKKDKP
3442	HDRRKRLKP
3443	AKKRSRVRP
3444	HKKKKRFKW
3445	HKKRKRFRN
3446	AKKKKRVCS
3447	HKRRKRFIP
3448	MEKRKRLRP
3449	HKRKAKDRW
3450	HRRRARMEP
3451	HKKRLREKT
3452	KPKKKRMKN
3453	QKRRKRRRC
3454	HRKKARVRW
3455	HKRRARLRP
3456	HKKRKRFWT
3457	HKKKKRLAP
3458	HRKKKKQRN
3459	HKKRKKARP
3460	HKKRLRTKP
3461	HEKRKREQP
3462	HCKRKRVRW

SEQ ID NO	581 to 589 Region
3463	HKKKKKSRP
3464	TKKKDRHKP
3465	HKRKLRFRP
3466	HEKRKKARD
3467	AKKKKRFRP
3468	HQRKARMKT
3469	AKKRKRQKN
3470	AKRKLRMRW
3471	MKKRKKFKN
3472	HKRKARLRS
3473	HDKRKKQQP
3474	HKKKKRRCM
3475	HKKRGRGRW
3476	HPKRKRTCP
3477	ACKKKKQQP
3478	PKKRGRTQP
3479	HKKRKKERP
3480	HKRRKRRRW
3481	SKKRKRMRP
3482	HLKKGRHRP
3483	TKKKDKHKC
3484	AQKKAKARP
3485	AKKRSKQRP
3486	HCRKARQQP
3487	HKRRSRLKW
3488	HDRRKRSAA
3489	HKRRTRVRP
3490	EKRRKRVQP
3491	HDRKKKTQC
3492	SKRRKRFGP
3493	HQKKLKERP
3494	HLKRKRVKP
3495	HPKRKKQQW
3496	HKRKKKTRL
3497	HPKRLKVRP
3498	HKKKKRTQW
3499	HRKRKRTGP
3500	HKKRKRSKT
3501	HRKRKRMRC
3502	HKKRKRQAA
3503	HKRRARHRT
3504	TKKRKKSRN
3505	QKKRKRQRY

SEQ ID NO	581 to 589 Region
3506	HKKKARQKN
3507	HKKRKRECS
3508	TKKRKRQIC
3509	HDKRKRIKP
3510	HDRRKKMRP
3511	TKRRARTKY
3512	HKKRKKFRP
3513	HKKRARLRP
3514	AKKRARMRP
3515	QRKRARVRN
3516	HPKRKKTKP
3517	TKKKKRFKW
3518	HKKRKKHCP
3519	HQKKKRKCP
3520	HKRRKKTRS
3521	HKKKKKTRT
3522	HDKRKRLQP
3523	CKRKKRTCP
3524	HKKKLQTKN
3525	KPKKKRVNH
3526	TKKKKRTRT
3527	HGKKKRVKP
3528	TKKKKRTRP
3529	HKKKKRTRP
3530	HDKRKKQRE
3531	HKKKKRLRS
3532	HKKRAKLRP
3533	HKKKAKDRP
3534	KKKKKRLRP
3535	MKRKKRFRC
3536	HCKKAKQRP
3537	TRPRKRTKP
3538	HDRKGKQRP
3539	HKRRAKFRT
3540	HRKRGRLRP
3541	HKKRKKQQP
3542	HKKKKRQRS
3543	HDKKARVKP
3544	HEKKGRMRP
3545	KKKRKRHRP
3546	KKRKKRVRP
3547	AKKRLRHRP
3548	HKRKGKFRP

SEQ ID NO	581 to 589 Region
3549	HDRKAKVRP
3550	HQRKKKMQW
3551	HKKRSRQKS
3552	HKKRGRFRE
3553	HKKKKKARW
3554	HCKRARTAH
3555	HKKRQRMRC
3556	HKKRARQAP
3557	HKRRAKVIP
3558	HCRKDKTRW
3559	TKKRARLRP
3560	HRRKKKLAS
3561	HKKRAKQKY
3562	AKKRKKQHP
3563	HPKRKRQKP
3564	HKRKARVRP
3565	HKKKKRARP
3566	HKKKKKMRC
3567	HKKKAKTRP
3568	HQKRKKQRP
3569	HRKKLRCRW
3570	IKKKKKMRS
3571	HKKRSRLRP
3572	HRRKKRVGP
3573	HKRRDRQRS
3574	HQKRGRVRT
3575	HKKRGKMRP

[0196] In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 2514 – SEQ ID NO: 3575.

[0197] **TABLE 7** provides additional 581 to 589 region sequences predicted to confer retina tissue tropism or preference, generated and selected using machine learning.

TABLE 7 – Additional Exemplary 581 to 589 Region Sequences for Retinal Targeting

SEQ ID NO	581 to 589 Region
3576	KGRRKKVSG
3577	AQKKVKKFG
3578	HKKRRKVWH
3579	KSKIKKYAG
3580	QNKKKKWSW
3581	HKKKLKWVS
3582	KKKKPVTWG
3583	KVKTKKKWA
3584	KTKKIKSHG
3585	KRKKAARKP
3586	KQKIKKSSG
3587	KKKKTRHQR
3588	KVKKKVCGG
3589	KKRPKRRQC
3590	MAKRKKWRP
3591	KTKKKHTSD
3592	RNKKKKRCW
3593	CKKKKRKGC
3594	KMRKKKCEQ
3595	KKKFVKMTH
3596	KTKAFKKLG
3597	KVKRKRKAG
3598	KVKTCKKPQ
3599	MKKLKKLWC
3600	KWKKKKGIF
3601	FKKKGKAHA
3602	LKKMKKQAC
3603	KTRKTKWSP
3604	KAKWYKKGN
3605	KRKRRRKKS
3606	KKKVWIKSQ
3607	KYKNKKWNS
3608	NVKRYRHAQ
3609	RTKKRRSCG
3610	IPKKKRKWC
3611	KGKLKKHCT
3612	HRKKKRQWS
3613	KPKKAKQQQ
3614	HKKKMGRGH
3615	KKKTRKVQE
3616	NKKHKKRGM
3617	KKKSKITNH
3618	LCKKKKRFQ
3619	KAKRQRWRP

SEQ ID NO	581 to 589 Region
3620	QYKKKKRVS
3621	TKKRRRRMT
3622	KARKLKIQG
3623	KTHRKKKFM
3624	TKRKKKIGP
3625	SKKRNKVCT
3626	KSKFHKQKA
3627	KKLKAKVCM
3628	KLRKKRTRG
3629	HKKRRKSHH
3630	RKKKRYKIV
3631	KKKNKLHVQ
3632	KSKWVKKWH
3633	RKRKKARTP
3634	KKKSKHMQA
3635	KRKRAKVNC
3636	NWKKKKVCT
3637	IKKKKKHND
3638	KHKMKKHVG
3639	KKKKMHPCT
3640	KVKGRKIFK
3641	KKKKLKSWF
3642	NRKRRRKKM
3643	KAKRPKSKA
3644	KKARKKFVA
3645	KKRKIPRKG
3646	GRKKFKIKN
3647	KVKVKKGYW
3648	KVRKEKTKH
3649	MKKKKRLLV
3650	KHRKSKTRT
3651	YKKRRKRWA
3652	KKRGKKFSP
3653	KLKKRGKGG
3654	ATKRKKKAL
3655	KKKKAHATY
3656	KHKKKHYHN
3657	HRKRTRYGC
3658	KMKRKKSNQ
3659	KRKRQKQYQ
3660	AHKKKKHLT
3661	KSRKSKGKG
3662	QTKRRKKGC
3663	KGKKFKKGV

SEQ ID NO	581 to 589 Region
3664	KAKQKWVKF
3665	RVKRCRRCA
3666	RAKRPRRQW
3667	KQKKKQYPQ
3668	KVKRWRGQQ
3669	CKRRRKRYI
3670	KKKYRKRRG
3671	KRRKKGNAT
3672	SKKRLKSHG
3673	KKKRKSHNS
3674	KKKDQKACV
3675	LRKKKKQTG
3676	TRKRKKKVK
3677	VKKKQKSHE
3678	KKKKFKNVE
3679	RAKQKKKQS
3680	KMRKSKVCP
3681	ARKRKKSCC
3682	MKHKKKWCH
3683	QHKKKKRYA
3684	KRKMIKKCM
3685	KKMKKRQTG
3686	KNKKKKKMC
3687	KCKRKRRRG
3688	AKKKRKVIM
3689	HRRKQRRYQ
3690	KKRKQKRGM
3691	KKARKTKSH
3692	KKRKFNRAA
3693	KRKKSRSYG
3694	MKKVKKKTG
3695	KGRRQKRAA
3696	KNKKKREAT
3697	YKKMKRKQV
3698	KRKKKPNDQ
3699	NKRKKRGGP
3700	TARKKKCKM
3701	STKRKKKGN
3702	HKKRGRSMH
3703	KKRKYHCDW
3704	KCKSKKKIA
3705	YKRKWKHCE
3706	TIKKFKRKH
3707	RAKRKRKNM

SEQ ID NO	581 to 589 Region
3708	AKKRKKDWS
3709	KARKARRFF
3710	KKKKHLSNM
3711	KKKALKRPM
3712	KGKRQKKQE
3713	CHKNFKKKG
3714	KKKTNKCTN
3715	RTKKRKCFA
3716	RIRKRKQRQ
3717	KKRIMKKSH
3718	APRKKKEKG
3719	KTKKFKWRV
3720	QKRKEKKCC
3721	LKKRKRVAA
3722	RVKRKRYWQ
3723	CKKLWKKHH
3724	KKKWIRRKD
3725	KLRKMKKTP
3726	RKKKKAWAT
3727	KVKKWGWKT
3728	IKKKIKIAG
3729	RVKRARHYS
3730	KKRRCQRGQ
3731	KKKKWWQCA
3732	KAKFTKKYQ
3733	RRKKAKHCS
3734	KRKKYKWQL
3735	TKAKKKAPV
3736	IRRKKKNGS
3737	HKKRKRCNN
3738	QSKRKKRKW
3739	RHRKKRQYP
3740	KQRKKKTAN
3741	KARAKKLKA
3742	KKRRYRHEY
3743	KRKRRHHTH
3744	KKKGYKCMW
3745	KVKKAKQIF
3746	KKKVKMHIG
3747	VYKNKKVKS
3748	KKHKTKAHH
3749	MAKKKKWQI
3750	RKRKIRRNC

SEQ ID NO	581 to 589 Region
3751	KKKKCRLQW
3752	KKKRNKAWW
3753	KKKRKDRAY
3754	CKKTKKYFT
3755	MKKKQKNTY
3756	KKKGKGINS
3757	CKKGRKKWM
3758	KKRRYKCAH
3759	QAKKKKKQG
3760	KKKRKARMD
3761	RMKRRRHSS
3762	TNKPKKCKG
3763	PKKRKFVKG
3764	KKRKGTGGW
3765	NKKVQKKPC
3766	TGKKKKWQP
3767	QGKKKKVNG
3768	KYRKWKRTM
3769	KRRRARQSS
3770	KSKKNSYKN
3771	KSKVTKTKG
3772	KSRKRRTQW
3773	KKKQNKWKW
3774	KNKFTKMKS
3775	MKKMKKCSG
3776	KMKRKKGQS
3777	KKLRKKSCG
3778	KFKKKHIME
3779	KVKWNKKCT
3780	KAKKKVRLC
3781	KKKHTTSKG
3782	HKKRRARAH
3783	NKKRKRGHY
3784	KKKKRFHFN
3785	KCKRKHVAS
3786	HKKKVKSHN
3787	VVKWKKCKT
3788	KSKNKKGCN
3789	KCKKKQNHV
3790	KGKRKRKHS
3791	KIRKHKKDN
3792	NKRKRKYKG
3793	KVKWKQKVG

SEQ ID NO	581 to 589 Region
3794	KMKHKKHSA
3795	AKKAQKQKQ
3796	KKKAKSYDN
3797	KSKTFKYGG
3798	KTKPKKCGG
3799	KAKRKTFVS
3800	KVRKKRQHA
3801	KTRKYKIYQ
3802	KKKKSMRHR
3803	QKKKKSCHG
3804	HKGKKKALG
3805	KVKMRKKNT
3806	KRKNKKSFW
3807	YVKRRKKKN
3808	KKKCKWGMM
3809	GKKGNKCKQ
3810	VKKKIKVST
3811	KWKRKCKGQ
3812	KKQKKRTYT
3813	KTRAKKKTT
3814	KKKKYHHDT
3815	WKKRKKAGF
3816	CCKTKKQKG
3817	KARRRKRYP
3818	KKKKTRVIE
3819	QQKAKKCKG
3820	KCKKKIRWT
3821	KKKLKRRAN
3822	VAKRRRKCC
3823	KQKKSKYTH
3824	KKKMRKREH
3825	KRKKKWKAH
3826	KRMKKKRAY
3827	SRKKKKKMS
3828	KKKQGRFKE
3829	GIRKKKKTT
3830	LVKPKKKAQ
3831	KIKGRKKHC
3832	KGKCKKTHH
3833	KLKKRKSVN
3834	KARKSKRAT
3835	KPRKKKGSE
3836	KRKRMRNMH

SEQ ID NO	581 to 589 Region
3837	HKRKKPPKE
3838	KKKSKYSGV
3839	RSRKKRRGM
3840	KRKRHKHQS
3841	HKRKGKSKW
3842	KKRKLKWFW
3843	KQKVKKENC
3844	GKKKGKRMN
3845	KHKKCIKCA
3846	KTRKRRAYC
3847	SKKTYKKAY
3848	TKKKGKQYH
3849	KIKMKKLQF
3850	KSRMKKLKT
3851	KKRRRWRYM
3852	SKKRVKSSG
3853	KNKRKKNHD
3854	MKHKKKQQN
3855	RTKKRRRQH
3856	KQKIKKMGF
3857	QSRKKKRNS
3858	KGKKRKQMH
3859	YNKKKKHSG
3860	KGKAKKRRH
3861	KKAKGKAYP
3862	MIKIKKKGT
3863	KKKKVYRYS
3864	KKKKTVPAW
3865	CFKKRKKGV
3866	KCKRTKKRN
3867	KVKCKKHSG
3868	KVKKMKSMW
3869	KVRRYKRLS
3870	NKQRKKKQC
3871	KAKTKRHKD
3872	KVKRMKMTA
3873	MKKKKVRYH
3874	KSKCKKGRA
3875	TCKWKKAKH
3876	KVKRVRKYW
3877	FKKKTKCMG
3878	KTKKKTTMF
3879	MRRKKKQVY

SEQ ID NO	581 to 589 Region
3880	KKKRKRRES
3881	RKKKKKAGD
3882	CGRKKKRCD
3883	KVKKRKMYM
3884	KKKRKKIGL
3885	HKKRRRYPY
3886	KKKKAHCSC
3887	KVRKTKACI
3888	SQKKKRVKH
3889	LMRKKKQVP
3890	KKKAKSTDC
3891	CRKKKKAHV
3892	KKKCRKHQY
3893	KARKKFKTN
3894	KGRKKRHPG
3895	KVKKSKHMM
3896	KRKQKFAKH
3897	KNRMKKKHC
3898	LCKSFKKKF
3899	KAKKRRQFH
3900	KLKRRRRHS
3901	EKKKKRRVC
3902	KASKKKRYH
3903	GIKKKKSVM
3904	TKKRKRVKM
3905	VCKKKKMKH
3906	HIKKKKGFG
3907	KKRQKKMCA
3908	CKKKMKTGW
3909	HKRRRFTGY
3910	KRRKHKKMM
3911	QCKKQKQKS
3912	IKRRKKCMH
3913	KNKAQKKPA
3914	KWKKMKLFM
3915	KRRRRARGW
3916	KVKGRKKYP
3917	NKKHKKCHS
3918	KKKRVGQVA
3919	KAKPKKNHC
3920	TMKRKKHQC
3921	KRKGVKKRQ
3922	KRKKMTKSL

SEQ ID NO	581 to 589 Region
3923	KKRRQKTVQ
3924	RVRRRKSTG
3925	ATKKKRKNM
3926	KKKFKNWTY
3927	RTKRYRWRC
3928	RTKAKKTKS
3929	KKKMGKKCN
3930	KAKRFKLYT
3931	KKKKCWMEQ
3932	KGKKNKMIY
3933	KKKRVSWSC
3934	RHKKKKDAH
3935	KKKWKASQC
3936	KSKKFKLSY
3937	KTRKVKWCM
3938	RKKKKRRSM
3939	RFKKKKRFA
3940	KFKKKCYAW
3941	KKKKSRTRH
3942	HKRKKSWHL
3943	KKKRNRRSA
3944	RKKRVRNSH
3945	CKRKKKHTL
3946	HKRKQRQRC
3947	AKKKKKHKP
3948	KWKMKKWMP
3949	RRKRRHSAT
3950	RIKRKRWSS
3951	HKKYCKKTS
3952	RVRRRKWCE
3953	KSKRCKFKQ
3954	KKKKMMCNH
3955	KVKKVRKYH
3956	KKKKVFKTH
3957	KTKKKSYDM
3958	KTKLKKMFS
3959	TKKTMKKAN
3960	ARKKKKKRG
3961	KWRKAKAKY
3962	KKRKQKSTH
3963	KRKRKITSD
3964	RAKRIRIRC
3965	KTKTLKTKF

SEQ ID NO	581 to 589 Region
3966	QARKKKRLG
3967	KTKKKLMGN
3968	IKKRRKLHP
3969	KKKKKFRCS
3970	KQKFGKKAG
3971	KKRKIVCGY
3972	KKRGKKKGH
3973	KKKGQKGYA
3974	LRRRKKNRY
3975	KVKKIKNRD
3976	KRKRFKNDK
3977	KRRKTNRQP
3978	KTKRYRFHN
3979	KARRKRCQC
3980	KTKKRRSSN
3981	QVKKKKRLM
3982	KVKRKKIGW
3983	RSRKRKSYV
3984	KRRKFKRSD
3985	MKMKKKRGH
3986	KKKKFIKSL
3987	KVKRRKRRM
3988	KVKKGQQKC
3989	VKKSVKKIC
3990	KKKAKHGWE
3991	KTKRKRAYW
3992	KKFKCKNSW
3993	RRKRFRFYS
3994	TRRKGKRCN
3995	KKKKMYHSS
3996	KVRKKKDHC
3997	SKKRYKRGS
3998	KNKKCKFSN
3999	HKRKSQHHA
4000	KVKKKRLSA
4001	KAKRKRRHN
4002	RAKKKKRAG
4003	KRRRQRRHH
4004	KTKKKAKCV
4005	KVKKYKAHY
4006	KLKKKRRYF
4007	RVKKKRQAE
4008	KNKKVVKHH

SEQ ID NO	581 to 589 Region
4009	KFKKMRKAT
4010	KKKKRSYMP
4011	KMKSKKCAG
4012	RKKKKQLGI
4013	KFRKRKIYS
4014	KIRKRRQHT
4015	KRKKKMRPA
4016	KAKKQKTTE
4017	SMKKFKKMS
4018	KKKVLKTVE
4019	KSKVKKHGW
4020	KQKKIIKCF
4021	KRKKNKMGP
4022	KSKKNKWQQ
4023	KKKRIQCHV
4024	KIKTKKKMA
4025	KRKRCVWRS
4026	KKRKKNTFS
4027	PKKKKRWTP
4028	VKKSKKQTN
4029	KKKAKHIEC
4030	KAKKNKGHY
4031	VKHRKKVKY
4032	KTKQKKHCC
4033	KTHKKKGSY
4034	IKKSKKAFG
4035	TRKIKKQKG
4036	KAKKMKMSW
4037	KKKRSLKIE
4038	KKKRKKTIY
4039	KAKHKKQIE
4040	CRKKKRRMW
4041	KKRRKGMGF
4042	KVRKAKVQQ
4043	CKKKKSVCF
4044	MAKRKKRRH
4045	MKHKKKNHV
4046	KSKKRKMTT
4047	KCKKNKHHP
4048	KKKRLRGRG
4049	IVKKGKHKS
4050	SKRKKKIVW
4051	KTKMRKKNA

SEQ ID NO	581 to 589 Region
4052	KKKYSKNTC
4053	AKKKKGMKW
4054	KSKKGKTSP
4055	MIKKIKKCG
4056	RFKRKKMKM
4057	HTRKMKTHF
4058	KTKKSKVAM
4059	GRKKRKKSD
4060	KRKCIKQKF
4061	KRKKGRKAE
4062	QQKKKKATW
4063	KRRKRGYST
4064	KMKRYRWHY
4065	CMKRKKKQP
4066	RKKKKWWST
4067	KKKKYQVFT
4068	KIKMYKKFN
4069	SKKKQKCLV
4070	RKRKKRRIY
4071	IKKRYKHLV
4072	KIKYSKKTG
4073	NAKRYRQHY
4074	KRRRIQRSM
4075	KVKKKGRSD
4076	RTKRNRKCQ
4077	KKRSKSKCS
4078	KCKNAKKVG
4079	HKRRCRHRY
4080	RHKKKKEHC
4081	HKKTKKNSS
4082	KCKKRKFMP
4083	KNKRVKKMG
4084	MKRRKKKWI
4085	NKKNKKVNN
4086	AVKRKRRMQ
4087	KKKRQRGWF
4088	KSKTKSKVC
4089	KVKHVKKQS
4090	NNKKRKKFQ
4091	IKKMKKARM
4092	KVKLKKICH
4093	KFHKKKQSW
4094	KCKKWKIMM

SEQ ID NO	581 to 589 Region
4095	KGKSGKTKM
4096	VRRRKKRWA
4097	KKKAKNYTY
4098	HKKRKPTVY
4099	KVRKRRYCA
4100	KKKRRRNAW
4101	KSKSKKMFR
4102	KKKRKVYGM
4103	SRRRKKNKH
4104	RKRKKRYHM
4105	KPKRKSCKH
4106	KTKRRKSMC
4107	AKKKFKYNN
4108	RRKRIKSSQ
4109	KKKGRRKNR
4110	KAKGFKKMD
4111	RRKKAKHVH
4112	YKKRKKCGM
4113	KARRMKRQK
4114	SAKKKKWDS
4115	VHKKKKSCW
4116	QVKVKKKCL
4117	KAKRFRWRS
4118	KKKIYKLHN
4119	KKHMKKSQV
4120	RRRRKKFTP
4121	KKKWIKGWG
4122	QAKKKKVHA
4123	QKKKMRKFS
4124	KKRCKKCSS
4125	KRHRAKKKH
4126	MAKRYRWWS
4127	KKKYFKKVY
4128	KKKKKPRSG
4129	RQKKRKAGS
4130	KRKRRIGRT
4131	KSKKKIRAS
4132	KRRKMRQVS
4133	LVKKSKKNG
4134	RKKKKMGWN
4135	KAKVHKKRN
4136	KKRLCKWKV
4137	KSRKMKFMC

SEQ ID NO	581 to 589 Region
4138	GGRRKKRYY
4139	LKKKTGRKP
4140	KAKRCKRWY
4141	LYKKRKKCI
4142	KAKAFKSSQ
4143	SKRKNKSCT
4144	KQKKKGDAR
4145	ILKRKKKSL
4146	KVKKKQVNG
4147	HRRRTKRFQ
4148	KVKKKTVGP
4149	KALKKKGWG
4150	SKKRKKQKH
4151	KVKPKKHLA
4152	KKKSIKVVP
4153	KKRRAKNCP
4154	KTRKGKKHG
4155	ISRKKKQAG
4156	KAKKKRNQA
4157	VKKRKRVWT
4158	QKKRQRYPS
4159	KKKGVKNRS
4160	KRRKIKKGG
4161	KRKRPRQSC
4162	RKRKRIGGT
4163	KKKRSRRSC
4164	RKKKRCKSS
4165	KTKKPKQHP
4166	HKKKKCNWC
4167	KQRKIKRYP
4168	KTKKKQRAN
4169	KSKNKTTKC
4170	RFKRKKFIS
4171	KKKMKSRHP
4172	KCKSKRHHK
4173	KRKTKKHPQ
4174	KSRKTKYCK
4175	RTKRSRSNY
4176	KRARKKAKC
4177	AAKRKKKCC
4178	KKKRYRRYW
4179	TKKRYKRMY
4180	KKRRIRNYG

SEQ ID NO	581 to 589 Region
4181	KRKKNLKAN
4182	VLKHKKKSC
4183	KTCKKKWMG
4184	KRRKLRRGG
4185	KNKKKHWRP
4186	KSRKTKTGW
4187	KKSRKRKQF
4188	HKKGFKKWY
4189	KAKRKKWLH
4190	KKKRFVMRG
4191	KTKKQRKAV
4192	KGKKSKQGG
4193	RKKQQKNKA
4194	KFRKKHTLP
4195	RKKRYRWCQ
4196	HKKKKHFYA
4197	VKKRNRRTM
4198	RKKKMKGAG
4199	KKKSMARKW
4200	KTKKTKAWG
4201	KTRRKKHTD
4202	LKRKKPKCQ
4203	QVKGKKAKP
4204	IKKRRRFGP
4205	NGKHKKKCF
4206	KMKACKKAG
4207	KKKRNKIYS
4208	KKKKGNYLT
4209	KKKQYKSWV
4210	KFKKMKRKM
4211	KQKRSKAYC
4212	KGKKRGRQM
4213	KKKKHWFVA
4214	KARWKKRHG
4215	RKKRKRRNN
4216	KKCKKKVPA
4217	VTKKKKVRT
4218	SVRKKKKAA
4219	AKKHMKKVG
4220	TKKKKRYHN
4221	KWRKFKCYH
4222	HKRKRHMNP
4223	RKKTKKAFT

SEQ ID NO	581 to 589 Region
4224	IQKKKKCWL
4225	KYRKYKTSS
4226	KSKRYKTCC
4227	VKKKSKVTS
4228	KSKRKGHNK
4229	RKKMKRQKE
4230	KNKRKAKWP
4231	KRKKRGSWG
4232	KARRVRRYY
4233	QKKKVKKCW
4234	VRKRQRQCT
4235	RKRKWKCHC
4236	KVKKKAVVY
4237	KVKKVKISP
4238	KKKKHQPVA
4239	KRRRKTGSQ
4240	QNKKKKAYI
4241	AKKKCKKWT
4242	TKKRRKSPS
4243	KCKRRKKAG
4244	KNKRRKKLY
4245	KVKASKRKC
4246	KKKRFSQVF
4247	KGKWKKFIG
4248	HIRKKKYGN
4249	KLKWKKMWC
4250	KRRKNRYWA
4251	HKKKIKRCD
4252	KCKKKSTYS
4253	KKFKVKHIC
4254	QKKVMKKCG
4255	HKRKICGHH
4256	KVKKKRCRK
4257	KTRKKNHGT
4258	KKQKKRSQN
4259	KKARRKRYH
4260	KSKKHKHDH
4261	KSKDKKQWQ
4262	AKKRKRVAW
4263	SPKKKKWRT
4264	KFKKTKWKF
4265	KRKVKKLMF
4266	KFRKVKTAT

SEQ ID NO	581 to 589 Region
4267	YKKMKKCAY
4268	RKKKDRRKC
4269	HKRRRKTPP
4270	KAKKKNFVI
4271	GKKHTKGKQ
4272	KMKSKKMQQ
4273	RAKRYKKTA
4274	NCKRKKGNK
4275	KKKHMKIGN
4276	KYKFKKWST
4277	KSKRYRMMV
4278	KKKKAKMDG
4279	TNKKKKKAV
4280	KLKKFKRDW
4281	KQKRRRRCM
4282	KKKWLKNIY
4283	KVKMKKIWA
4284	KKKSSKSFC
4285	KKRKHINKA
4286	KRKRKRRCH
4287	YKKKMKWML
4288	AKKGKKQMT
4289	CKKFQKKFA
4290	NKRRIKHRQ
4291	IKKRRKTQN
4292	RKKQKKRTS
4293	RSKRRKACG
4294	YGRKKKQCK
4295	RTKKKKVCS
4296	KAKTKGYKN
4297	KSKKKRNQQ
4298	KLKRTRRSW
4299	RTRKVKHKC
4300	KVKRYRNHW
4301	QRRRNKRQQ
4302	KKRRYHSWA
4303	KKKSKKNSA
4304	KVKWKKDQG
4305	VKKGMKKQY
4306	KVRRKRRPS
4307	YVRKKKFGG
4308	KVKKKRIQF
4309	MKGKKKCAG

SEQ ID NO	581 to 589 Region
4310	KKKWVKTFW
4311	NKKHRKKGH
4312	KKKRHQVVK
4313	MWKRKKVKC
4314	KGRRKRSAM
4315	KCRKKQAKN
4316	KKRKHARVH
4317	KLKVKKVGS
4318	KCKRQKRCA
4319	HIKFKKKQC
4320	AKKNKKWFT
4321	KQKIVKKWM
4322	KTKRIRHHQ
4323	KIRKKRRRL
4324	GFKKKKKQQ
4325	RKKRGKCYG
4326	KVKKRKTNG
4327	KKKRRSNLS
4328	KRKSGKNKS
4329	KKRKTHATK
4330	KCKKRGRTK
4331	QKKCKKRAI
4332	QKKFRKKQQ
4333	KQKRIKKLG
4334	KKKLKGWHV
4335	KKKKMYFSY
4336	KTKKVKYWN
4337	RKKFLKRKG
4338	IKKRKKTQW
4339	KFKPKKAYA
4340	KKRKRSAKS
4341	LAKPKKKAN
4342	KVKRKSNKT
4343	KKKCKLAMF
4344	KKKANKHMD
4345	KTRKRRLYA
4346	RKRRHKGRP
4347	RKKKKQASY
4348	KKKKTRHKS
4349	HKKIKKYVS
4350	KKKLGKCRW
4351	QKRKIRRMA
4352	RHKKKRHCQ

SEQ ID NO	581 to 589 Region
4353	KKKKGKGIA
4354	KKKKYWMIH
4355	KKKRPKATT
4356	KGKKKSVYP
4357	KSKKKRRFD
4358	MIKKVKTKG
4359	KSKKKAQMH
4360	CKKYKKYNY
4361	KKRRTRHSF
4362	KHKAMKFKN
4363	HKRKKKLGV
4364	KVRRKKNAP
4365	KKKITKRGA
4366	MKKKKKVCC
4367	KVRKRKKCA
4368	KFKRKNCKQ
4369	SVKKKKNVS
4370	GPKKKKWSS
4371	RKKRHGKGC
4372	KVKMCKQKW
4373	HKRKGHWVQ
4374	KFKKKINFW
4375	RKKRGRKES
4376	TKKRKPKGS
4377	HKKRNRFCT
4378	KRKCKAKGN
4379	KTRKSKKDR
4380	KIKRKRKHM
4381	TKRRHKRQV
4382	KKKTCKLGH
4383	KKKKAQRHT
4384	KKKCKRKYA
4385	HKKNIKKHW
4386	EKKRKKWYS
4387	KKKHCKLHW
4388	KLKSKKRGR
4389	STKRRRRAS
4390	KRKKSMMKT
4391	AKKKIKKVG
4392	KRKRWKKLF
4393	KVKKSKAHM
4394	KKRRWRHHH
4395	RSRKVKRHY

SEQ ID NO	581 to 589 Region
4396	KKKKTLHTN
4397	CKKKRKQHC
4398	TKKTKKQQP
4399	KKKRLKHSD
4400	MARKKKSRT
4401	NKKPRKVKW
4402	VKKRKRNHV
4403	KVKKMKWKR
4404	KKRKNKEFI
4405	KKKGKRHRG
4406	LAKHKKHKH
4407	KQKKMKRQD
4408	KAKWKKWSW
4409	LKRKKRKDC
4410	KKRKWHYYG
4411	KAKKKHSRV
4412	KQKKKRRTT
4413	KKKCKNSGT
4414	QKRKRKLSE
4415	CKKLKKTGY
4416	RKKKPKMQM
4417	RRRRSKSKA
4418	HKKSWKKYP
4419	KKKWKVVNW
4420	KKKVQKMHP
4421	KKRKKGSWA
4422	KIRRYKRQA
4423	KKFKKKSAN
4424	SKRKKRKWG
4425	MSRKKKRST
4426	KKRRHGRWY
4427	KKKKSSTGP
4428	KVRKTKIGE
4429	KKRRTCRHQ
4430	KKRKGIRGT
4431	HKRKKHNQM
4432	RKKRHKGNQ
4433	LCKKKKRTC
4434	LKKPKKTCN
4435	KIKHKKWLV
4436	KKKKKIQMQ
4437	KVKRKQQLC
4438	RCRKRKSIC

SEQ ID NO	581 to 589 Region
4439	SKKRRRRMS
4440	ICKKKRLKG
4441	KLRKFKGKY
4442	KLKRKKNVQ
4443	RMKKKRQIM
4444	KKRRQKVKH
4445	KKKSKKMFE
4446	HRKRVRVRF
4447	KMKKKRCPA
4448	SARKKKWCC
4449	HKKRKQTGT
4450	KKKACKKSA
4451	KIKKTRKNH
4452	VKKKLKTGA
4453	KFKARKHKT
4454	KHKSHKKQL
4455	RKNKKKHNA
4456	CRKKKKIKC
4457	HHKRQRAHH
4458	CVRKKKQVG
4459	SFKWKKKQY
4460	HGKQKKKCC
4461	KARRMKNWS
4462	KKKRFGRQK
4463	KNKKMKKAA
4464	KTKVKKVAH
4465	KKKNYKSSY
4466	QKKGRKKNL
4467	TRRKKRRPC
4468	KGKVSKKQS
4469	RNRKKKWCC
4470	KKKKRKNHR
4471	LHKKKKGNW
4472	HTKKKKFAP
4473	NKKKFKTVQ
4474	KFRKKRWVP
4475	KKKKQNHGC
4476	VNKKKKHAA
4477	SMKKKRKAS
4478	SKKKQKARP
4479	TGKKKKHYW
4480	YCKKWKIKN
4481	TKRKKKQFH

SEQ ID NO	581 to 589 Region
4482	KKQKKHRMP
4483	KTRNKKPKC
4484	HAKGKKKCM
4485	KKKKCPHAQ
4486	KKKRVKDKQ
4487	KKKTQRHHN
4488	KKKWWKKSQ
4489	KVKRKGHCQ
4490	KVKRSKHCQ
4491	KIRKKKDMQ
4492	KKKIRKNFY
4493	SKRKYKKTG
4494	KKKPKHVCA
4495	KRRKHIRRH
4496	CRKKTKQKV
4497	RARKKKCFF
4498	IKKCKKRVM
4499	HKKRNRKSK
4500	KKRFKKAFG
4501	CIKKKKYMN
4502	KRKKQYKVC
4503	KMKTYKIKQ
4504	KHQKKKRSG
4505	YKKMKKAMI
4506	KAKKKKKKF
4507	HVKKKKWNG
4508	KKRCKKHGS
4509	YKKKTKYSS
4510	KKRRYRHAG

[0198] In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 3576 – SEQ ID NO: 4510.

[0199] **TABLE 8** provides additional 581 to 589 region sequences predicted to confer retina tissue tropism or preference, generated and selected using machine learning.

TABLE 8 – Additional Exemplary 581 to 589 Region Sequences for Retinal Targeting

SEQ ID NO	581 to 589 Region
4511	KHKKKGGPQ
4512	RKQKKKAWC
4513	KKRKRAPKI

[0200] In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having

one or two amino acid substitutions relative to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 4511 – SEQ ID NO: 4513.

[0201] Features for Retina Tissue-Tropic AAV VP Capsid Polypeptides. The present disclosure provides features of 581 to 589 region sequences that enhance retina tissue tropism or preference, as determined from a primary screen. In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains one or more basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains two or more basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains three or more basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains four or more basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains one basic amino acid residue (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains two basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains three basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains four basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains five basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains six basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains seven basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains eight basic amino acid residues (e.g., K, R, or H). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains nine basic amino acid residues (e.g., K, R, or H).

[0202] In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains no more than three acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains no more than two acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains no more than one acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains no acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina

tissue tropism or preference contains one acidic amino acid residue (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains two acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains three acidic amino acid residues (e.g., D or E).

[0203] In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains more basic amino acid residues (e.g., K, R, or H) than acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains one or more basic amino acid residues (e.g., K, R, or H) and no acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains two or more basic amino acid residues (e.g., K, R, or H) and no more than one acidic amino acid residue (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains two or more basic amino acid residues (e.g., K, R, or H) and no acidic amino acid residues (e.g., D or E). In some embodiments, a 581 to 589 region with retina tissue tropism or preference contains three or more basic amino acid residues (e.g., K, R, or H) and no more than two acidic amino acid residues (e.g., D or E).

[0204] In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$, wherein X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are each independently any amino acid) comprises K, R, or H at position X^3. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K or R at position X^3. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K at position X^3. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises R at position X^3. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K, R, or H at position X^6. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K or R at position X^6. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K at position X^6. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises R at position X^6. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K, R, or H at position X^1. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K or R at position X^1. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K at position X^1. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises R at position X^1. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K, R, or H at position X^4. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises K or R at position X^4. In some embodiments, a 581 to

589 region having a sequence of SEQ ID NO: 5014 comprises K at position X^4. In some embodiments, a 581 to 589 region having a sequence of SEQ ID NO: 5014 comprises R at position X^4.

[0205] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^1 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 1726, 374, 1442, 933, 1748, 4142, 1434, 1358, 1191, 3732, 4110, 4039, 4411, 4506, 4270, 4156, 3780, 4036, 4030, 4016, 1550, 3899, 1247, 1855, 1181, 3919, 1639, 3664, 1244, 4140, 3930, 4117, 4189, 4001, 3799, 3643, 3619, 1240, 1686, 1479, 1307, 1575, 4296, 1665, 3871, 4135, 1605, 4408, 3604, 1274, 4149, 1313, 3741, 1938, 3709, 1727, 3893, 1280, 3622, 1784, 3834, 1752, 1983, 1743, 3979, 4461, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 1857, 2510, 2316, 1904, 1219, 1486, 1512, 1481, 1516, 3820, 3789, 4252, 4047, 4330, 4082, 4094, 1574, 1248, 4078, 1872, 1426, 3785, 3687, 4318, 4243, 3866, 3704, 4172, 1621, 4315, 1192, 1513, 1856, 2476, 3324, 2769, 2678, 1561, 3296, 375, 2343, 2348, 376, 377, 1395, 1584, 4093, 4453, 3940, 3778, 4374, 4210, 4009, 4264, 4339, 4368, 1738, 378, 1610, 4194, 4474, 4013, 4266, 1771, 1759, 1922, 3860, 3832, 1349, 1381, 3663, 1642, 1185, 4356, 3932, 1233, 4212, 3858, 1198, 4192, 3611, 1919, 1819, 3790, 3712, 1969, 4095, 1887, 4468, 1720, 4247, 934, 1790, 2002, 1657, 1663, 1336, 3894, 1554, 1494, 1405, 3576, 4314, 3695, 1851, 1850, 4362, 1815, 3845, 4511, 3656, 3638, 1406, 1596, 4454, 1443, 1661, 935, 4504, 1359, 1734, 3650, 1910, 1305, 1648, 3831, 4435, 1208, 1988, 4451, 1993, 1986, 3849, 1718, 4068, 1835, 1425, 1428, 1282, 4380, 1658, 1452, 1687, 4024, 379, 4072, 3791, 4491, 4323, 4014, 1304, 1440, 1511, 1981, 1676, 1547, 4422, 1283, 3861, 1383, 3644, 3691, 4259, 1749, 1418, 1176, 4216, 1924, 1421, 1387, 3992, 4423, 4253, 1618, 1871, 1256, 3748, 4119, 1297, 1586, 1251, 1299, 1954, 4450, 3990, 4029, 4097, 3890, 3796, 1389, 3711, 4344, 1578, 1476, 4343, 1202, 4413, 4384, 3808, 1647, 1475, 3892, 3674, 1739, 3926, 3595, 1943, 3756, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 3781, 1535, 1210, 4492, 4365, 4118, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 4350, 4334, 3821, 1932, 3929, 4171, 1258, 3824, 3631, 4465, 4494, 1320, 1398, 3828, 1204, 1223, 1284, 1685, 3773, 4209, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4327, 4037, 4163, 3918, 4486, 1243, 3933, 4178, 1662, 1643, 4152, 3634, 3617, 4445, 4303, 1370, 3838, 4199, 4284, 1213, 4382, 1399, 1187, 3714, 1828, 4487, 3615, 1842, 1501, 3746, 4018, 4420, 3606, 4121, 3724, 3935,

1941, 4419, 4282, 1955, 1949, 4310, 4488, 1577, 4127, 1288, 1171, 3670, 4052, 3627, 3777, 936, 1371, 3685, 1325, 1940, 380, 4482, 4258, 3812, 1581, 1860, 4124, 4508, 4500, 3652, 3972, 1309, 1630, 1528, 3717, 1217, 3692, 4430, 3764, 4316, 4285, 3645, 3971, 4421, 1172, 4026, 2740, 3125, 3546, 1725, 1206, 3842, 4404, 3690, 3962, 4513, 4340, 4329, 4410, 3703, 4136, 1763, 1487, 3589, 3907, 4153, 2707, 3730, 4426, 4180, 4041, 3923, 4444, 3851, 4429, 4361, 1441, 4394, 4302, 3758, 4510, 3742, 1868, 4077, 1710, 1939, 1335, 1666, 1407, 4187, 1193, 1188, 1196, 1724, 1717, 1200, 1646, 1997, 1975, 1701, 4280, 1613, 4006, 1984, 1351, 3653, 3833, 1593, 2561, 4442, 3900, 4298, 1761, 4388, 1820, 1597, 4317, 4249, 1341, 1203, 1680, 4441, 3628, 3725, 1945, 937, 4206, 1588, 1439, 3794, 4447, 1838, 3776, 3658, 4064, 1377, 4011, 4272, 4503, 1324, 1367, 3594, 3680, 1300, 1750, 938, 3913, 3774, 1877, 1987, 1862, 3998, 1380, 4185, 3686, 3696, 4463, 1350, 4008, 4230, 3853, 4244, 4083, 381, 1909, 3897, 1546, 382, 3613, 3273, 3452, 3525, 1229, 4105, 3835, 383, 1263, 1234, 3970, 1492, 3856, 3586, 1175, 4321, 4020, 4144, 1224, 1199, 3667, 2778, 4412, 4407, 1812, 1810, 3823, 1416, 1427, 1507, 1878, 4333, 3146, 4281, 4211, 1179, 3843, 1669, 1677, 1524, 1525, 1974, 384, 1979, 1456, 1239, 4167, 3740, 1876, 1388, 1967, 1474, 385, 1342, 1471, 4176, 1232, 1989, 4125, 1741, 1508, 1580, 4060, 4378, 1576, 1212, 1893, 3921, 3585, 1174, 1396, 4061, 4015, 1207, 3698, 3825, 3922, 4021, 4181, 1598, 1916, 1429, 4502, 4231, 1321, 4390, 3693, 3734, 1382, 3684, 1747, 3806, 3896, 3635, 1768, 4025, 3976, 3840, 3963, 4286, 1502, 3836, 4161, 3659, 3743, 4130, 3605, 1385, 1783, 4392, 4328, 1316, 4173, 4265, 1246, 1985, 1629, 1829, 1737, 3826, 1473, 1992, 1883, 1656, 1837, 1914, 1839, 1834, 3984, 4495, 3910, 4160, 3671, 4184, 4132, 4250, 1503, 1237, 1523, 1417, 4063, 1562, 3977, 1971, 1707, 1847, 1792, 3769, 4074, 1534, 4239, 4003, 3915, 1689, 1776, 1599, 1265, 1410, 1823, 1498, 1329, 939, 386, 940, 387, 1655, 3874, 4261, 3626, 1791, 3579, 1644, 3936, 4054, 4260, 4359, 4131, 4297, 4357, 4022, 3770, 4046, 1222, 1996, 3788, 4169, 1925, 3953, 4228, 4226, 4277, 4101, 1889, 1369, 3797, 4088, 4019, 3771, 3632, 1402, 388, 1520, 1767, 1466, 1194, 4137, 1908, 1927, 1758, 3772, 3661, 4186, 4174, 1170, 3850, 1315, 1611, 1530, 1859, 2209, 4183, 1408, 1403, 941, 4033, 3623, 3596, 1461, 1848, 1173, 1928, 1459, 1765, 1826, 3719, 1931, 3584, 4004, 3591, 3967, 4168, 3957, 3878, 4165, 4191, 3980, 4058, 4200, 4336, 3958, 1260, 4051, 3798, 4032, 1774, 4322, 3991, 4106, 1641, 1570, 3978, 3965, 4464, 3813, 4154, 1365, 4257, 3846, 4345, 4379, 3603, 1693, 3937, 3801, 1787, 1214, 4483, 4201, 1898, 1845, 1226, 1220, 4245, 1347, 3867, 1900, 3640, 3916, 4089, 1209, 3745, 3988, 3975, 4236, 4075, 4146, 4256, 4308, 4000, 4148, 3588, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 3727, 4005, 4092, 4372, 4283, 1553, 3805, 4151, 1281, 1681, 4489, 3982, 4437, 3597, 4342, 3872, 3987, 4490, 3876, 3668, 4300, 1679, 1242, 3598, 3583, 3647, 389, 4304, 3793, 3779, 1937, 1907, 4042, 3648, 3996, 3800,

4367, 4099, 1807, 3887, 4428, 1625, 1390, 1884, 1682, 4364, 4306, 3869, 1278, 1672, 942, 1505, 1542, 1709, 1915, 3600, 3914, 1968, 3948, 1670, 3811, 1865, 1362, 943, 1716, 3961, 1506, 4221, 1376, 944, 1683, 4276, 1445, 1721, 1632, 3607, 1328, 1455, 1913, 1497, 1317, 1951, 1778, 1379, 3768, 4225, 1668, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 571, 1401, 4438, 1895, 1264, 572, 1912, 573, 3939, 4170, 4056, 1271, 1065, 1521, 1221, 1066, 1451, 1654, 1067, 3934, 4080, 4352, 574, 1700, 3739, 1565, 1419, 1811, 3950, 1690, 1397, 3716, 1569, 1465, 1437, 1674, 4337, 1285, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4229, 4292, 4193, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 1729, 4223, 1540, 4455, 1068, 1069, 4512, 1723, 1070, 3750, 3633, 4070, 4104, 4162, 4235, 1863, 4346, 1881, 1071, 1814, 1572, 2418, 575, 4443, 3761, 1346, 1587, 1072, 3592, 576, 1891, 4469, 2430, 1275, 577, 1950, 1963, 4129, 1073, 1296, 1360, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1556, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 2185, 2279, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 2222, 578, 3928, 4295, 3715, 3855, 3609, 1990, 4076, 4175, 3927, 1757, 1650, 4299, 1773, 2004, 1267, 1364, 579, 1462, 1879, 4007, 3729, 3665, 3722, 1691, 1712, 1074, 1624, 1751, 1394, 3924, 3952, 580, 581, 2003, 1343, 2203, 1559, 1250, or 1555.

[0206] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^2 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 285, 1626, 299, 3809, 4271, 3844, 1436, 300, 1515, 1617, 3646, 4059, 1431, 1331, 310, 3804, 1363, 1934, 1602, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113,

1345, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 2772, 3230, 3043, 2922, 3581, 3524, 2869, 2610, 3298, 2775, 3108, 2603, 3614, 2612, 2860, 3187, 3238, 3786, 4385, 3016, 3436, 2876, 2987, 3532, 3438, 3561, 3259, 2663, 2890, 3433, 3071, 3018, 2580, 2755, 3015, 2540, 3398, 2664, 2583, 2830, 2644, 2641, 3513, 2725, 2723, 3338, 3556, 2866, 2514, 2932, 2753, 2862, 2899, 2605, 2989, 3096, 3124, 2985, 2716, 3145, 3017, 2591, 2640, 3033, 1853, 3216, 3316, 3412, 2971, 3256, 3153, 3575, 3339, 2915, 2531, 3552, 3475, 3060, 3375, 2756, 3382, 2847, 2859, 3251, 3702, 3423, 2537, 2801, 3076, 2696, 3092, 3459, 3144, 3441, 2802, 3479, 2907, 3512, 3518, 3021, 2871, 3032, 2647, 2945, 3045, 2763, 3313, 3034, 3315, 3541, 2746, 2669, 2524, 3003, 2732, 3166, 3046, 3306, 2873, 3364, 3253, 3215, 3061, 2804, 2722, 2964, 2990, 2836, 4098, 4449, 3173, 2762, 3737, 2628, 3507, 2564, 3031, 2872, 3360, 2658, 2930, 2904, 3244, 3217, 3311, 3445, 2840, 3372, 2958, 3098, 3356, 3456, 3388, 2624, 3207, 2576, 2742, 2665, 2815, 3052, 3421, 2593, 3242, 2535, 2966, 2898, 2858, 2943, 2668, 2798, 3196, 2528, 2713, 3001, 2691, 2948, 2767, 2544, 3302, 2734, 2893, 2592, 2861, 3502, 2969, 2582, 3229, 2676, 2545, 3255, 3330, 2547, 3257, 2882, 3151, 3088, 2883, 3318, 2645, 2733, 2587, 3500, 3008, 2715, 2845, 3183, 2654, 3233, 3267, 2741, 2827, 2704, 3091, 2832, 2736, 3177, 3271, 2835, 2908, 3176, 2947, 3292, 3191, 2517, 3026, 3082, 3392, 3381, 2584, 2712, 3213, 3451, 2634, 3150, 2810, 3303, 2573, 3460, 2615, 3394, 2828, 3329, 4377, 4499, 3555, 2974, 3782, 3629, 3578, 3885, 2817, 3248, 2954, 3334, 3571, 3345, 3551, 3384, 3422, 1357, 1844, 2530, 2973, 4418, 4081, 3951, 1764, 1671, 1852, 334, 1843, 3449, 3185, 3399, 2786, 3055, 3472, 3397, 2601, 3564, 3277, 4373, 3548, 3179, 3407, 3841, 3347, 3142, 4255, 4431, 3241, 3077, 2700, 3147, 2648, 3283, 2829, 3278, 2581, 2536, 4363, 2848, 3410, 2797, 2523, 2520, 2721, 3496, 2571, 3198, 3219, 3030, 2673, 2921, 3837, 3301, 3322, 2705, 3239, 2949, 3369, 3396, 2892, 2897, 2766, 3174, 3297, 2550, 2889, 2933, 2793, 2627, 2677, 3119, 2596, 3226, 3172, 3089, 2868, 2839, 3942, 3120, 3286, 2843, 3465, 1564, 3946, 4222, 1504, 3999, 2682, 1875, 2865, 3539, 3168, 2864, 3308, 3557, 2940, 3109, 3503, 2625, 3455, 3114, 2595, 3331, 2978, 2518, 2521, 4079, 3024, 3573, 2952, 2653, 1769, 3180, 2813, 2652, 2600, 2816, 3201, 3188, 3270, 2997, 2992, 3009, 3520, 2936, 3275, 3165, 3447, 3131, 3305, 2809, 2792, 2729, 2814, 2619, 3266, 2825, 3066, 2857, 2998,

3064, 2681, 3035, 3279, 2764, 3480, 3127, 2912, 3010, 2607, 3211, 3111, 3041, 1573, 3909, 4269, 3487, 3489, 3019, 335, 1266, 1415, 2980, 3428, 1355, 3454, 2851, 2881, 3232, 3458, 3326, 3353, 2927, 3212, 2950, 3376, 3208, 3062, 3612, 3195, 3385, 2686, 2602, 3569, 3123, 2727, 1622, 2821, 2636, 2750, 2850, 3050, 2925, 3336, 3540, 2689, 3139, 2526, 3361, 3022, 3427, 3107, 3140, 3371, 3276, 2831, 3501, 2924, 3366, 3199, 3101, 3321, 3499, 2917, 2683, 2800, 2812, 3340, 3227, 3148, 3657, 4446, 1746, 1464, 1886, 2666, 3246, 3130, 3560, 3236, 2730, 3572, 1607, 3689, 2968, 1457, 1500, 909, 337, 1184, 3450, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 4147, 4498, 1518, 3728, 3637, 3570, 3429, 4091, 2870, 2995, 4338, 3205, 2880, 3261, 1994, 3968, 4291, 4204, 4071, 4034, 1742, 2037, 352, 2820, 3912, 3287, 1218, 1190, 1959, 1840, 3736, 1283, 3861, 1383, 3644, 3691, 4259, 1749, 1418, 1176, 4216, 1924, 1421, 1387, 3992, 4423, 4253, 1618, 1871, 1256, 3748, 4119, 1297, 1586, 1251, 1299, 1954, 4450, 3990, 4029, 4097, 3890, 3796, 1389, 3711, 4344, 1578, 1476, 4343, 1202, 4413, 4384, 3808, 1647, 1475, 3892, 3674, 1739, 3926, 3595, 1943, 3756, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 3781, 1535, 1210, 4492, 4365, 4118, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 4350, 4334, 3821, 1932, 3929, 4171, 1258, 3824, 3631, 4465, 4494, 1320, 1398, 3828, 1204, 1223, 1284, 1685, 3773, 4209, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4327, 4037, 4163, 3918, 4486, 1243, 3933, 4178, 1662, 1643, 4152, 3634, 3617, 4445, 4303, 1370, 3838, 4199, 4284, 1213, 4382, 1399, 1187, 3714, 1828, 4487, 3615, 1842, 1501, 3746, 4018, 4420, 3606, 4121, 3724, 3935, 1941, 4419, 4282, 1955, 1949, 4310, 4488, 1577, 4127, 1288, 1171, 3670, 4052, 3627, 3777, 936, 1371, 3685, 1325, 1940, 380, 4482, 4258, 3812, 1581, 1860, 4124, 4508, 4500, 3652, 3972, 1309, 1630, 1528, 3717, 1217, 3692, 4430, 3764, 4316, 4285, 3645, 3971, 4421, 1172, 4026, 2740, 3125, 3546, 1725, 1206, 3842, 4404, 3690, 3962, 4513, 4340, 4329, 4410, 3703, 4136, 1763, 1487, 3589, 3907, 4153, 2707, 3730, 4426, 4180, 4041, 3923, 4444, 3851, 4429, 4361, 1441, 4394, 4302, 3758, 4510, 3742, 1868, 4077, 1710, 1939, 1335, 1666, 1407, 4187, 1193, 1188, 1196, 1724, 1717, 1200, 1646, 4176, 1232, 1989, 4125, 1741, 1508, 1580, 4060, 4378, 1576, 1212, 1893, 3921, 3585, 1174, 1396, 4061, 4015, 1207, 3698, 3825, 3922, 4021, 4181, 1598, 1916, 1429, 4502, 4231, 1321, 4390, 3693, 3734, 1382, 3684, 1747, 3806, 3896, 3635, 1768, 4025, 3976, 3840, 3963, 4286, 1502, 3836, 4161, 3659, 3743, 4130, 3605, 1385, 1783, 4392, 4328, 1316, 4173, 4265, 1246, 1985, 1629, 1829, 1737, 3826, 1473, 1992, 1883, 1656, 1837, 1914, 1839, 1834, 3984, 4495, 3910, 4160, 3671,

4184, 4132, 4250, 1503, 1237, 1523, 1417, 4063, 1562, 3977, 1971, 1707, 1847, 1792, 3769, 4074, 1534, 4239, 4003, 3915, 1689, 1776, 1599, 1265, 1410, 1823, 1498, 954, 955, 2437, 4139, 1482, 3602, 4434, 3721, 1592, 1825, 1698, 1519, 1352, 4202, 4409, 1977, 1917, 2382, 3675, 1833, 3974, 419, 4309, 4045, 3854, 3682, 2491, 444, 445, 1972, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3873, 3755, 1216, 3599, 3775, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3694, 446, 3985, 3535, 1306, 4084, 3282, 447, 1353, 2168, 3879, 2698, 1894, 1882, 1817, 1880, 490, 1018, 3917, 3616, 4311, 1800, 4473, 4085, 4401, 1310, 3783, 3765, 1538, 3870, 491, 1948, 3699, 1735, 3792, 4290, 2074, 492, 1019, 2012, 1803, 3642, 497, 1322, 1261, 4027, 3478, 3763, 2959, 1293, 2462, 517, 3197, 1595, 3413, 1675, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 3803, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 1449, 2121, 1044, 3720, 4351, 4414, 1673, 3453, 3254, 2501, 1050, 3515, 2219, 1433, 1323, 4301, 1569, 1465, 1437, 1674, 4337, 1285, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4229, 4292, 4193, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 1729, 4223, 1540, 4455, 1068, 1069, 4512, 1723, 1070, 3750, 3633, 4070, 4104, 4162, 4235, 1863, 4346, 1881, 1360, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1556, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 1858, 596, 597, 598, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 599, 3847, 4993, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 1412, 2324, 605, 1368, 3827, 4103, 606, 607, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 4879, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 3815, 2005, 1964, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, or 2250.

[0207] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962,

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1159, 1953, 1160, 1201, 727, 3787, 3747, 730, 1846, 3815, 2005, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 734, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1628, 3705, 1195, 3859, 1164, 1165, 1166, 1745, 1973, 1168, 3807, 4307, 1454, or 1781.

[0208] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^4 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 739, 4177, 1289, 15, 743, 3477, 3051, 2982, 2877, 746, 3036, 3426, 3073, 3169, 3362, 2784, 3192, 1638, 25, 1703, 1836, 3660, 30, 32, 752, 1653, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 2633, 757, 1952, 3122, 2551, 3718, 2216, 3484, 3577, 1308, 1230, 3960, 2994, 3080, 2589, 3681, 51, 761, 3925, 3654, 763, 764, 57, 4086, 1740, 767, 772, 2599, 2706, 70, 3865, 1549, 1361, 3882, 1942, 1312, 4501, 1413, 3593, 4043, 1806, 3908, 4397, 1615, 2006, 3945, 2854, 3523, 3669, 1356, 777, 4065, 84, 1484, 778, 87, 3891, 4456, 4040, 4496, 2001, 1478, 1189, 1490, 1885, 2270, 1180, 786, 4458, 1970, 1590, 98, 1298, 101, 1688, 794, 107, 1849, 797, 1579, 111, 112, 113, 1444, 801, 114, 115, 119, 120, 122, 1760, 123, 124, 806, 125, 126, 127, 128, 129, 130, 134, 811, 814, 139, 1326, 144, 816, 1302, 150, 152, 821, 160, 161, 162, 1651, 1483, 179, 180, 183, 185, 187, 1391, 198, 199, 831, 204, 833, 207, 3901, 3312, 2649, 1301, 4386, 3028, 1896, 1522, 3490, 216, 218, 1612, 225, 228, 229, 234, 239, 849, 850, 1536, 241, 246, 248, 855, 249, 252, 253, 261, 4966, 864, 263, 4749, 2296, 1241, 866, 268, 868, 269, 270, 873, 874, 1252, 273, 1591, 274, 1980, 878, 1539, 3601, 3877, 1930, 1420, 1678, 1460, 1799, 1374, 1290, 1354, 290, 2391, 4324, 294, 4138, 3903, 892, 3829, 298, 3844, 1436, 300, 1515, 1617, 1961, 303, 1589, 893, 4370, 3646, 4059, 1331, 1558, 1552, 320, 1958, 1491, 1635, 332, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3414, 3093, 2996, 3141, 3544, 3102,

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3803, 4123, 4233, 3129, 3087, 3505, 4158, 1044, 3720, 4351, 4414, 1673, 3453, 3254, 1649, 543, 4240, 3580, 2598, 4062, 2841, 1049, 3515, 1433, 1323, 4301, 1051, 3738, 1270, 3857, 1056, 3662, 1057, 3981, 1063, 568, 570, 3620, 1064, 4002, 3964, 3707, 3666, 1348, 4273, 4497, 1401, 4438, 1895, 1912, 3939, 4170, 4056, 1221, 1654, 1067, 3934, 4080, 4352, 574, 3739, 1565, 3950, 1397, 3716, 1569, 1465, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 4455, 4512, 3750, 3633, 4070, 4104, 4162, 4235, 4346, 1572, 4443, 3761, 1346, 3592, 1891, 4469, 1275, 577, 1963, 4129, 1296, 1360, 3733, 4111, 3993, 4108, 3949, 1556, 1435, 1424, 1830, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 4293, 1827, 3839, 3983, 4395, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1650, 4299, 1773, 2004, 1267, 1364, 4007, 3729, 3665, 3722, 1712, 1751, 3924, 3952, 1343, 4114, 1704, 4448, 1786, 3354, 586, 3432, 2891, 587, 1903, 2077, 1080, 1563, 2274, 595, 2559, 2590, 2738, 4478, 4069, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 1412, 4017, 4477, 1794, 4263, 3072, 2199, 3888, 604, 605, 1368, 3827, 4103, 607, 1571, 1438, 3701, 4389, 4897, 1603, 2154, 1715, 4369, 1652, 1733, 4218, 1798, 621, 1667, 1384, 3700, 1788, 1600, 1102, 1423, 2771, 1339, 3070, 2557, 2795, 2906, 3299, 3118, 4779, 2028, 1614, 1947, 630, 4479, 3766, 1106, 634, 1108, 635, 638, 3706, 3735, 3390, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1585, 3221, 2643, 2739, 3920, 1801, 4279, 2502, 1117, 2965, 2695, 3293, 3264, 2076, 657, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 667, 1133, 1134, 673, 1933, 1731, 1793, 3342, 683, 1146, 687, 3822, 1601, 692, 3905, 1414, 696, 1695, 4115, 701, 1544, 702, 703, 4031, 2010, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 1532, 1493, 1854, 1510, 705, 1153, 4476, 1375, 712, 1245, 715, 4234, 1154, 1314, 4096, 720, 1311, 721, 722, 4217, 726, 3815, 2005, 1964, 1262, 4480, 4294, 1582, 3439, 2833, 4287, 4509, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 1195, 3859, 3807, 4307, 1454, or 1781.

[0209] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^5 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 2498, 4177, 742, 16, 17, 18, 745, 3477, 1548, 2982, 3426, 3073, 3169, 747, 3362, 4942, 23, 28, 2038, 3660, 750, 31, 32, 1640, 34, 37, 4925, 1205, 4288, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635,

3446, 3053, 3688, 4320, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 1225, 3178, 3006, 3252, 2991, 2642, 2519, 3363, 2633, 42, 755, 44, 756, 46, 1952, 758, 2410, 2551, 3718, 1308, 1230, 3960, 1378, 2589, 3681, 760, 53, 4951, 4591, 762, 3925, 55, 3654, 763, 60, 61, 4086, 1740, 766, 1966, 63, 2041, 64, 769, 770, 2384, 771, 65, 772, 2197, 68, 3816, 69, 2599, 70, 3865, 1549, 3882, 75, 4501, 76, 774, 1413, 776, 3757, 3593, 4043, 4397, 4415, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 1356, 81, 82, 4065, 83, 84, 1294, 87, 3891, 4456, 4040, 1189, 1490, 90, 92, 782, 94, 1831, 1867, 4458, 1936, 100, 792, 2007, 4556, 795, 104, 106, 1849, 2509, 110, 1906, 798, 2359, 2461, 4864, 1344, 116, 120, 121, 803, 1463, 805, 1760, 123, 124, 806, 127, 2085, 130, 132, 809, 1978, 134, 813, 139, 815, 1326, 141, 142, 145, 4816, 1302, 817, 146, 818, 148, 149, 4546, 150, 153, 156, 157, 163, 164, 166, 169, 823, 824, 1483, 175, 177, 178, 179, 826, 827, 182, 183, 829, 184, 185, 190, 191, 192, 2361, 195, 1391, 197, 2223, 201, 202, 4775, 1334, 837, 3901, 3312, 212, 4386, 3028, 213, 1446, 214, 215, 1896, 3490, 217, 219, 223, 225, 2088, 4542, 226, 227, 230, 843, 844, 237, 845, 239, 849, 852, 1536, 854, 244, 245, 248, 855, 251, 253, 255, 257, 858, 860, 262, 863, 4535, 865, 264, 1241, 265, 1477, 267, 867, 1252, 273, 275, 1980, 277, 281, 1892, 879, 1539, 881, 1295, 282, 285, 1626, 2082, 1374, 1620, 4564, 289, 887, 888, 889, 4324, 293, 4138, 296, 3903, 892, 3829, 298, 301, 302, 1589, 4370, 2342, 309, 4059, 310, 1779, 1558, 1552, 317, 320, 898, 321, 2016, 2134, 324, 325, 327, 1635, 4484, 1756, 4609, 332, 4635, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3214, 3163, 2541, 3090, 3097, 3462, 3037, 3419, 2780, 2931, 1276, 2789, 3228, 2657, 3189, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3102, 3466, 3461, 2788, 2660, 3344, 2720, 3379, 2826, 3249, 3527, 4460, 3352, 4319, 3906, 4248, 3804, 1363, 1404, 4349, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 3092, 3459, 3144, 3441, 2802, 3479, 2907, 3512, 3518, 3021, 2871, 3032, 2647, 2945, 3045, 2763, 3313, 3034, 3315, 3541, 2746, 2669, 2524, 3003, 2732, 3166, 3046, 3306, 2873, 3364, 3253, 3215, 3061, 2804, 2722, 2964, 2990, 2836, 4098, 4449, 3173, 2762, 3737, 2628, 3507, 2564, 3031, 2872, 3360, 2658, 2930, 2904, 3244, 3217, 3311, 3445, 2840, 3372, 2958, 3098, 3356,

3456, 3388, 2624, 3207, 2576, 2742, 2665, 2815, 3052, 3421, 2593, 3242, 2535, 2966, 2898, 2858, 2943, 2668, 2798, 3196, 2528, 2713, 3001, 2691, 2948, 2767, 2544, 3302, 2734, 2893, 2592, 2861, 3502, 2969, 2582, 3229, 2676, 2545, 3255, 3330, 2547, 3257, 2882, 3151, 3088, 2883, 3318, 2645, 2733, 2587, 3500, 3008, 2715, 2845, 3183, 2654, 3233, 3267, 2741, 2827, 2704, 3091, 2832, 2736, 3177, 3271, 2835, 2908, 3176, 2947, 3292, 3191, 2517, 3026, 3082, 3392, 3782, 3629, 3578, 3885, 4081, 1764, 1852, 4431, 3241, 3077, 2700, 3147, 2648, 3283, 2829, 3278, 2581, 2536, 4363, 2848, 3410, 2797, 2523, 2520, 2721, 3496, 2571, 3198, 3219, 3030, 2673, 2921, 3837, 3301, 3322, 2705, 3239, 2949, 3369, 3396, 2892, 2897, 2766, 3174, 3297, 2550, 2889, 2933, 2793, 2627, 2677, 3119, 2596, 3226, 3172, 3089, 2868, 2839, 3942, 4222, 1504, 3180, 2813, 2652, 2600, 2816, 3201, 3188, 3270, 2997, 2992, 3009, 3520, 2936, 3275, 3165, 3447, 3131, 3305, 2809, 2792, 2729, 2814, 2619, 3266, 2825, 3066, 2857, 2998, 3064, 2681, 3035, 3279, 2764, 3480, 3127, 2912, 3010, 2607, 3211, 3111, 3909, 4269, 3019, 1415, 3020, 2748, 2646, 2787, 2760, 3158, 3170, 2703, 3494, 3404, 2675, 2749, 3341, 3355, 2594, 3495, 2884, 3516, 3042, 2737, 2923, 3563, 2855, 3476, 2611, 2937, 3383, 2875, 3223, 2878, 1808, 2951, 3519, 2579, 2853, 3387, 3401, 3007, 3568, 3152, 3367, 3358, 336, 3290, 3550, 3309, 2613, 2765, 1355, 2881, 3232, 3458, 3326, 3353, 2927, 3212, 2950, 3376, 3208, 3062, 3612, 3195, 3385, 2686, 1622, 3361, 3022, 3427, 3107, 3140, 3371, 3276, 2831, 3501, 2924, 3366, 3199, 3101, 3321, 3499, 2917, 2683, 1464, 3560, 3236, 2730, 3572, 1607, 909, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 3002, 2338, 4472, 1472, 1529, 4507, 1583, 340, 912, 2013, 913, 2277, 1594, 4440, 917, 343, 344, 345, 346, 350, 351, 4498, 3637, 3570, 3429, 4091, 4338, 3205, 2880, 3261, 3968, 4291, 4204, 4034, 2820, 3912, 3287, 1218, 1190, 4145, 354, 3610, 4224, 1840, 3736, 1770, 4155, 932, 363, 1279, 2156, 1722, 368, 1566, 370, 4967, 372, 1211, 2494, 1726, 1748, 1191, 4039, 4411, 4506, 4270, 4156, 3780, 1550, 3899, 1181, 3919, 1639, 3664, 4189, 4001, 3799, 1240, 1686, 1479, 1307, 1575, 4296, 1665, 3871, 1605, 4408, 4149, 3741, 3893, 1280, 1983, 3979, 3817, 1489, 4214, 3902, 1857, 1904, 3820, 3789, 4252, 4330, 4082, 3785, 3687, 4243, 3704, 4172, 4315, 1192, 2769, 2678, 3296, 2343, 4093, 4453, 3940, 3778, 4374, 4339, 4368, 4194, 4474, 4013, 1771, 1759, 3860, 3832, 1381, 4356, 1233, 4212, 3858, 1198, 3611, 1919, 1819, 3790, 1969, 4247, 1790, 3894, 1554, 3576, 4314, 1851, 1850, 4511, 3656, 3638, 1406, 1443, 1661, 4504, 3831, 4435, 1208, 1988, 3849, 1835, 4380, 4024, 4491, 4323, 4014, 1511, 1981, 1676, 1547, 1383, 3644, 3691, 4259, 1176, 4216, 1924, 1387, 4423, 1256, 4119, 1251, 3990, 4029, 4097, 3890, 3796, 4343, 1202, 4413, 4384, 3808, 3892, 3926, 3756, 4405, 4109, 1210, 4492, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3784, 4470, 4010, 4334, 3821, 4171, 3824, 3631, 4494, 1320, 1204, 1223, 1284, 1685, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4100, 4327, 3634,

3617, 4445, 4303, 1370, 3838, 1187, 3615, 3746, 3935, 1941, 4419, 1171, 3670, 3777, 936, 3685, 1325, 1940, 4482, 4258, 3812, 4124, 4508, 4500, 3652, 3972, 1630, 4421, 1172, 4026, 2740, 3125, 3546, 4513, 4340, 1763, 1487, 3589, 3907, 4041, 3851, 4077, 4187, 1193, 1196, 1724, 1717, 1200, 1975, 1613, 4006, 3653, 3833, 1593, 4442, 3900, 4388, 1820, 4317, 4249, 3628, 3794, 4447, 3776, 3658, 1377, 4011, 4272, 3594, 4185, 3686, 3696, 1350, 4230, 3853, 4244, 1909, 3897, 1546, 3273, 3452, 3525, 4105, 3835, 383, 1263, 1492, 3856, 3586, 1175, 4144, 1224, 1199, 3667, 2778, 4412, 1507, 3146, 4281, 1179, 3843, 3740, 1388, 1474, 1342, 1471, 4176, 1741, 1508, 4378, 1212, 4015, 1207, 3698, 3825, 4231, 3806, 3896, 3963, 4286, 3743, 4130, 3605, 4173, 4265, 1246, 1737, 3826, 1473, 1992, 1883, 1656, 3671, 4063, 1847, 4239, 3915, 1265, 1498, 1329, 3874, 4261, 1791, 3579, 4359, 4131, 4297, 4357, 4046, 3788, 4169, 1925, 4228, 4101, 1889, 1369, 4088, 4019, 1194, 3772, 3850, 1315, 1530, 1859, 4183, 1408, 4033, 3623, 1928, 1459, 1765, 4004, 3591, 3967, 4168, 3957, 3878, 3980, 3958, 4051, 3798, 4032, 3991, 4106, 1641, 4464, 3813, 4257, 3846, 4345, 1787, 1214, 4483, 4201, 1220, 3867, 3640, 3916, 1209, 4236, 4075, 4146, 4256, 4308, 4000, 4148, 3588, 3883, 4326, 4092, 4283, 1553, 3805, 4151, 1281, 1681, 4489, 3982, 4437, 3597, 4342, 3987, 3583, 3647, 389, 4304, 3793, 1937, 3996, 3800, 4367, 4099, 1390, 4364, 4306, 1278, 1672, 1542, 1915, 3600, 3948, 3811, 1362, 4276, 1445, 1721, 1632, 3607, 1317, 1778, 1668, 391, 4406, 4341, 1480, 393, 394, 395, 946, 3618, 4433, 1177, 947, 950, 400, 4471, 401, 402, 954, 3602, 4434, 3721, 1825, 4202, 4409, 406, 1631, 1684, 3889, 410, 412, 2352, 1905, 417, 418, 3675, 1833, 3974, 419, 964, 420, 421, 969, 4733, 1272, 971, 423, 3830, 973, 426, 1708, 428, 4141, 3749, 1619, 975, 4044, 3590, 1706, 4400, 979, 2895, 3448, 438, 982, 2433, 983, 442, 3862, 2435, 443, 4309, 4045, 3854, 3682, 444, 445, 4366, 3425, 3231, 3649, 2759, 2724, 3873, 3599, 3775, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 3694, 446, 3985, 3535, 4084, 3282, 988, 2107, 990, 451, 452, 453, 992, 993, 1696, 996, 3116, 1386, 999, 458, 3879, 460, 461, 462, 2339, 1003, 4425, 1645, 1004, 466, 2328, 468, 1231, 1468, 2496, 473, 474, 2108, 1273, 1007, 1744, 1659, 478, 1009, 1012, 4313, 482, 1499, 484, 2513, 2205, 4592, 1458, 4274, 2122, 4905, 4205, 2000, 488, 1894, 3917, 3616, 4311, 4085, 4401, 1310, 3783, 1538, 3870, 1948, 3699, 1735, 3792, 2202, 4090, 2378, 2012, 3642, 1020, 2302, 4665, 4781, 500, 1022, 1023, 4686, 505, 507, 508, 509, 1025, 1732, 1816, 3636, 1028, 516, 1366, 4572, 2489, 1261, 4027, 3763, 2959, 1293, 3197, 1448, 1032, 519, 2420, 522, 3759, 1215, 4122, 1730, 524, 526, 3966, 1035, 527, 528, 529, 530, 531, 1036, 532, 533, 536, 537, 3767, 1929, 1041, 3683, 1043, 4906, 542, 1338, 1796, 4331, 4332, 4466, 3803, 3087, 3505, 1449, 1044, 4414, 3453, 3254, 544, 546, 1045, 547, 4240, 3580, 4680, 549, 550, 2598, 551, 3819, 1259, 4062, 554, 1049, 1050, 1433, 555, 1052, 1053, 3738, 3857, 2089, 1056, 2193, 1257, 1238, 3662, 1059, 1060, 4203, 3981, 1303, 4116, 567, 569, 3620,

4002, 3679, 3707, 4497, 4438, 1264, 3939, 4170, 4056, 1271, 1451, 1654, 3934, 4080, 4352, 574, 3739, 1565, 1419, 3950, 3716, 1465, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4164, 3630, 4229, 4292, 4215, 1729, 4223, 4455, 4512, 3633, 4070, 4104, 4162, 4443, 3761, 1587, 3592, 1891, 4469, 1963, 4129, 1360, 3949, 1861, 4120, 1292, 4293, 3839, 3983, 3928, 4295, 3715, 3855, 3609, 1990, 4007, 3722, 1624, 3924, 3952, 580, 2003, 1343, 582, 4114, 1818, 1704, 4448, 584, 1078, 1786, 585, 1832, 586, 2891, 587, 4936, 1082, 4459, 2113, 590, 2308, 593, 1858, 597, 2738, 4150, 3260, 3481, 4439, 1268, 4050, 3377, 4424, 3492, 1412, 4477, 4263, 3072, 2009, 3888, 3827, 4103, 1438, 609, 610, 611, 3701, 4389, 613, 4369, 617, 1921, 1373, 1870, 4218, 1099, 1702, 4801, 623, 3700, 1788, 625, 4878, 1423, 1339, 3875, 628, 2557, 2906, 2029, 4876, 1103, 631, 4479, 3766, 632, 1104, 1105, 634, 4651, 1108, 1813, 636, 638, 641, 4581, 1112, 2164, 3735, 3390, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 4398, 1269, 3624, 4481, 1432, 3295, 1568, 1766, 2643, 2739, 4760, 1115, 3920, 644, 645, 646, 4279, 3762, 1637, 1509, 2200, 1117, 4780, 2965, 2695, 650, 651, 653, 654, 655, 658, 4035, 2910, 3391, 2808, 3676, 2852, 3284, 3537, 1319, 4467, 1802, 1227, 660, 4812, 2364, 1124, 1125, 665, 4917, 1127, 1129, 1132, 1133, 2236, 673, 4557, 1136, 1139, 678, 4737, 4531, 679, 680, 1144, 681, 4525, 2415, 685, 2445, 3822, 690, 691, 1601, 4621, 3905, 695, 1149, 696, 2027, 2160, 1795, 1372, 4115, 2194, 1920, 4031, 1393, 1277, 1400, 4402, 4157, 4028, 704, 1902, 1510, 4182, 1153, 4476, 2053, 710, 1375, 715, 4096, 717, 1155, 719, 1311, 722, 4217, 1156, 723, 1157, 1627, 4566, 1158, 724, 725, 1953, 1201, 3787, 3747, 1846, 3815, 1822, 1537, 1318, 4294, 733, 734, 3439, 2833, 4505, 4267, 3697, 4112, 2967, 3651, 1805, 1163, 3859, 2275, 737, 1167, 1745, 3807, or 4307.

[0210] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^6 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 1308, 3960, 1378,

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2575, 2942, 2886, 2758, 2594, 3495, 2884, 3516, 3042, 2737, 2923, 3563, 2855, 3476, 2611, 2937, 3383, 3497, 3402, 3162, 2662, 2875, 3223, 2878, 1808, 3285, 2757, 3057, 2951, 3519, 2579, 2853, 3387, 3401, 3493, 3393, 1608, 3365, 2885, 3574, 3081, 3007, 3568, 3152, 3367, 3358, 336, 3468, 3290, 3550, 3132, 2726, 2879, 3190, 3309, 2613, 2765, 3106, 1355, 3454, 2851, 2881, 3232, 3458, 3326, 3353, 2927, 3212, 2950, 3376, 3208, 3062, 3612, 3195, 3385, 2686, 2602, 3569, 3123, 2727, 1622, 2821, 2636, 2750, 2850, 3050, 2925, 3336, 3540, 2689, 3139, 2526, 3361, 3022, 3427, 3107, 3140, 3371, 3276, 2831, 3501, 2924, 3366, 3199, 3101, 3321, 3499, 2917, 2683, 2800, 2812, 3340, 3227, 3148, 3657, 4446, 1464, 1886, 2666, 3246, 3130, 3560, 3236, 2730, 3572, 3689, 2968, 1457, 3450, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 4147, 3002, 2986, 910, 2979, 2542, 1762, 4472, 1529, 4057, 1976, 4507, 1583, 1711, 2013, 1594, 4440, 344, 920, 921, 4498, 3728, 3637, 3570, 3429, 4091, 2870, 2995, 4338, 3205, 2880, 3261, 3968, 4291, 4204, 4071, 4034, 1742, 2820, 3912, 3287, 1218, 1190, 4145, 354, 1782, 927, 3610, 356, 4224, 1918, 1959, 1840, 3736, 1770, 929, 930, 931, 4155, 360, 361, 362, 364, 1279, 365, 1543, 366, 367, 4049, 1633, 1722, 369, 1495, 1566, 373, 1211, 1726, 1442, 1748, 4142, 1434, 1358, 1191, 3732, 4110, 4039, 4506, 4156, 4036, 4030, 4016, 3899, 1247, 1855, 3919, 1244, 4140, 3930, 4117, 4189, 4001, 3643, 3619, 1240, 1575, 3871, 4135, 4408, 3604, 1274, 4149, 3741, 1938, 3709, 3622, 3834, 1983, 1743, 3979, 4461, 4113, 3817, 4232, 4214, 3902, 1219, 1486, 1512, 1516, 4047, 4082, 4094, 1574, 1248, 4078, 1872, 1426, 3687, 4318, 4243, 3866, 3704, 4172, 1856, 3324, 2769, 2678, 1561, 3296, 377, 1395, 1584, 4093, 4453, 4210, 4009, 4264, 4339, 1738, 4474, 4013, 4266, 1771, 1759, 1922, 3860, 3832, 1349, 1381, 3663, 1185, 3932, 3858, 1198, 4192, 3611, 1919, 3790, 3712, 4095, 1887, 4468, 1720, 4247, 934, 1790, 2002, 1657, 1336, 3894, 3576, 4314, 3695, 1850, 4362, 1815, 3638, 4454, 1661, 4504, 1359, 3650, 1305, 1648, 3831, 4435, 4451, 1993, 3849, 1718, 4068, 1835, 1425, 1428, 4380, 1658, 1452, 4024, 4072, 3791, 4491, 4323, 4014, 1304, 1511, 1981, 1676, 4422, 1283, 3861, 3644, 4259, 1418, 1176, 4216, 1421, 3992, 4423, 4253, 3748, 4119, 1297, 1954, 4450, 3711, 4344, 1578, 4384, 3892, 3674, 3595, 4405, 3973, 4109, 4159, 3744, 4387, 4275, 4492, 4365, 4118, 4278, 3751, 3678, 4353, 3175, 2970, 1228, 3534, 3437, 3406, 3641, 4470, 3941, 4348, 3587, 3818, 4350, 3821, 3929, 3824, 4465, 1398, 3828, 1284, 3773, 4209, 3014, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4163, 4486, 4178, 1643, 4152, 4445, 4303, 4284, 1213, 4382, 1399, 3714, 4487, 3615, 4018, 4420, 4121, 3724, 4282, 4310, 4488, 4127, 3670, 4052, 3627, 3777, 1371, 3685, 4258, 3812, 1581, 4124, 4508, 4500, 3652, 3972, 1528, 3717, 2740, 3125, 3546, 3842, 4404, 3690, 3962, 4136, 3589, 3907, 4153, 2707, 4180, 3923, 4444, 4361, 4394, 3758, 4510, 3742, 1710, 1407, 4187, 1193, 1188, 1196, 1724, 1717, 1200, 1997, 1701, 4280, 4006, 1984, 3833,

2561, 4442, 3900, 4298, 1761, 4388, 1597, 4317, 4249, 1341, 1203, 1680, 4441, 3628, 3725, 1945, 937, 4206, 1588, 1439, 3794, 4447, 3776, 3658, 4064, 4011, 4272, 4503, 1324, 3594, 3680, 1300, 1750, 3913, 3774, 1877, 1987, 3998, 3686, 3696, 4463, 3853, 4244, 4083, 1909, 3897, 1546, 3613, 3273, 3452, 3525, 1229, 3835, 1234, 3970, 3856, 3586, 1175, 4321, 2778, 4412, 4407, 3823, 1427, 1507, 1878, 4333, 3146, 4281, 4211, 3843, 1677, 1524, 1525, 1974, 1239, 4167, 3740, 1342, 1471, 4176, 1232, 1989, 4125, 1741, 1580, 4060, 1576, 1212, 3921, 1174, 4061, 4021, 3693, 3734, 1382, 3684, 3806, 3635, 3976, 3840, 4286, 3836, 4161, 3659, 3605, 4392, 4328, 1316, 4173, 4265, 1246, 1629, 1829, 3826, 1992, 1656, 1914, 1839, 3984, 3910, 4160, 4184, 4132, 4250, 1792, 3769, 1534, 4003, 1689, 1599, 1265, 1410, 1823, 1498, 1329, 386, 940, 1655, 3874, 4261, 3626, 3579, 1644, 3936, 4054, 4260, 4297, 4357, 4022, 4046, 1222, 1996, 3788, 3953, 4226, 4277, 4101, 3797, 4019, 3771, 3632, 1402, 4137, 3772, 3661, 4186, 4174, 1170, 3850, 1315, 1611, 1859, 4183, 1403, 4033, 3623, 3596, 1461, 1848, 1173, 1928, 1765, 3719, 3584, 4165, 4191, 3980, 4058, 4200, 4336, 3958, 1260, 4051, 3798, 4032, 1774, 4322, 3991, 4106, 3978, 3965, 4464, 3813, 4154, 1365, 3846, 4345, 4379, 3603, 3937, 3801, 1787, 1214, 4483, 4201, 1845, 1220, 4245, 1347, 3867, 1900, 3640, 3916, 4089, 3745, 3975, 4256, 4308, 4000, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 4005, 4092, 4372, 4283, 3805, 4151, 3982, 3597, 3872, 3987, 4490, 3876, 3668, 4300, 1679, 1242, 3598, 3583, 3647, 4304, 3779, 1907, 4042, 3648, 3996, 3800, 4367, 4099, 1807, 3887, 4428, 1625, 1390, 1884, 1682, 4364, 4306, 3869, 1278, 942, 1505, 1709, 3600, 3914, 3948, 1865, 1716, 3961, 1506, 4221, 1376, 1683, 4276, 1721, 1632, 3607, 1455, 1913, 1497, 1317, 1951, 1778, 3768, 4225, 1668, 390, 4406, 4341, 1480, 1714, 1422, 397, 3618, 4433, 1177, 3898, 398, 950, 400, 1965, 4471, 953, 401, 403, 955, 1482, 3602, 4434, 3721, 1592, 1825, 1698, 1519, 1352, 4409, 1977, 405, 1631, 1684, 409, 3889, 2117, 411, 413, 414, 415, 961, 1905, 416, 963, 3675, 1833, 3974, 965, 970, 1897, 1272, 4133, 3830, 972, 424, 427, 1708, 4141, 3749, 1619, 975, 4044, 3590, 1944, 4126, 1923, 1706, 432, 976, 978, 4400, 1606, 980, 2604, 2895, 436, 3448, 2188, 438, 1692, 442, 3862, 4055, 4358, 2276, 985, 1664, 443, 4309, 4045, 3854, 3682, 1972, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3755, 1216, 3599, 3775, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3694, 3985, 3535, 1306, 4084, 3282, 1780, 448, 990, 991, 1485, 992, 1728, 993, 994, 1696, 997, 3116, 1869, 456, 1386, 1000, 3879, 2698, 460, 1001, 461, 1447, 1002, 1003, 463, 464, 4425, 465, 1004, 466, 469, 1231, 1468, 470, 1005, 476, 1273, 1744, 1488, 1659, 1604, 479, 1013, 1014, 481, 4313, 1499, 1016, 4073, 1777, 485, 4274, 487, 1775, 4205, 1526, 1697, 2000, 488, 1894, 1882, 1817, 1880, 490, 1018, 3917, 3616, 4311, 4473, 4085, 4401, 3783, 3765, 1538, 3870, 491, 3699, 3792, 4290, 494, 2421, 4090, 2012, 1803, 3642, 1322, 1020, 502, 1333, 504, 1890, 507, 3608, 1732, 1864, 1816, 1531, 513, 3636, 514, 1699,

1027, 1366, 4950, 4027, 3478, 2959, 1293, 3197, 1595, 3413, 518, 1032, 1033, 1675, 1797, 2315, 521, 1999, 3759, 1215, 4122, 1730, 3966, 1035, 4973, 528, 3911, 3289, 1821, 530, 532, 1874, 533, 1038, 538, 539, 3767, 1929, 3683, 1338, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 3720, 4351, 4414, 3453, 3254, 1649, 544, 4240, 3580, 1046, 548, 549, 2598, 552, 553, 3819, 1259, 4062, 554, 2841, 3515, 1433, 1323, 4301, 555, 558, 3738, 1567, 559, 1054, 1270, 3857, 2175, 1257, 1238, 3662, 561, 1058, 563, 1061, 4203, 1899, 3981, 1062, 1303, 4116, 1946, 3620, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 1401, 4438, 1895, 1264, 1912, 573, 3939, 4170, 4056, 1271, 1521, 1221, 1451, 3934, 4080, 4352, 1700, 3739, 1419, 1811, 3950, 1690, 3716, 1569, 1437, 1674, 4337, 1285, 4268, 1183, 3881, 3938, 4198, 4416, 4229, 4292, 4193, 4325, 4375, 4432, 4215, 3944, 4195, 4223, 1540, 4455, 4512, 1723, 3750, 4070, 4104, 4235, 1863, 4346, 1881, 1814, 4443, 3761, 1587, 3592, 576, 4469, 1275, 1950, 4129, 1296, 1551, 3733, 4111, 3993, 4108, 1287, 1713, 1556, 1736, 1995, 1705, 1861, 4120, 4417, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 3928, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1757, 4299, 1773, 1364, 1462, 4007, 3729, 3665, 3722, 1691, 1712, 1624, 1751, 1394, 3924, 3952, 581, 2003, 1559, 1250, 1555, 4114, 1818, 1076, 4448, 1078, 1786, 3354, 1832, 3432, 2891, 1903, 4459, 589, 1563, 1084, 591, 592, 594, 595, 1858, 596, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 4439, 3852, 3997, 3847, 4050, 3377, 4424, 4143, 4493, 3492, 1412, 4017, 4477, 1794, 602, 4263, 3072, 2009, 1754, 3888, 603, 604, 1368, 3827, 4103, 1571, 1438, 611, 1093, 612, 1094, 3701, 4389, 614, 615, 1332, 1715, 4369, 1652, 1541, 1921, 1733, 1373, 1870, 619, 4218, 1798, 1702, 1384, 3700, 1788, 1600, 624, 2473, 1423, 2771, 1339, 3875, 3070, 2015, 2557, 2795, 2906, 2103, 3299, 3118, 4576, 1103, 1614, 1947, 631, 4479, 3766, 1107, 635, 1813, 636, 2431, 637, 1109, 639, 3706, 1110, 640, 642, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1568, 1766, 3221, 2643, 2739, 3920, 647, 1801, 4279, 3762, 1637, 1509, 648, 1117, 1119, 2965, 2695, 3293, 4722, 1121, 653, 1122, 3264, 655, 656, 657, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3537, 3994, 1319, 4467, 1623, 660, 1123, 664, 1126, 1128, 1129, 1130, 670, 1527, 671, 1772, 1137, 5005, 1933, 1731, 1793, 3342, 1140, 1141, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 1920, 4999, 1544, 703, 4031, 4305, 1636, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 4028, 3989, 704, 1493, 1902, 1152, 4182, 707,

708, 709, 4476, 1375, 713, 714, 1841, 4234, 1154, 1314, 4096, 718, 719, 720, 2063, 1311, 721, 4217, 1627, 1158, 1953, 1201, 3787, 729, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 2423, 1745, 1973, 3807, 4307, 1169, 1454, or 1781.

[0211] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^7 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 740, 15, 742, 743, 17, 22, 24, 1836, 32, 36, 2450, 39, 752, 753, 1998, 3059, 2519, 757, 48, 1952, 50, 52, 760, 2389, 54, 2346, 58, 4086, 1660, 1966, 768, 2402, 772, 71, 72, 2453, 3882, 775, 1806, 3669, 1356, 2132, 81, 84, 85, 87, 4040, 88, 1885, 782, 783, 784, 785, 94, 788, 2173, 98, 2007, 102, 113, 799, 4848, 1444, 4821, 2329, 115, 119, 2290, 123, 806, 128, 134, 812, 145, 817, 154, 2149, 821, 167, 171, 4596, 183, 830, 191, 194, 2071, 195, 4920, 831, 2223, 207, 3901, 211, 212, 213, 215, 224, 4782, 845, 846, 849, 850, 854, 247, 248, 2245, 255, 261, 264, 265, 1477, 270, 874, 876, 279, 882, 1930, 285, 286, 886, 2119, 2468, 887, 888, 4138, 297, 3844, 302, 893, 307, 308, 2155, 1431, 2312, 900, 1635, 906, 2799, 2128, 2918, 1363, 4251, 2622, 3333, 3474, 3614, 2732, 3166, 3151, 3088, 2883, 3318, 2645, 2733, 3213, 3782, 1844, 2523, 2520, 2997, 2681, 3035, 3279, 2764, 3480, 2787, 1808, 3101, 3689, 4147, 1762, 1976, 340, 1594, 2439, 348, 4498, 1518, 1782, 926, 357, 359, 932, 363, 369, 1873, 3780, 4140, 4001, 3709, 3834, 1752, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 3820, 4330, 1872, 3687, 4318, 375, 4210, 3860, 4212, 3695, 1851, 4504, 1910, 1428, 4323, 4422, 4259, 1176, 3711, 4365, 4383, 3969, 4128, 3802, 3863, 3821, 4171, 3824, 4462, 3760, 3753, 2783, 3880, 3943, 4163, 4178, 4199, 3724, 3670, 4482, 3692, 4430, 4316, 3645, 3690, 3589, 3730, 4426, 3851, 4429, 1335, 1717, 1997, 1975, 4280, 4006, 3900, 4298, 4388, 1341, 1350, 1909, 4412, 4407, 4281, 4167, 1893, 3585, 4015, 1747, 4286, 3826, 1473, 1914, 3984, 4495, 4184, 3977, 1707, 4074, 4003, 3915, 1410, 1498, 940, 4131, 4357, 1925, 1466, 1611, 1530, 4168, 4245, 4075, 3987, 1679, 4306, 3869, 3768, 393, 2265, 3618, 4433, 947, 399, 401, 402, 4139, 1352, 406, 415, 418, 420, 4919, 431, 4044, 976, 433, 434, 435, 442, 3873, 3411, 3985, 987, 1485, 2262, 457, 458, 4425, 466, 467, 468, 1468, 474, 1008, 1012, 1016, 4518, 1697, 490, 3616, 2247, 2302, 499, 500, 501, 509, 2110, 512, 1797, 520, 525, 3966, 1038, 537, 1041, 3683, 2165, 542, 4331, 3129, 1044, 4351, 3453, 1047, 1323, 4301, 557, 3738, 559, 1270, 3857, 1056, 2186, 1057, 1059, 565, 566, 3981, 567, 3620, 4002, 3666, 3939, 1221, 1397, 1437, 4337, 4268, 3938, 4292, 4215, 3750, 3633, 4070, 3592, 1827, 3839, 4395, 3855, 3665, 1624, 2395, 1818, 586, 587, 1903, 1080, 1081, 1082, 589, 1084, 1085, 594, 596, 4439, 3997, 1962, 1087, 4777, 606, 607, 610, 1094, 4389, 1603, 1095, 616, 618, 622, 1104, 4536, 3706, 2481, 3100, 3200, 3621, 4179, 1432, 4381, 643, 1115, 644, 2307, 2477, 652, 657, 658, 3994, 4467,

661, 663, 665, 4600, 1137, 1933, 4840, 1140, 678, 680, 683, 686, 692, 693, 696, 2081, 2280, 698, 1400, 4197, 1532, 1854, 706, 711, 712, 4570, 714, 1841, 1314, 4096, 2249, 726, 1846, 2385, 1318, 733, 3651, 1165, 4839, 4968, 4684, or 1454.

[0212] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is a basic amino acid residue. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 739, 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 52, 760, 53, 762, 4659, 54, 3925, 55, 3654, 56, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 2399, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 75, 1312, 4501, 76, 77, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 1180, 92, 785, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 794, 795, 104, 105, 106, 1849, 108, 4736, 1579, 110, 1906, 113, 1444, 1344, 116, 802, 117, 118, 2158, 121, 803, 804, 1463, 805, 122, 2058, 124, 125, 127, 4994, 807, 132, 809, 810, 133, 1978, 812, 135, 136, 137, 138, 813, 4673, 140, 815, 1326, 141, 142, 143, 144, 145, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 151, 152, 153, 154, 155, 819, 820, 157, 821, 159, 160, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 180, 826, 827, 181, 828, 182, 183, 4641, 829, 184, 185, 186, 187, 188, 189, 830, 191, 192, 193, 194, 195, 196, 1391, 197, 2223, 200, 201, 202, 203, 204, 205, 832, 833, 206, 834, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 215, 1896, 1522, 3490, 838, 2241, 217, 218, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 226, 227, 230, 231, 842, 232, 233, 235, 844, 236, 237, 2150, 851, 852, 853, 1536, 240, 854, 242, 243, 244, 245, 246, 247, 855, 4634, 249, 250, 251, 252, 253, 254, 255, 857, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 869, 870, 271, 871, 872, 272, 874, 1252, 273, 1591, 275, 1980, 276, 876, 877, 277, 278, 279, 1892, 879, 1539, 880, 1295, 3601,

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[0213] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^6 of SEQ ID NO: 5014 is a basic amino acid residue. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 4884, 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 4889, 21, 3192, 4942, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 2450, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 759, 50, 1308, 3960, 1378, 2994, 3080, 2589, 3681, 51, 760, 2389, 762, 3925, 3654, 763, 4626, 59, 60, 4086, 1740, 1660, 62, 1966, 63, 2438, 768, 66,

67, 2197, 68, 3816, 2599, 2706, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 1312, 4501, 76, 1413, 775, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 1356, 2132, 4065, 1294, 1484, 85, 86, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 780, 1180, 92, 781, 782, 783, 2356, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 1936, 1590, 98, 99, 789, 790, 1298, 101, 1688, 791, 792, 2007, 102, 103, 104, 105, 107, 108, 1579, 110, 1906, 111, 798, 112, 799, 800, 2461, 1444, 801, 114, 115, 1344, 116, 802, 117, 118, 119, 121, 803, 1463, 1760, 124, 806, 126, 128, 807, 129, 131, 808, 2281, 133, 1978, 811, 812, 135, 136, 137, 138, 814, 140, 1326, 141, 142, 143, 2344, 816, 1634, 1302, 817, 818, 147, 148, 149, 150, 151, 154, 155, 819, 820, 156, 157, 2295, 158, 161, 162, 165, 822, 168, 169, 170, 823, 172, 1651, 173, 1483, 174, 825, 176, 178, 180, 827, 181, 828, 4911, 184, 185, 186, 188, 189, 830, 192, 193, 194, 196, 1391, 197, 198, 199, 200, 201, 202, 203, 4775, 205, 832, 206, 834, 207, 208, 209, 210, 835, 836, 1334, 3901, 3312, 2649, 1450, 4386, 3028, 1446, 2206, 215, 1522, 3490, 217, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 225, 4751, 228, 229, 230, 231, 2448, 842, 232, 233, 4782, 234, 235, 238, 847, 239, 850, 851, 853, 1536, 240, 241, 242, 243, 244, 245, 246, 247, 4923, 4696, 250, 251, 254, 255, 857, 256, 258, 259, 859, 260, 861, 862, 4966, 864, 263, 4970, 2318, 865, 2326, 264, 1241, 266, 1477, 867, 268, 868, 269, 270, 869, 870, 271, 871, 872, 272, 873, 4655, 4972, 1252, 1591, 875, 274, 275, 1980, 276, 876, 877, 2066, 277, 278, 280, 2323, 1892, 1539, 2214, 881, 882, 3601, 3877, 1930, 1460, 282, 1799, 284, 4553, 4772, 1626, 286, 1374, 1620, 1290, 1354, 887, 1956, 889, 4765, 292, 4324, 4138, 891, 296, 3903, 297, 3829, 3809, 4271, 3844, 1436, 300, 1617, 1961, 5010, 302, 304, 305, 2147, 1589, 4370, 307, 3646, 4059, 1431, 1331, 312, 1779, 313, 896, 1558, 1552, 318, 319, 322, 1958, 2454, 323, 324, 901, 1491, 328, 329, 330, 4820, 4484, 1756, 907, 4584, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3414, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 4248, 1557, 3804, 1602, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527,

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[0214] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is a basic amino acid residue and X^6 of SEQ ID NO: 5014 is a basic amino acid residue. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 35, 36, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 45, 756, 48, 1952, 3122, 2551, 3718, 3484, 3577, 759, 3960, 1378, 2994, 3080, 2589, 3681, 760, 762, 3925, 3654, 60, 4086, 1740, 1660, 62, 1966, 63, 768, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 1312, 4501, 76, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 4065, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 1180, 92, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 104, 105, 108, 1579, 110, 1906, 1444, 1344, 116, 802, 117, 118, 121, 803, 1463, 124, 807, 133, 1978, 812, 135, 136, 137, 138, 140, 1326, 141, 142, 143, 1634, 1302, 817, 818, 147,

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[0215] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 760, 53, 3925, 55, 3654, 56, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 3882, 3713, 1942, 1312, 4501, 76, 77, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 90, 91, 779, 1180, 92, 785, 786, 94,

95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 794, 795, 104, 105, 106, 1849, 108, 1579, 110, 1906, 113, 1444, 1344, 116, 802, 117, 118, 121, 803, 804, 1463, 805, 122, 124, 125, 127, 807, 132, 809, 810, 133, 1978, 812, 135, 136, 137, 138, 813, 140, 815, 1326, 141, 142, 143, 144, 145, 1634, 1302, 817, 146, 818, 147, 148, 149, 151, 152, 153, 154, 155, 819, 820, 157, 159, 160, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 826, 827, 181, 828, 182, 829, 184, 185, 186, 187, 188, 189, 830, 191, 192, 193, 194, 195, 196, 1391, 197, 200, 201, 202, 203, 204, 205, 832, 833, 206, 834, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 215, 1896, 1522, 3490, 838, 217, 218, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 226, 227, 230, 231, 842, 232, 233, 844, 236, 237, 851, 852, 853, 1536, 240, 854, 242, 243, 244, 245, 246, 247, 249, 250, 251, 252, 253, 254, 255, 857, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 264, 1241, 265, 266, 866, 1477, 267, 867, 869, 870, 271, 871, 872, 272, 1252, 273, 1591, 275, 1980, 276, 876, 877, 277, 278, 279, 1892, 1539, 880, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 282, 1799, 283, 1626, 1374, 287, 1620, 1290, 1354, 888, 291, 1956, 889, 292, 4324, 293, 4138, 891, 3903, 297, 3829, 3809, 4271, 3844, 1436, 1515, 1617, 1961, 304, 306, 1589, 4370, 308, 309, 894, 3646, 4059, 1431, 1331, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 898, 321, 322, 899, 1958, 901, 325, 902, 326, 1491, 329, 330, 905, 4484, 1756, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 1888, 4248, 1557, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 1345, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920,

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[0216] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^6 of SEQ ID NO: 5014 is K or R. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469,

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5005, 1933, 1731, 1793, 3342, 1140, 1141, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 1920, 4999, 1544, 703, 4031, 4305, 1636, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 4028, 3989, 704, 1493, 1902, 1152, 4182, 707, 708, 709, 4476, 1375, 713, 714, 1841, 4234, 1154, 1314, 4096, 718, 719, 720, 2063, 1311, 721, 4217, 1627, 1158, 1953, 1201, 3787, 729, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 2423, 1745, 1973, 3807, 4307, 1169, 1454, or 1781.

[0217] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is not D. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 2167, 52, 760, 53, 2389, 4755, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 2140, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2379, 81, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 4556, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 1579, 110, 1906, 111, 2428, 798, 2075, 112, 2411, 113, 2359,

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1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 4628, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 2275, 1166, 4968, 4912, 2423, 737, 1167, 4989, 4684, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0218] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^6 of SEQ ID NO: 5014 is not D. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 2167, 52, 760, 53, 2389, 4934, 4951, 4755, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773,

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1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4606, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 4879, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4642, 722, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 2024, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4628, 4294, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4835, 2259, 4571, 2275, 1166, 4968, 2250, 2423, 737, 1167, 4989, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0219] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is not D and X^6 of SEQ ID NO: 5014 is not D. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777,

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[0220] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is not E. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107,

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3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4516, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 2191, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4606, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 4879, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4642, 722, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 730, 731, 2024, 1846, 2507, 2368, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 2275, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0221] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^6 of SEQ ID NO: 5014 is not E. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 2167, 52, 760, 53, 2389, 4934, 4951, 4755, 761, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2132, 2379, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 787, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 4585, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 109, 1579, 110, 1906, 111, 2428, 798, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4864, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 144, 145, 816, 4654, 2125, 4663, 4810, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159,

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4875, 4627, 4515, 4876, 4965, 4605, 4576, 2028, 4985, 4850, 1103, 4757, 4747, 1614, 1947, 2237, 630, 631, 4997, 4618, 4479, 3766, 632, 1104, 1105, 4886, 1106, 2432, 633, 1107, 4530, 634, 2371, 4651, 1108, 4536, 635, 1813, 636, 2431, 4866, 4991, 4814, 4560, 4956, 637, 4555, 1109, 4941, 4577, 4633, 2213, 638, 639, 3706, 1110, 640, 1111, 641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4524, 4881, 4837, 4888, 4648, 642, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 4629, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4603, 4762, 4819, 2221, 4636, 4992, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 2477, 4724, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 4714, 4979, 4812, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 2456, 4606, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 677, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 718, 1155, 719, 720, 2063, 1311, 721, 4642, 722, 4833, 4903, 4885, 4666, 2249, 4217,

1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 2024, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4628, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0222] A VP capsid polypeptide may have a 581 to 589 region having a sequence of SEQ ID NO: 5014, wherein X^3 of SEQ ID NO: 5014 is not E and X^6 of SEQ ID NO: 5014 is not E. In some embodiments, the 581 to 589 region has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 52, 760, 53, 2389, 4934, 4951, 761, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2132, 2379, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 787, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 4585, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792,

2007, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 109, 1579, 110, 1906, 111, 2428, 798, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 144, 145, 816, 4654, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 2170, 4809, 4520, 180, 826, 827, 181, 828, 4695, 4911, 182, 4582, 4873, 4596, 2020, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 2114, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 2187, 4914, 4947, 196, 1391, 197, 4534, 4726, 4788, 198, 199, 4920, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4953, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 5007, 4542, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2393, 2448, 841, 842, 232, 233, 4782, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 4704, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4923, 2245, 4696, 855, 4634, 856, 249, 250, 251, 252, 253, 254, 255, 857, 2115, 4880, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 4966, 863, 864, 263, 4749, 4970, 2296, 2318, 865, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 4977, 268, 868, 269, 4668, 5002, 270, 869, 870, 271, 871, 872, 272, 4822, 4709, 873, 4655, 4972, 2392, 874, 1252, 273, 1591, 4975, 875, 274, 2025, 275, 1980, 276, 876, 877, 2066, 277, 278, 279, 4670, 280, 2323, 2288, 2334, 4689, 281, 878, 1892, 879, 1539, 2214, 2215, 880, 2327, 881, 882, 4601, 883, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 2306, 884, 282, 1799, 283, 284, 4988, 4553, 4772, 4817, 2260, 285, 1626, 2082, 885, 286, 1374, 886, 2119, 2468, 287, 1620, 1290, 2425, 2482, 4671, 2282, 288, 2354, 1354, 2033, 289, 887, 290, 888, 291, 1956, 2467, 889, 2357, 4547, 4765, 292, 4794, 2391, 4324, 890, 294, 295, 4138, 891, 2297, 296, 2224, 3903, 297, 892, 3829, 298, 299, 3809, 4271, 3844, 1436, 300, 1515, 1617, 4701, 2174, 301, 1961, 4649, 5010, 302, 303, 304, 305, 2452, 2147, 306, 2293, 1589, 893, 4370, 4841, 2342, 307, 308, 309, 894, 2246, 2155, 3646, 4059, 1431, 1331, 310, 311, 4836, 4948, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 317, 2312, 318, 319, 897, 320, 898, 321, 322, 899, 1958, 2022, 2016, 900, 2454, 323, 2427,

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1332, 1715, 4369, 1652, 1096, 617, 1541, 618, 1921, 1733, 1373, 1870, 619, 4218, 1798, 2387, 1097, 1098, 1099, 1100, 620, 1702, 621, 622, 4801, 2398, 2239, 1101, 1667, 1384, 623, 4745, 3700, 1788, 1600, 624, 2098, 625, 4550, 4721, 4960, 4878, 2473, 4792, 4675, 1102, 1423, 626, 2771, 627, 1339, 3875, 628, 629, 3070, 4565, 2118, 4818, 2557, 2795, 2906, 2103, 4869, 2029, 3299, 3118, 4932, 4838, 4901, 4657, 4646, 4875, 4627, 4515, 4876, 4965, 4605, 4576, 2028, 4985, 4850, 1103, 4747, 1614, 1947, 2237, 630, 631, 4618, 4479, 3766, 632, 1104, 1105, 4886, 1106, 2432, 633, 1107, 4530, 634, 2371, 4651, 1108, 4536, 635, 1813, 636, 2431, 4866, 4991, 4814, 4560, 4956, 637, 4555, 1109, 4941, 4577, 2213, 638, 639, 3706, 1110, 640, 1111, 641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4524, 4881, 4837, 4888, 4648, 642, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 2456, 4606, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 677, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4476, 2053, 710,

1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 718, 1155, 719, 720, 2063, 1311, 721, 4642, 722, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 730, 731, 2024, 1846, 2507, 2368, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

[0223] RPE Tissue-Tropic AAV VP Capsid Polypeptides. Described herein are engineered AAV VP capsid polypeptides comprising a variant 581 to 589 region predicted to confer increased RPE tissue tropism compared to a wild type AAV VP capsid polypeptide (e.g., a wild type AAV5 capsid polypeptide of SEQ ID NO: 1), generated and selected using machine learning. In some embodiments, an RPE tissue-tropic engineered AAV VP capsid polypeptide may also have tropism for choroid tissue. **TABLE 9** provides 581 to 589 region sequences predicted to confer RPE tissue tropism or preference.

TABLE 9 – Additional Exemplary 581 to 589 Region Sequences for RPE Targeting

SEQ ID NO	581 to 589 Region
4514	QTEFVCSGK
4515	TEINDTKST
4516	TNLPMEMIP
4517	HPDPTAEYA
4518	NHDVTPREY
4519	EPTACGVEI
4520	EAVQTAEHN
4521	DPNQCWMMN
4522	TWLELDMEC
4523	HATVFDENN
4524	TIPMHDQAK
4525	TWLDKHCVA
4526	PPTVTQCMH
4527	TVPCNGEHS
4528	NEHTDVQGE
4529	HATMCNQKS
4530	TGTVMQKAD
4531	TVPMKGMEE
4532	NMTHTQNEI
4533	DQTLCEEPP
4534	EHTIFGESG
4535	EVENKIYGH
4536	THGSVCRPD
4537	VATPECQAY
4538	GNEPDVQYN
4539	NEHSTGKAC
4540	NTDWLCDMN
4541	TNMMCNEGP
4542	EPDYKVAQP
4543	PETVGYKHC
4544	DTQFLDMVK
4545	NATMYVEER
4546	DVNPRGEAI
4547	GDNVTVEAP
4548	TITCQEARC
4549	SSHNLCCVT
4550	TATAHCMEG
4551	TPFADLCVC
4552	YTDSANNAI
4553	FQMQMHAYA
4554	TTDFAGMVQ
4555	THTCNWAEQ
4556	DALNREEAC
4557	TVENKSADA

SEQ ID NO	581 to 589 Region
4558	TVEMWNYCC
4559	IEPATPHCD
4560	THQNTFLTV
4561	HAVNTCEEQ
4562	MQNPFYEQT
4563	MEQKNETSG
4564	FVTDKEAVA
4565	TCTDIFHQA
4566	VTLMKDSAC
4567	ENEPGQTAC
4568	VYHCPSEED
4569	TTCWINNEG
4570	VQCVCLRNY
4571	YQDTFHEAN
4572	PEQTKACYA
4573	QATPCCEQP
4574	GNEACPKQI
4575	VEHTVCEIC
4576	TEQFAKNSA
4577	TIDVTHAAC
4578	PSTVNHCFT
4579	DHTPGGEPP
4580	TNTPASHDA
4581	TILMKHASQ
4582	EESQTVLIY
4583	SEIASHKLT
4584	HAQMQHCYV
4585	DADTWVMMC
4586	NGTSAPCML
4587	YICPSHNLN
4588	TVEIWNHDT
4589	MILTHTDVK
4590	TNLPDHMSY
4591	ATGQKEMIC
4592	NATFKNEMP
4593	NYQFCNEAA
4594	CQTVHYCPI
4595	NEVIAYCRH
4596	EFDPPNRYH
4597	TVLEMWMMC
4598	MVQATHCSI
4599	NEDVYHSEC
4600	TTVNLNREP
4601	FIPATNAGS

SEQ ID NO	581 to 589 Region
4602	NHDTCNEGW
4603	TNEDQHCAI
4604	PTEQTNAEA
4605	TEPGDHCEY
4606	TVDQMYAIA
4607	TMQSVNKGA
4608	NTENEAHAQ
4609	HAQNREACN
4610	TVEPTFAGY
4611	TMVQHTKSI
4612	YTFQCNAEA
4613	EAQFNSEHT
4614	NQTPGDKDG
4615	EHFNPVEYT
4616	PNEQYGNWI
4617	PPVQVGFAS
4618	TGHMNCEYY
4619	LNTVCYDKY
4620	NQTACYKWD
4621	VAYQKVEPT
4622	VTPPTNQYC
4623	NETDVEMMK
4624	EATGCNESD
4625	VATQCSAER
4626	ATVMTHSAC
4627	TEHQFAQKS
4628	YGEETSMTC
4629	TMEQTHNEY
4630	IPCPTCYGH
4631	EACDGVKIH
4632	DAQCYGLPS
4633	TIEWMNEMY
4634	ETHVQYMPD
4635	HATIRGEHQ
4636	TNEMGVERY
4637	QTQAPDCYA
4638	TWFIYCMEH
4639	NEQYCEHIT
4640	LHCCTCKEY
4641	EFHVCYADN
4642	VTDAYGYEP
4643	TQCMWDNEN
4644	TIMQMHNEG
4645	TNDPLVMEC

SEQ ID NO	581 to 589 Region
4646	TEHCWMYTC
4647	EFQACSKYA
4648	TIQPFMASD
4649	GLPQCNEHR
4650	NETWVVCMK
4651	THDVRCFFA
4652	VLTNEEKDC
4653	ELTFHNEYP
4654	DTVNMYLRQ
4655	EVTVWHEHN
4656	CVTAEHNWI
4657	TEHAYVKAI
4658	SETHTCYGV
4659	ATHLVQMYQ
4660	PAQAWVQTC
4661	HAQATFEVC
4662	VHNAQVEMA
4663	DVENLCAQA
4664	PETVNHKHA
4665	NTCPKANEG
4666	VTFMMNQCK
4667	VMTPPNEYC
4668	EVQIYSEAP
4669	YTDAFANEH
4670	FALCCNEPQ
4671	FVTIYAEAC
4672	IATPPDEQC
4673	DTHWLCCEV
4674	TPGEYHMEC
4675	TATVECCRW
4676	LWLFHPFAK
4677	DITPACLHA
4678	PETWLGEPC
4679	YQADCDATP
4680	QNLDKSGAC
4681	NEYVTCQGD
4682	ATQMIWMQH
4683	HATNYVIES
4684	YTCESDREA
4685	NTFNEYAWL
4686	NTLNKNAYG
4687	TVESLNCCP
4688	TMIMWYKGA

SEQ ID NO	581 to 589 Region
4689	FAQPVYEGQ
4690	VEEATCFVT
4691	DATMIMYYQ
4692	NHTNWCESS
4693	PTEAITCQA
4694	ASDFICKEC
4695	EDQACNHSN
4696	ETGQNHMCP
4697	TVENWGMAQ
4698	PNENQHQYL
4699	NTEIACQLK
4700	VTQNACLRN
4701	GLDAIYQMK
4702	ATVNDYLRP
4703	MPCAQHALI
4704	ESDATCCTD
4705	TWLCPVEEP
4706	HACQQVEAA
4707	VQTADMQAS
4708	TVEYLVHMP
4709	EVTCNWAQY
4710	NFQVTHKQI
4711	HNTATNDMQ
4712	LNTMMVQIK
4713	VQYQENARP
4714	TSEAPHQYK
4715	VKPEFHNLY
4716	TTTVENEMG
4717	DMQNTNHAI
4718	VETVTDAQC
4719	TMQYAWMSP
4720	NATVFEACN
4721	TATFHYAWP
4722	TPPNDKEEN
4723	TMLNSGEFN
4724	TPEVMHNTA
4725	MVHATNADS
4726	EHTVANEAS
4727	NTNADVAER
4728	HNTNWCEEY
4729	IPVTFNNET
4730	TPNPTDMEI
4731	VEQMYNEPP

SEQ ID NO	581 to 589 Region
4732	VNEFYHQIW
4733	LVDQKNMMQ
4734	TINEFHMQS
4735	TMCFNGEYH
4736	DEHATQCYA
4737	TVNWRGEQA
4738	VPVNPGEHK
4739	VITQTNHEG
4740	VTPWCFEAC
4741	ENTCFYHFD
4742	AINAYNEEH
4743	VAQGFANEA
4744	ATQPTPMAH
4745	TAQNVTEFD
4746	PFQQFNEAI
4747	TFHAFIQYK
4748	TMQMTDQAH
4749	ETVRTGSNC
4750	VEWACTNEQ
4751	EPCPTHKAG
4752	NSEFDVARG
4753	MVTAEWADI
4754	LVHAFYEQR
4755	ATEPPGVES
4756	VECMQHEHY
4757	TFEMFNEGP
4758	LITLCYEFH
4759	MQLPVTMRG
4760	TMDCKWMQC
4761	NACTCNNEH
4762	TNEFMWEKA
4763	HEAQYNEHI
4764	MIGVTNHAP
4765	GEFVTHNLT
4766	ATQHIYDAA
4767	YTQYEVACP
4768	MQTDHMCQK
4769	CENLGVEFK
4770	TSDVAWEGH
4771	TVTAFYEIP
4772	FQTAPHQYC
4773	TVEQCSHAG
4774	ENEPPVTVI

SEQ ID NO	581 to 589 Region
4775	EIQDKHEAL
4776	SNQQCEEVI
4777	SQTIACREN
4778	MQTPSHKSA
4779	TEERDGNAC
4780	TPDMKGYQP
4781	NTESKGEAC
4782	EQTVFHRLC
4783	HIDVQCEPD
4784	TPVQNHHIC
4785	PSDALTFAI
4786	EQGAFCGEP
4787	DENWGVEYS
4788	EHVQCDAID
4789	PETFAGVQA
4790	ENEMCPMMN
4791	DKELCNESC
4792	TATPHQKLA
4793	VEHCYNEGF
4794	GETVHACKI
4795	NHTPTDQIA
4796	NEFVTHYQT
4797	TNLNYFHYA
4798	MQNADMTAI
4799	TEVINEASH
4800	TPDNLHEGY
4801	TADSKVEPN
4802	VEVQCNEQT
4803	GVQCNTLMI
4804	NTLNLVAKD
4805	NTPQLHNEI
4806	APTPTCCSA
4807	TITFCYKSD
4808	IIPPDVQMK
4809	EATVTNDFY
4810	DVEPLVATC
4811	VQCPLYMHP
4812	TSEQKHEAS
4813	PVTPYGEEL
4814	THPMAYKEQ
4815	YAQPCTEFP
4816	DVHAKYMAH
4817	FQTINDKSA

SEQ ID NO	581 to 589 Region
4818	TDHWEMKPI
4819	TNEFQNMQY
4820	GYQPWHECI
4821	DHTQLVREA
4822	EVTADNHEN
4823	TIYPAGEAQ
4824	VLDNTHNEA
4825	VATPTCYGN
4826	VTPNEYLPG
4827	TGQATEMQN
4828	VEQCLVAAC
4829	VPMQCDVDA
4830	SETVWMKHA
4831	TILVCCQAY
4832	PILFHNETP
4833	VTECPVEQP
4834	DIIQCVLVT
4835	YQAPPHATC
4836	GSDACYKFQ
4837	TIPQNTAPV
4838	TDVQGHMCI
4839	YQCPPDRHA
4840	TVLCGERIH
4841	GPTAEACFC
4842	NEQSCTAHI
4843	TNLIMCMYV
4844	TSAPYVEEP
4845	HMLIYGNYH
4846	NETDCYASA
4847	TAEMVVHCA
4848	DGTPMVRYY
4849	TQMASYAEH
4850	TEVTFNLHQ
4851	TVEMTCMMY
4852	EHLCNTKAA
4853	QHQAFHEAC
4854	PTTVFHDMP
4855	TAEMNYAIA
4856	HMTCFNEHA
4857	HHTPAGYYQ
4858	TNTPDGEDC
4859	VEEPTHSVQ
4860	TDKHGEMII

SEQ ID NO	581 to 589 Region
4861	VACNWGSLT
4862	TPPILCEMA
4863	YMPVNNEQI
4864	DIEFKCEHY
4865	LVLVPTDAA
4866	THLHICNPD
4867	MAQPGVFYA
4868	TITFVQEVC
4869	TDMPANASE
4870	TVLNCMEEN
4871	FQEDFYALI
4872	QTVVEHCPP
4873	EETAIPADC
4874	MQEPPDMYY
4875	TEHFHNMPK
4876	TELNRGEDI
4877	TPVWQNEGK
4878	TATIRDEDY
4879	VRDSLEART
4880	ETNACDART
4881	TIPPANEHA
4882	SATFPNEYA
4883	EPVPDYEHG
4884	AADTVHMQY
4885	VTFIEHLNQ
4886	TGLIFAEMG
4887	HVEFIGSAY
4888	TIQCPCEAY
4889	AEGVTHAII
4890	EPNVTVAAS
4891	NTVEPDNQA
4892	NWLVEWKAD
4893	TILPVYEHP
4894	VTVMIHAIC
4895	VSMQMHAKC
4896	TITFLCEED
4897	STQKCYEHG
4898	TWLVCCNKS
4899	TSTVENMDP
4900	MIEPCGMLQ
4901	TECCNGESD
4902	IATVHCMMK
4903	VTEMVHAAY

SEQ ID NO	581 to 589 Region
4904	NEQHTVEMR
4905	NECFKVEHD
4906	QILMKCETV
4907	HATFNCEVQ
4908	TEEMLVCPP
4909	TQHALDMAR
4910	TVFLHAHIA
4911	EEQGEKATI
4912	YSAVQDEER
4913	AWVATCNDQ
4914	EHNSTYEFD
4915	ENEMMQNDT
4916	TVLVHGMEN
4917	TTFAKNEGC
4918	TMGVQCMEC
4919	LTEPLDRAA
4920	EIDPACRHT
4921	VTCQNEAAC
4922	PFTVAYEGN
4923	ETDAFHAYA
4924	VRLNFCEFD
4925	AITDKNEGC
4926	YHCPFGMQP
4927	YAEQFTAKI
4928	ENTALNDCG
4929	DITNLCESC
4930	ERLPWVQCD
4931	SITCPGESY
4932	TDTVFPMDR
4933	DRLNFCEHC
4934	ATDAPCEYG
4935	TKLYHYMET
4936	SETCKYAIC
4937	HTVCCEFEG
4938	NTPFHDCYG
4939	FAQITEKHA
4940	MHTSLVEPC
4941	TICPFDENG
4942	AEPQKHEAC
4943	HSEQNGEPR
4944	TPQNLNHAH
4945	TVHTCLEAG
4946	GPESPVNEN

SEQ ID NO	581 to 589 Region
4947	EHQFTCEAC
4948	GSHAWMQVT
4949	TMQMCFKYA
4950	PILPCKEHC
4951	ATDNKNHSE
4952	TVHLCYADI
4953	ENDFINYGR
4954	TVLPNYEHA
4955	LVTNACVEI
4956	THQPFCKHA
4957	PEQWYGSAI
4958	WVTMHQCCK
4959	MEQATWECC
4960	TATFQCCYQ
4961	VQDAIYCYA
4962	ERDACLEIT
4963	TVEMFAKHY
4964	ENETHYKDI
4965	TENPFHEQP
4966	ETSKPHYGC
4967	IVTNKNECC
4968	YQTWPGRDS
4969	NIVLCNEHT
4970	ETVSTHAIY
4971	DQCATQNAI
4972	EVVQNHMIP
4973	QAVHCKEAC
4974	ENEFTCCYK
4975	EWLNNSAHA
4976	YGDAYHAST
4977	EVLACDKEG
4978	NQTDFAQQC
4979	TSENMIESP
4980	DATFQDCYA
4981	MQYQVHAAP
4982	MQTMCNDKY
4983	TPVIFNEVG
4984	ATQNIMAGN
4985	TEQMCSKYA
4986	NEQWCYKHP
4987	NYTVIHYEA
4988	FQCPSGERA
4989	YSTCPNECN

SEQ ID NO	581 to 589 Region
4990	TVLPMIEER
4991	THNTFGYAC
4992	TNEVTCQKT
4993	SKPPGSEQS
4994	DQHCLWEAC
4995	TNMATDEYC
4996	TEEQIGPAC
4997	TGEMFNKSS
4998	TNFQADEPR
4999	VIQQFKEAC
5000	STVSYHNEA
5001	NLLPDVERG
5002	EVQPGDKCY
5003	NEDVTPCEC
5004	TWPPWCNLI
5005	TVHACKNEF
5006	NTDWLTHEA
5007	EPDANYCYS
5008	QATSTNHDA
5009	DTQNVEMAA
5010	GLVAVHEEC
5011	PEQTCYEMT
5012	NWLDGDQAC
5013	VTTVMHAIN

[0224] In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 75% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 77.7% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having at least 88.8% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, an RPE tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having a sequence of any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013.

581 to 589 Regions for Ocular Tissue Targeting

[0225] In some embodiments, provided herein are AAV5 VP capsid polypeptide having at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 of AAV5 VP1, wherein said at least one mutation drives increased ocular tissue tropism. In some embodiments, the at least one mutation may comprise mutating one or more amino acid residues to positively charged amino acid residues (e.g., K, R, or H). In some embodiments, the at least one mutation may comprise mutating one or more negatively charged amino acid residues (e.g., E or D) to residues that are not negatively charged. In some embodiments, the 581 to 589 region comprises a sequence having at least 75% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, the 581 to 589 region comprises a sequence having at least 77.7% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, the 581 to 589 region comprises a sequence having at least 88.8% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO:

2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two amino acid substitutions relative to any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. In some embodiments, a retina tissue-tropic VP capsid polypeptide comprises a 581 to 589 region having one or two conservative amino acid substitutions relative to any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013.

Numbered Embodiments

[0226] The following embodiments recite non-limiting permutations of combinations of features disclosed herein. Other permutations of combinations of features are also contemplated. In particular, each of these numbered embodiments is contemplated as depending from or relating to every previous or subsequent numbered embodiment, independent of their order as listed. 1. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. 2. The VP capsid polypeptide of embodiment 1, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513. 3. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. 4. The VP capsid polypeptide of embodiment 3, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 4514 – SEQ ID NO: 5013. 5. The VP capsid polypeptide of any one of embodiments 1-4, wherein the 581 to 589 region confers increased retinal pigment epithelium tissue-tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. 6. The VP capsid polypeptide of embodiment 5, wherein the retinal pigment epithelium tissue tropism is at least 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, or at least 500-fold higher than the wild type AAV5 VP capsid

polypeptide of SEQ ID NO: 1. 7. The VP capsid polypeptide of any one of embodiments 1-6, wherein the 581 to 589 region confers increased choroid tissue-tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. 8. The VP capsid polypeptide of embodiment 7, wherein the choroid tissue tropism is at least 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, or at least 500-fold higher than the wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. 9. The VP capsid polypeptide of any one of embodiments 5-8, wherein the 581 to 589 region further confers increased retina tissue tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. 10. The VP capsid polypeptide of any one of embodiments 1-9, wherein the 581 to 589 region confers decreased photoreceptor tissue-tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1. 11. The VP capsid polypeptide of any one of embodiments 1-10, wherein the VP capsid polypeptide comprises an amino acid sequence at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 98.5%, at least 99%, or at least 99.5% identical to SEQ ID NO: 1. 12. The VP capsid polypeptide of any one of embodiments 1-11, wherein the VP capsid polypeptide has a sequence of SEQ ID NO: 2, wherein residues 581 to 589 of SEQ ID NO: 2 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$) correspond to the 581 to 589 region. 13. The VP capsid polypeptide of any one of embodiments 1-12, wherein the VP capsid polypeptide is capable of assembling into a recombinant viral capsid. 14. The VP capsid polypeptide of any one of embodiments 1-13, comprising at least one amino acid substitution as compared to each of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8. 15. The VP capsid polypeptide of any one of embodiments 1-14, wherein the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region relative to a wild type VP capsid polypeptide of SEQ ID NO: 1. 16. The VP capsid polypeptide of any one of embodiments 1-15, wherein the 581 to 589 region confers on a recombinant viral capsid assembled from the VP capsid polypeptide improved stability compared to a wild type AAV capsid comprising a peptide of SEQ ID NO: 1. 17. The VP capsid polypeptide of any one of embodiments 1-16, wherein the 581 to 589 region confers lower toxicity upon administration to a subject compared to a wild type VP capsid polypeptide of SEQ ID NO: 1. 18. The VP capsid polypeptide of any one of embodiments 1-17, wherein the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region that contributes to reduced production of neutralizing antibodies relative to a wild type VP capsid polypeptide of SEQ ID NO: 1. 19. The VP capsid polypeptide of any one of embodiments 1-18, wherein the VP capsid polypeptide further comprises one or more mutations

outside of the 581 to 589 region that improves manufacturability relative to a wild type VP capsid polypeptide of SEQ ID NO: 1. 20. A recombinant viral adeno-associated virus (rAAV) capsid comprising the VP capsid polypeptide of any one of embodiments 1-19, wherein the rAAV capsid preferentially targets retinal pigment epithelium tissue. 21. A recombinant viral adeno-associated virus (rAAV) capsid comprising the VP capsid polypeptide of any one of embodiments 1-19, wherein the rAAV capsid preferentially targets choroid tissue. 22. The rAAV capsid of embodiment 20 or embodiment 21, further comprising a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region. 23. A recombinant adeno-associated virus (rAAV), comprising the VP capsid polypeptide of any one of embodiments 1-19 assembled into a recombinant viral capsid and a payload encapsidated by the recombinant viral capsid. 24. The rAAV of embodiment 23, wherein the rAAV preferentially targets retinal pigment epithelium tissue. 25. The rAAV of embodiment 23 or embodiment 24, wherein the rAAV preferentially targets choroid tissue. 26. The rAAV of any one of embodiments 23-25, further comprising a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region. 27. The rAAV of any one of embodiments 23-26, wherein the payload encodes a therapeutic polynucleotide or a therapeutic peptide. 28. The rAAV of embodiment 27, wherein the payload encodes a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, or an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof. 29. The rAAV of embodiment 27, wherein the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA. 30. The rAAV of embodiment 27, wherein the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor. 31. A pharmaceutical composition comprising the VP capsid polypeptide of any one of embodiments 1-19, the rAAV capsid of any one of embodiments 20-22, or the rAAV of any one of embodiments 23-30. 32. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013. 33. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises

the VP capsid polypeptide of any one of embodiments 1-19. 34. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013. 35. A method of delivering a payload to a choroid tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of embodiments 1-19. 36. A method of delivering a payload to a choroid tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and (ii) delivering the payload to the choroid tissue. 37. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide of any one of embodiments 1-19; and (ii) delivering the payload to the retinal pigment epithelium tissue. 38. A method of delivering a payload to a choroid tissue of a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide of any one of embodiments 1-19; and (ii) delivering the payload to the choroid tissue. 39. The method of any one of embodiments 36-38, comprising administering the rAAV via intravitreal administration. 40. The method of any one of embodiments 36-38, comprising administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration. 41. The method of any one of embodiments 32-40, further comprising expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload. 42. The method of any one of embodiments 32-41, further comprising producing a therapeutic effect upon expression of the payload. 43. The method of embodiment 42, wherein the therapeutic effect is produced upon administration of from 1×10^5 to 5×10^{14} rAAVs. 44. The method of embodiment 42 or embodiment 43, comprising administering an amount of the rAAV sufficient to produce the therapeutic effect without producing a toxicity in the subject. 45. A method of treating a condition in a subject, the method comprising

administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013. 46. A method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of embodiments 1-19. 47. The method of embodiment 45 or embodiment 46, further comprising expressing the payload in a retinal pigment epithelium tissue of the subject. 48. The method of any one of embodiments 45-47, further comprising expressing the payload in a choroid tissue of the subject. 49. The method of any one of embodiments 45-48, further comprising producing a therapeutic effect in the subject. 50. A method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and (ii) expressing the payload in a retinal pigment epithelium tissue of the subject, thereby treating the condition in the subject. 51. A method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of embodiments 1-19; and (ii) expressing the payload in a retinal pigment epithelium tissue of the subject, thereby treating the condition in the subject. 52. A method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of embodiments 1-19; and (ii) expressing the payload in a choroid tissue of the subject, thereby treating the condition in the subject. 53. A method of treating a condition in a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide of any one of embodiments 1-19; (ii) delivering the payload to a retinal pigment epithelium tissue of the subject; and (iii) producing a therapeutic effect in the retinal pigment epithelium tissue, thereby treating the condition. 54. A method of treating a condition in

a subject, the method comprising: (i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide of any one of embodiments 1-19; (ii) delivering the payload to a choroid tissue of the subject; and (iii) producing a therapeutic effect in the choroid tissue, thereby treating the condition. 55. The method of any one of embodiments 50-54, comprising administering the rAAV via intravitreal administration. 56. The method of any one of embodiments 50-54, comprising administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration. 57. The method of any one of embodiments 45-56, wherein the condition is an ocular condition. 58. The method of embodiment 57, wherein the ocular condition is achromatopsia, macular degeneration, cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis. 59. The method of embodiment 57 or embodiment 58, wherein the ocular condition is Stargardt disease. 60. The method of any one of embodiments 32-59, further comprising delivering the rAAV to a retinal pigment epithelium tissue with higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. 61. The method of any one of embodiments 39-53, further comprising delivering the rAAV to a retinal pigment epithelium tissue with higher tissue tropism than for photoreceptor tissue. 62. The method of any one of embodiments 39-54, comprising delivering the rAAV to a retinal pigment epithelium tissue with at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. 63. The method of any one of embodiments 32-59, further comprising delivering the rAAV to a choroid tissue with higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. 64. The method of any one of embodiments 39-53, further comprising delivering the rAAV to a choroid tissue with higher tissue tropism than for photoreceptor tissue. 65. The method of any one of embodiments 39-54, comprising delivering the rAAV to a choroid tissue with at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. 66. The method of any one of embodiments 39-65, comprising administering from 1×10^5 to 5×10^{14} rAAVs. 67. The method of any one of embodiments 39-66, wherein the payload encodes a therapeutic protein, therapeutic

polynucleotide, a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof. 68. The method of embodiment 67, wherein the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA. 69. The method of embodiment 67, wherein the therapeutic protein is selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I, ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, and RS1. 70. The method of embodiment 67, wherein the therapeutic polynucleotide targets an mRNA encoding a protein selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I, ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, or RS1. 71. The method of embodiment 67, wherein the payload encodes a therapeutic polynucleotide targeting ABCA1, ABCA4, or CRB1 or a transgene encoding ABCA1, ABCA4, or CRB1. 72. The method of embodiment 67, wherein the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor. 73. The method of embodiment 72, wherein the component of the CRISPR/Cas system comprises a Cas3, a Cas8, a Cas10, a Cas9, a Cas4, a Cas12, a Cas13, a guide RNA, or a combination thereof. 74. The method of embodiment 72, wherein the ADAR enzyme is ADAR1 or ADAR2. 75. The method of embodiment 72, wherein the transcriptional activator is VP64. 76. The

method of embodiment 72, wherein the transcriptional repressor is KRAB. 77. The method of any one of embodiments 67-76, further comprising expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload. 78. The method of any one of embodiments 67-77, comprising expressing the therapeutic polypeptide or the therapeutic polynucleotide at a higher level in a retinal pigment epithelium tissue compared to a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1. 79. The method of embodiment 78, comprising expressing the therapeutic polypeptide or the therapeutic polynucleotide in a retinal pigment epithelium tissue at a level that is at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher compared to the wild type AAV5 capsid. 80. The method of any one of embodiments 32-79, comprising producing a toxicity in the subject that is lower than a toxicity produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1. 81. The method of any one of embodiments 32-80, comprising producing a toxicity in the subject that is lower than a toxicity produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retinal pigment epithelium tissue. 82. The method of any one of embodiments 32-81, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1. 83. The method of any one of embodiments 32-82, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV2 capsids. 84. The method of any one of embodiments 32-83, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV8 capsids. 85. The method of any one of embodiments 32-84, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV9 capsids. 86. The method of any one of embodiments 32-85, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retinal pigment epithelium tissue.

EXAMPLES

[0227] Below are examples of specific embodiments for carrying out the present invention. The examples are offered for illustrative purposes only and are not intended to limit the scope of the present invention in any way. Efforts have been made to ensure accuracy with respect to numbers used (e.g., amounts, temperatures, etc.), but some experimental error and deviation should, of course, be allowed for.

[0228] The practice of the present invention will employ, unless otherwise indicated, conventional methods of protein chemistry, biochemistry, recombinant DNA techniques and pharmacology, within the skill of the art. Such techniques are explained fully in the literature.

EXAMPLE 1

Identification of 581 to 589 Region Sequences that Confer Ocular Tissue Tropism

[0229] This example describes identification of 581 to 589 region sequences that confer ocular tissue tropism. The high throughput capsid engineering system is schematized in **FIG. 1**.

[0230] Tissues were harvested and transducing capsid genes are labeled with unique molecular identifiers and barcodes. These variant sequences/unique molecular identifiers (UMIs)/barcodes were parameterized, and machine learning algorithms were used to identify deterministic features of specific tissue targeting/detargeting capsids.

[0231] **FIG. 2A** provides a side view (top panel) and top view (bottom panel) of key residues of known AAV capsids that have been shown to interact with target cells. **FIG. 2B** illustrates salient features of the AAV capsid library, showing the region of introduced diversity, with residue numbering corresponding to the numbering of amino acids in AAV5 VP1. The library plasmid includes the invariant rep and diversified cap coding sequences between AAV inverted terminal repeats (ITRs; a cis-packaging approach).

[0232] The recombinant AAV library was administered to two non-human primates (NHPs), one male and one female. The library was administered via bilateral intravitreal injection of 3.2 x 10^{12} viral genomes in 50 µL per eye as follows. Animals were sedated/anesthetized to effect and placed in dorsal recumbency. Topical Proparacaine was applied to the eye. The conjunctival fornices were flushed with a 1:50 dilution of betadine solution/saline and the eyelid margins swabbed with undiluted 5% betadine solution. The eye was draped, and a wire eyelid speculum placed. A caliper was used to mark a spot 3.0 mm posterior to the limbus on the inferotemporal bulbar conjunctiva. The conjunctiva at the marked spot was swabbed with undiluted 5% betadine solution. Conjunctival forceps were used to fixate the globe position while a

STACLEAR™ syringe with 31 g needle was inserted at the marked spot, through the sclera and advanced into the vitreous humor. The injection needle was positioned to face the posterior axis of the globe and 50 µL of AAV5 library was delivered into the vitreous by slowly depressing the syringe plunger. The needle was held in place for at least 30 seconds to lessen reflux of the injected material. Subsequently, the needle was removed and the episcleral tissues approximated to the site of insertion grasped with the conjunctival forceps to further lessen reflux of the injected material. An identical injection procedure was then performed on the contralateral eye.

[0233] Four weeks post-injection, the animals were euthanized, and tissues were collected for analysis. For the ocular dissections, both eyes first had a maximum volume of aqueous and vitreous humor collected. The retina was separated from the retinal pigment epithelium (RPE)/choroid. The RPE/choroid was frozen in liquid nitrogen as a stand-alone tissue. The retina was further dissected into 5 pieces; superior, inferior, temporal, nasal, central (including fovea and optic disc) and frozen in liquid nitrogen.

[0234] The frozen specimens were mechanically dissociated in TRIZOL™ Reagent using QIAGEN® GENTLEMACS™ as follows. Tissue was homogenized using a GENTLEMACS™ dissociator. The tissue was spun down at 3000xg for 2-3 minutes. A 15ml MAXTRACT® QIAGEN® protocol was used to extract the AAV episomal DNA. Samples were added to MAXTRACT® High Density Tubes. Between 1 and 6 mL were added to 15 mL tubes and between 5 and 20 nM were added to 50 mL tubes, avoiding any insoluble material. In some instances, GLYCOBLUE™ was added as a co-precipitant. Lysis reagent and 0.2 mL chloroform per mL lysis reagent was added to each tube, and the tubes were capped and thoroughly mixed for at least 15 seconds to mix the organic and aqueous phases to form a pseudo-homogeneous suspension. Tubes were incubated at room temperature for 2 to 3 min. Following incubation, the samples were centrifuged at 1500 x g for 5 min at 4°C to separate the phases or until sample is completely phased (pink is no longer visible in the aqueous layer). The resulting sample contained three phases. The upper of the three phases was a colorless aqueous phase containing cellular RNA and AAV episomal DNA. The upper layer was transferred to a new tube by gently decanting into the new tube. For precipitation of RNA/episomal DNA from the aqueous phase, 0.5 mL of isopropanol was added per 1 mL of lysis reagent used previously and mixed thoroughly. The tubes were incubated at room temperature for 10 min and centrifuged at 4200xg for 10 to 15 min at 4 °C. A swinging bucket rotor was used to pellet the RNA and episomal DNA to the bottom of the tube. Following centrifugation, the supernatant was carefully discarded without disrupting the pellet, which was visible as a gel-like white (or blue if co-precipitant was used) pellet at the bottom of the tube. At least 1 mL of freshly made 75% ethanol

per 1 mL lysis reagent used previously was added. Samples were mixed by vortexing for a few seconds then centrifuged at 4200xg for 5 min at 4 °C. The supernatant was discarded, and the remaining liquid was aspirated following a quick spin. The pellet, containing RNA, was briefly air-dried for about 5 minutes without completely drying the pellet. The RNA pellet was redissolved in 250 µL of RNase-free water prewarmed to 37 °C. In some instances, the RNA was treated with 6 µL per 100 µL RNase Cocktail Enzyme Mix (THERMO FISHER SCIENTIFIC®; AM2286) at 37 °C for 30 min. to remove RNA. The treated mixture was purified with a Zymo DNA Clean and Concentrator kit-25 (D4033) following the manufacturer's protocol.

[0235] Next generation sequencing (NGS) of recovered AAV episomal DNA was performed using a semi-nested 3-round PCR amplification that appends unique molecular identifiers (UMIs) in the first round of PCR. The completed amplicon contained both UMIs and NGS adapters with dual indexes for sample demultiplexing. The first round of PCR was performed as follows. Four reactions were prepared per tissue sample. Each 100 µL PCR reaction contained 20 µL episomal DNA per reaction as a template. PCR cycling was performed (1. 98 °C for 30s; 2. 98 °C for 15s; 3. 66.6 °C annealing for 45s; 4. 72 °C for 45s; 5. Repeat steps 2-4 for 5 cycles; 6. 72 °C for 2 min). The amplified product was cleaned using CYTIVA® SERA-MAG™ Select bead clean-up following the manufacturer's protocol (1:1 bead:sample).

[0236] The second round of PCR was performed as follows. 23 µl of cleaned up PCR 1 reaction was used as a template. 2 µL of primers (10µM) and and 25 µL of 2x master mix Phusion polymerase with HF buffer (NEB, M0531L) was added per reaction. PCR cycling was performed (1. 98 °C for 30s; 2. 98 °C for 10s; 3. 62 °C for 30s; 4. 72 °C for 20s; 5. Repeat steps 2-4 for 18 cycles; 6. 72 °C for 5min; 7. 4 °C hold). The amplified product was cleaned using CYTIVA® SERA-MAG™ Select bead clean-up following the manufacturer's protocol (0.75:1 bead:sample).

[0237] Quantitative PCR (qPCR) with SYBR was performed as follows. 4 µL of cleaned up PCR 2 reaction was used as a template. 1 µL of primers at 20 µL of master mix (containing SYBR) was added. PCR cycling was performed (1. 98 °C for 30s; 2. 98 °C for 10s; 3. 72 °C for 20s and plate read; 4. Repeat steps 2 and 3 for 29 more times; 5. 72 °C for 5m). Amplification and cycle threshold (Ct) values were recorded. Following determination of Ct values, qPCR was repeated as described above but with endpoint at 3-4 cycles above Ct value for each sample. The amplified product was cleaned using CYTIVA® SERA-MAG™ Select bead clean-up following the manufacturer's protocol (1.25:1 bead:sample).

[0238] The libraries were pooled and checked for quality. Presence of a 296 bp band for each sample was verified by gel electrophoresis. Samples were quantified on a QUBIT™ flex with High Sensitivity reagents, pooling equal amounts (in ng) together. A TAPESTATION™ automated electrophoresis system was used to confirm quality and quantify each pool. Samples were sequenced on an ISEQ™ for pooling and quality control of indexes. In some instances, depending on library diversity and depth of sequence desired, sequencing was performed on an ILLUMINA® HISEQ™ or NOVASEQ™.

[0239] To isolate the capsid variant sequence to use for all analyses, raw demultiplexed data were processed using the following procedure executed using NEXTFLOW™ and custom PYTHON® scripts. Paired end sequencing reads were merged using Fastp v0.21.0 and the following parameters: --correction –merge –average_qual 30. This removed reads with an average sequencing quality score < Q30 and corrected base calls using the read with the higher Phred quality score at that position. Capsid variant sequences were extracted by aligning with zero mismatches in the five nucleotide sequences flanking the variant sequence, and UMI sequences were isolated as the first 12 nucleotides of the read. Extracted variant sequences were then conservatively clustered within an edit distance of four to collapse/suppress error. The sequence at the center of each cluster (i.e., the consensus sequence) was then translated into its amino acid sequence, and data were filtered respect to sequence quality and abundance. Sequences were removed if containing one of the codons excluded from library synthesis ('CTC', 'CTA', 'TTA', 'AGG', 'CGA', 'CGT', 'TAA', 'TAG', 'TGA').

[0240] Analysis was performed using the R programming language, and the number of unique variant sequences within each tissue was determined, as shown in **FIG. 4**. Number of viral genomes recovered per mg from each tissue is shown in **FIG. 3**.

[0241] Enrichment of amino acid residues at each position in the 581 to 589 region (AAV5 VP1 581-589) was determined for the retina in comparison to various background amino acid frequencies, including all other eye tissues (**FIG. 5A** and **FIG. 5B**) or the aqueous/vitreous humor (**FIG. 5C** and **FIG. 5D**). **FIG. 6A** and **FIG. 6B** show heatmaps of amino acid enrichment and depletion at each residue position of the 581 to 589 region (581 to 589, corresponding to positions in the AAV5 VP1 sequence) for the two NHPs, as fold increased/decreased over the input viral library frequency (“ST2”). As seen in **FIG. 5A** – **FIG. 5D**, **FIG. 6A**, and **FIG. 6B**, positively charged amino acid residues (e.g., K and R) are favored for retinal tissue tropism.

EXAMPLE 2

AAV5 Variants with Tissue Tropism in Eye Tissues

[0242] This example describes engineered AAV5 variants with ocular tissue tropism that are discovered using the methods and systems described in **EXAMPLE 1**.

[0243] Positively charged residues, including lysine (K), arginine (R), and histidine (H), were identified as promoting ocular tissue tropism when included in the VP capsid polypeptide 581 to 589 region. Accordingly, an ocular tissue-tropic VP capsid polypeptide may comprise a K, R, or H amino acid residue at one or more of X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, or X^9 of SEQ ID NO: 2. Conversely, negatively charged residues, including aspartic acid (D) and glutamic acid (E), were identified as disfavoring ocular tissue tropism when included in the VP capsid polypeptide 581 to 589 region. Accordingly, an ocular tissue-tropic VP capsid polypeptide may comprise fewer D or E amino acid residues in the 581 to 589 region than a wild type VP capsid polypeptide (e.g., SEQ ID NO: 1), or D and E residues may be excluded from the 581 to 589 region entirely.

[0244] The present disclosure, thus, provides for rAAVs composed of engineered AAV5 VP1 capsid polypeptides having a SEQ ID NO: 2, wherein the X^1, X^2, X^3, X^4, X^5, X^6, X^7, X^8, and X^9 are independently selected from A, R, N, D, C, E, Q, G, H, I, L, K, M, F, P, S, T, W, Y, and V. Also encompassed herein are rAAVs composed of engineered AAV5 VP2 capsid polypeptides and engineered AAV5 VP3 capsid polypeptides having the 581 to 589 regions described herein at the regions in AAV5 VP2 (amino acid residues 445 to 453) and AAV5 VP3 (amino acid residues 389 to 397) corresponding to the amino acids in the AAV5 VP1 581 to 589 region.

[0245] From the primary screen described in **EXAMPLE 1**, certain generalizable trends were also observed for AAV5 variants with ocular tissue tropism. The presence of basic amino acid residues, including K, R, and H, in the 581 to 589 region was favorable for retina tissue tropism and enhanced capsid preference for retina tissue. Increasing the number of basic amino acid residues in the 581 to 589 region increased capsid preference for retina tissue. Basic residues had the largest favorable impact on retina tissue tropism when positioned at position X^3 of the 581 to 589 region, with reference to SEQ ID NO: 2, followed by positions X^6, X^1, and X^4, in order of impact. Conversely, the presence of acidic amino acid residues, including D and E, in the 581 to 589 region was unfavorable for retina tissue tropism and decreased capsid preference for retina tissue. Furthermore, capsids with 581 to 589 regions containing two or more basic amino acid residues exhibited greater preference for retina tissue with fewer acidic amino acid residues. Increasing the number of acidic amino acid residues in a 581 to 589 region decreased preference for retina tissue in capsids with 581 to 589 regions containing two or more basic amino acid residues.

EXAMPLE 3

Selection of Prospective Tissue-Tropic Capsid Variants for Secondary Screen

[0246] This example describes the selection of prospective tissue-tropic capsid variants for secondary screening. Prospective retinal pigment epithelium (RPE) tissue-tropic and retinal tissue-tropic AAV5 capsid polypeptide variants were identified using the primary screen described in **EXAMPLE 1**. An AAV5 capsid polypeptide variant was identified as a prospective tissue-tropic variant if it was found only in that tissue of a non-human primate (NHP) following intravitreal administration. Of the 218,937 AAV5 capsid polypeptide variants identified in retinal tissue, 218,803 AAV5 capsid polypeptide variants were found exclusively in retinal tissue, as shown in **FIG. 7**. From those variants, 1156 were found exclusively in retinal tissue across multiple replicates, of which 724 were found exclusively in retinal tissue in multiple NHPs. Prospective retinal tissue-tropic variants were prioritized for inclusion in the secondary screen if they were observed multiple times in retinal tissue. As shown in **FIG. 8**, variants with multiple observations ("y"), either in multiple NHPs or multiple replicates within a particular NHP, had higher predictive probabilities ("retina_score") of exhibiting retina-specific tropism compared to variants having a single observation ("n"), thus providing additional support for their inclusion in the secondary screen. Sequences found exclusively in retinal tissue across multiple replicates, corresponding to AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 738 – SEQ ID NO: 1169, were selected as prospective retinal tissue-tropic AAV5 capsid polypeptide variants for inclusion in the secondary screen. Sequences found exclusively in retinal tissue across multiple NHPs, corresponding to AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 14 – SEQ ID NO: 737, were selected as prospective retinal tissue-tropic AAV5 capsid polypeptide variants for inclusion in the secondary screen. Additionally, observed tissue-unique prospective retina tissue-tropic AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 1170 – SEQ ID NO: 2013 were selected using machine learning for inclusion in the secondary screen. A total of 724 tissue-unique prospective retina tissue-tropic variants observed in multiple NHP were included in the secondary screen. A total of 432 tissue-unique prospective retina tissue-tropic variants observed in multiple replicates were included in the secondary screen. A total of 844 other observed prospective retina tissue-tropic variants, top-ranked by machine learning, but only observed in one replicate of one NHP, were included in the secondary screen.

[0247] As shown in **FIG. 7**, 2069 AAV5 capsid polypeptide variants were identified in RPE tissue and 2065 AAV5 capsid polypeptide variants were identified exclusively in RPE tissue.

Observed RPE tissue-tropic AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 2014 – SEQ ID NO: 2513 were selected using machine learning for inclusion in the secondary screen. A total of 500 top ML-ranked tissue-unique prospective RPE tissue-tropic variants, having high predictive probability of being RPE-tropic and low predictive probability of being retina-tropic, were included in the secondary screen.

[0248] Additional prospective RPE tissue-tropic and retinal tissue-tropic engineered AAV5 capsid polypeptides to be included in the secondary screen were selected based on a machine learning analysis of the results of the primary screen performed in **EXAMPLE 1**. Synthetic AAV5 capsid polypeptide variants predicted to have retina tissue tropism or RPE tissue tropism were produced using input optimization through generative convolutional neural network (CNN) modeling; by sampling position weight matrices (PWMs) of amino acid frequencies for a tissue; or by sampling a uniform distribution of amino acid frequencies. These variants were then scored using the machine learning models trained using the observed capsid variants, with the top ML-ranked variants being selected for inclusion in the secondary screen. For retina tissue, synthetic sequences identified using input optimization had the highest predictive probabilities ("Average ML Score") of having retina-specific tropism, as shown in **FIG. 9**. **FIG. 9** shows the distributions of predicted probabilities of all variants with multiple observations in multiple NHPs or multiple replicates compared to all synthetic retina-tropic variants generated by machine learning, before secondary screen selection. **FIG. 10** shows the distributions of predicted probabilities of the variants selected for inclusion in the secondary screen, categorized by how the variant was identified.

[0249] AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 2514 – SEQ ID NO: 3575 were generated using convolutional neural network (CNN) input optimization as prospective retina tissue-tropic and selected for inclusion in the secondary screen. AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 3576 – SEQ ID NO: 4510 were generated by sampling PWMs, followed by scoring these sequences and selecting high-ranking sequences as prospective retina tissue-tropic for inclusion in the secondary screen. AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 4511 – SEQ ID NO: 4513 were generated by sampling a uniform distribution, followed by scoring these sequences as retina tissue-tropic for inclusion in the secondary screen. When selecting sequences for further screening, variants generated from sampling PWMs and variants generated from sampling a uniform distribution were considered together. A total of 2000 synthetic prospective retina tissue-tropic variants were included in the

secondary screen, including 1062 input optimized sequences, 935 sequences from sampling PWMs, and 3 sequences identified from uniform distribution sampling.

[0250] AAV5 capsid polypeptide variants with 581 to 589 regions having sequences of SEQ ID NO: 4514 – SEQ ID NO: 5013 were generated by sampling PWMs, followed by scoring these sequences and selecting high-ranking sequences as prospective RPE tissue-tropic for inclusion in the secondary screen. A total of 500 synthetic prospective RPE tissue-tropic variants were included in the secondary screen.

EXAMPLE 4

Secondary Screen to Identify Ocular Tissue-Tropic Engineered AAV Capsids

[0251] This example describes a secondary screen to identify ocular tissue-tropic engineered AAV capsids. Prospective tissue-tropic capsids identified from an *in vivo* primary screen, through machine learning, or both, such as the retina tissue-tropic and RPE tissue-tropic capsids identified in **EXAMPLE 3**, are introduced into an *in vivo* secondary screen to confirm tissue-tropic behavior of the identified capsids. The secondary screen includes capsids observed in the primary screen in RPE, choroid, retina, or combinations thereof. The barcoded secondary screen capsid library, including wild type AAV controls, is injected into a non-human primate (NHP) by intravitreal injection. Following injection, ocular tissues, including RPE/choroid, retina, vitreous humor, aqueous humor, and optic nerve, are isolated from the NHP, and the barcoded sequences are quantified. RPE and choroid tissues are isolated and analyzed together.

[0252] To identify RPE-targeting capsids in the functional screen, two versions of every candidate capsid in the library are encoded. The first version includes a payload sequence under transcriptional control of a universal promoter (e.g., CAG). The second version includes a payload sequence under transcriptional control of an RPE-specific promoter (e.g., BEST1). Capsids that infect RPE will show RNA expression from both the RPE-specific and universal promoters, whereas capsids infecting other cells will show expression from the CAG promoter and lack expression from the BEST1 promoter. Capsids found in RPE/choroid tissue that express from both the RPE-specific and universal promoters are identified as RPE tissue-tropic capsids. Capsids found in retina tissue are identified as retina tissue-tropic capsids.

EXAMPLE 5

Treatment of an Eye Disease or Condition with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0253] This example describes treatment of an ocular disease or condition with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid

polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue tropism, photoreceptor cell targeting, retinal pigment epithelial cell targeting, or combinations thereof. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA or miRNA targeting an mRNA encoded for by a gene implicated in the ocular disease or condition, or the therapeutic payload is a transgene. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of the ocular disease or condition is alleviated, or the subject is cured.

EXAMPLE 6

Treatment of Macular Degeneration with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0254] This example describes treatment of wet age-related macular degeneration with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5

Cap comprising a 581 to 589 region conferring retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in wet age-related macular degeneration, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, or SLC16A8 gene. The transgene is a gene encoding for an anti-VEGF antibody. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism compared with wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of wet age-related macular degeneration is alleviated, or the subject is cured.

EXAMPLE 7

Treatment of Glaucoma with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0255] This example describes treatment of glaucoma with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous

humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in glaucoma, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, CYP1B1, or LTBP2 gene. The transgene is optineurin. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of glaucoma is alleviated, or the subject is cured.

EXAMPLE 8

Treatment of Retinitis Pigmentosa with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0256] This example describes treatment of retinitis pigmentosa with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in the retinitis pigmentosa, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, or AGBL5 gene. The transgene is a NRL, RDH12, PRPH2 (RDS), RHO,

RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, SNRNP200, PRPF3, or AGBL5 gene. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared with wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of the retinitis pigmentosa is alleviated, or the subject is cured.

EXAMPLE 9

Treatment of Stargardt Disease with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0257] This example describes treatment of Stargardt disease with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region conferring retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in Stargardt disease, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by an ABCA1, ABCA4, or CRB1 gene. The transgene is ABCA1, ABCA4, or CRB1. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared wild

type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of Stargardt disease is alleviated, or the subject is cured.

EXAMPLE 10

Treatment of Uveal Melanoma with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0258] This example describes treatment of uveal melanoma with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in uveal melanoma, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, a HERC2/OCA2 gene. The transgene is an anti gp100 protein. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the

subject, at least one symptom of uveal melanoma is alleviated, a tumor size is reduced, or the subject is cured.

EXAMPLE 11

Treatment of Optical Neuropathy with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0259] This example describes treatment of optical neuropathy with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in optical neuropathy, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a Complex I, ND, OPA1, or RPE65 gene. The transgene is Complex I, ND, OPA1, or RPE65. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the

therapeutic payload. Upon administration to the subject, at least one symptom of ocular neuropathy is alleviated, or the subject is cured.

EXAMPLE 12

Treatment of Usher Syndrome with an AAV5-derived Virion Encapsidating a Therapeutic Payload

[0260] This example describes treatment of Usher syndrome with a variant AAV5-derived virion having any one of the engineered ocular tissue-tropic variant AAV5 VP capsid polypeptides disclosed herein, wherein the variant AAV5 virion encapsidates a therapeutic payload. Polynucleotide sequence encoding for AAV Rep, an AAV5-derived variant Cap and helper proteins and a therapeutic payload are transfected in cells to produce variant AAV5 virions, where the polynucleotide sequence encoding for the variant AAV5 Cap comprises at least one mutation in a 581 to 589 region, corresponding to residues 581 to 589 in the VP1 capsid polypeptide, and where the polynucleotide sequence encodes for a variant AAV5 Cap comprising a 581 to 589 region that confers retinal tissue targeting, retinal pigment epithelial cell targeting, or both. The 581 to 589 region has a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013, SEQ ID NO: 2514 – SEQ ID NO: 4513, SEQ ID NO: 2014 – SEQ ID NO: 2513, or SEQ ID NO: 4514 – SEQ ID NO: 5013. Each such variant is detargeted for vitreous humor and aqueous humor. The therapeutic payload is a guide RNA targeting an mRNA encoded for by a gene implicated in Usher syndrome, or the therapeutic payload is a transgene. The mRNA targeted by the guide RNA is an mRNA encoded for by a ADGRV1, CEP250, CLRN1, MYO7A, PROM1, USH1C, USH1G, or USH2A gene. The transgene is ADGRV1, CEP250, CLRN1, MYO7A, PROM1, USH1C, USH1G, or USH2A. The variant AAV5 virion encapsidating the payload is administered to a subject. The subject is a human or non-human animal. The route of administration is an intravitreal route of administration. The intravitreal route of administration is intravitreal injection. Upon administration to the subject, the variant AAV5 virions encapsidating the therapeutic payload exhibit enhanced ocular tissue tropism as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, a lower dose of the variant AAV5 virions encapsidating the therapeutic payload is administered as compared to wild type AAV5 virions encapsidating the therapeutic payload. Upon administration to the subject, at least one symptom of Usher syndrome is alleviated, or the subject is cured.

EXAMPLE 13

Singleplex Tertiary Screen to Validate Ocular Tissue-Tropic Engineered AAV Capsids

[0261] This example describes a tertiary screen, in singleplex, to identify ocular tissue-tropic engineered AAV capsids. Prospective tissue-tropic capsids identified from an *in vivo* secondary screen, through machine learning, or both, such as the retina tissue-tropic and RPE tissue-tropic capsids identified in **EXAMPLE 4**, are introduced into an *in vivo* tertiary screen, in singleplex, to confirm tissue-tropic behavior of the identified capsids when individually dosed in NHP. The tertiary screen includes capsids observed in the secondary screen in RPE, choroid, retina, or combinations thereof. The tertiary screen capsid library is injected into a non-human primate (NHP) by intravitreal injection. Following injection, ocular tissues, including RPE/choroid, retina, vitreous humor, aqueous humor, and optic nerve, are isolated from the NHP, and the barcoded sequences are quantified. RPE and choroid tissues are isolated and analyzed together. Prospective tissue-tropic capsids are compared to control, wild-type AAV to identify superior variant capsids of the present disclosure that target various compartments of the eye (e.g., RPE tissue-tropic capsids or retina tissue-tropic capsids).

[0262] While the invention has been particularly shown and described with reference to a preferred embodiment and various alternate embodiments, it is understood by persons skilled in the relevant art that various changes in form and details can be made therein without departing from the spirit and scope of the invention.

CLAIMS

WHAT IS CLAIMED IS:

1. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide,

wherein the 581 to 589 region comprises a sequence of SEQ ID NO: 5014 and further comprises at least one substitution relative to SEQ ID NO: 9; and

wherein the 581 to 589 region comprises one or more basic amino acid residues.

2. The VP capsid polypeptide of claim 1, wherein the 581 to 589 region comprises more basic amino acid residues than acidic amino acid residues.

3. The VP capsid polypeptide of claim 2, wherein the acidic amino acid residues are selected from the group consisting of D and E.

4. The VP capsid polypeptide of any one of claims 1-3, wherein the basic amino acid residues are selected from the group consisting of K, R, and H.

5. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581-589 region of the VP capsid polypeptide comprises a sequence of SEQ ID NO: 5014, wherein X^1, X^2, X^3, X^4, X^5, or X^6 of SEQ ID NO: 5014, or any combination thereof is K or R.

6. The VP capsid polypeptide of any one of claims 1-5, wherein X^1 of SEQ ID NO: 5014 is K or R.

7. The VP capsid polypeptide of claim 4, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 1726, 374, 1442, 933, 1748, 4142, 1434, 1358, 1191, 3732, 4110, 4039, 4411, 4506, 4270, 4156, 3780, 4036, 4030, 4016, 1550, 3899, 1247, 1855, 1181, 3919, 1639, 3664, 1244, 4140, 3930, 4117, 4189, 4001, 3799, 3643, 3619, 1240, 1686, 1479, 1307, 1575, 4296, 1665, 3871, 4135, 1605, 4408, 3604, 1274, 4149, 1313, 3741, 1938, 3709, 1727, 3893, 1280, 3622, 1784, 3834, 1752, 1983, 1743, 3979, 4461, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 1857, 2510, 2316, 1904, 1219, 1486, 1512, 1481, 1516, 3820, 3789, 4252, 4047, 4330, 4082, 4094, 1574, 1248, 4078, 1872, 1426, 3785, 3687, 4318, 4243, 3866, 3704, 4172, 1621, 4315, 1192, 1513, 1856, 2476, 3324, 2769, 2678, 1561, 3296, 375, 2343, 2348, 376, 377, 1395, 1584, 4093, 4453, 3940, 3778, 4374, 4210, 4009, 4264, 4339, 4368, 1738, 378, 1610, 4194, 4474, 4013, 4266, 1771, 1759, 1922, 3860, 3832, 1349, 1381,

3663, 1642, 1185, 4356, 3932, 1233, 4212, 3858, 1198, 4192, 3611, 1919, 1819, 3790, 3712, 1969, 4095, 1887, 4468, 1720, 4247, 934, 1790, 2002, 1657, 1663, 1336, 3894, 1554, 1494, 1405, 3576, 4314, 3695, 1851, 1850, 4362, 1815, 3845, 4511, 3656, 3638, 1406, 1596, 4454, 1443, 1661, 935, 4504, 1359, 1734, 3650, 1910, 1305, 1648, 3831, 4435, 1208, 1988, 4451, 1993, 1986, 3849, 1718, 4068, 1835, 1425, 1428, 1282, 4380, 1658, 1452, 1687, 4024, 379, 4072, 3791, 4491, 4323, 4014, 1304, 1440, 1511, 1981, 1676, 1547, 4422, 1283, 3861, 1383, 3644, 3691, 4259, 1749, 1418, 1176, 4216, 1924, 1421, 1387, 3992, 4423, 4253, 1618, 1871, 1256, 3748, 4119, 1297, 1586, 1251, 1299, 1954, 4450, 3990, 4029, 4097, 3890, 3796, 1389, 3711, 4344, 1578, 1476, 4343, 1202, 4413, 4384, 3808, 1647, 1475, 3892, 3674, 1739, 3926, 3595, 1943, 3756, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 3781, 1535, 1210, 4492, 4365, 4118, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 4350, 4334, 3821, 1932, 3929, 4171, 1258, 3824, 3631, 4465, 4494, 1320, 1398, 3828, 1204, 1223, 1284, 1685, 3773, 4209, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4327, 4037, 4163, 3918, 4486, 1243, 3933, 4178, 1662, 1643, 4152, 3634, 3617, 4445, 4303, 1370, 3838, 4199, 4284, 1213, 4382, 1399, 1187, 3714, 1828, 4487, 3615, 1842, 1501, 3746, 4018, 4420, 3606, 4121, 3724, 3935, 1941, 4419, 4282, 1955, 1949, 4310, 4488, 1577, 4127, 1288, 1171, 3670, 4052, 3627, 3777, 936, 1371, 3685, 1325, 1940, 380, 4482, 4258, 3812, 1581, 1860, 4124, 4508, 4500, 3652, 3972, 1309, 1630, 1528, 3717, 1217, 3692, 4430, 3764, 4316, 4285, 3645, 3971, 4421, 1172, 4026, 2740, 3125, 3546, 1725, 1206, 3842, 4404, 3690, 3962, 4513, 4340, 4329, 4410, 3703, 4136, 1763, 1487, 3589, 3907, 4153, 2707, 3730, 4426, 4180, 4041, 3923, 4444, 3851, 4429, 4361, 1441, 4394, 4302, 3758, 4510, 3742, 1868, 4077, 1710, 1939, 1335, 1666, 1407, 4187, 1193, 1188, 1196, 1724, 1717, 1200, 1646, 1997, 1975, 1701, 4280, 1613, 4006, 1984, 1351, 3653, 3833, 1593, 2561, 4442, 3900, 4298, 1761, 4388, 1820, 1597, 4317, 4249, 1341, 1203, 1680, 4441, 3628, 3725, 1945, 937, 4206, 1588, 1439, 3794, 4447, 1838, 3776, 3658, 4064, 1377, 4011, 4272, 4503, 1324, 1367, 3594, 3680, 1300, 1750, 938, 3913, 3774, 1877, 1987, 1862, 3998, 1380, 4185, 3686, 3696, 4463, 1350, 4008, 4230, 3853, 4244, 4083, 381, 1909, 3897, 1546, 382, 3613, 3273, 3452, 3525, 1229, 4105, 3835, 383, 1263, 1234, 3970, 1492, 3856, 3586, 1175, 4321, 4020, 4144, 1224, 1199, 3667, 2778, 4412, 4407, 1812, 1810, 3823, 1416, 1427, 1507, 1878, 4333, 3146, 4281, 4211, 1179, 3843, 1669, 1677, 1524, 1525, 1974, 384, 1979, 1456, 1239, 4167, 3740, 1876, 1388, 1967, 1474, 385, 1342, 1471, 4176, 1232, 1989, 4125,

1741, 1508, 1580, 4060, 4378, 1576, 1212, 1893, 3921, 3585, 1174, 1396, 4061, 4015, 1207, 3698, 3825, 3922, 4021, 4181, 1598, 1916, 1429, 4502, 4231, 1321, 4390, 3693, 3734, 1382, 3684, 1747, 3806, 3896, 3635, 1768, 4025, 3976, 3840, 3963, 4286, 1502, 3836, 4161, 3659, 3743, 4130, 3605, 1385, 1783, 4392, 4328, 1316, 4173, 4265, 1246, 1985, 1629, 1829, 1737, 3826, 1473, 1992, 1883, 1656, 1837, 1914, 1839, 1834, 3984, 4495, 3910, 4160, 3671, 4184, 4132, 4250, 1503, 1237, 1523, 1417, 4063, 1562, 3977, 1971, 1707, 1847, 1792, 3769, 4074, 1534, 4239, 4003, 3915, 1689, 1776, 1599, 1265, 1410, 1823, 1498, 1329, 939, 386, 940, 387, 1655, 3874, 4261, 3626, 1791, 3579, 1644, 3936, 4054, 4260, 4359, 4131, 4297, 4357, 4022, 3770, 4046, 1222, 1996, 3788, 4169, 1925, 3953, 4228, 4226, 4277, 4101, 1889, 1369, 3797, 4088, 4019, 3771, 3632, 1402, 388, 1520, 1767, 1466, 1194, 4137, 1908, 1927, 1758, 3772, 3661, 4186, 4174, 1170, 3850, 1315, 1611, 1530, 1859, 2209, 4183, 1408, 1403, 941, 4033, 3623, 3596, 1461, 1848, 1173, 1928, 1459, 1765, 1826, 3719, 1931, 3584, 4004, 3591, 3967, 4168, 3957, 3878, 4165, 4191, 3980, 4058, 4200, 4336, 3958, 1260, 4051, 3798, 4032, 1774, 4322, 3991, 4106, 1641, 1570, 3978, 3965, 4464, 3813, 4154, 1365, 4257, 3846, 4345, 4379, 3603, 1693, 3937, 3801, 1787, 1214, 4483, 4201, 1898, 1845, 1226, 1220, 4245, 1347, 3867, 1900, 3640, 3916, 4089, 1209, 3745, 3988, 3975, 4236, 4075, 4146, 4256, 4308, 4000, 4148, 3588, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 3727, 4005, 4092, 4372, 4283, 1553, 3805, 4151, 1281, 1681, 4489, 3982, 4437, 3597, 4342, 3872, 3987, 4490, 3876, 3668, 4300, 1679, 1242, 3598, 3583, 3647, 389, 4304, 3793, 3779, 1937, 1907, 4042, 3648, 3996, 3800, 4367, 4099, 1807, 3887, 4428, 1625, 1390, 1884, 1682, 4364, 4306, 3869, 1278, 1672, 942, 1505, 1542, 1709, 1915, 3600, 3914, 1968, 3948, 1670, 3811, 1865, 1362, 943, 1716, 3961, 1506, 4221, 1376, 944, 1683, 4276, 1445, 1721, 1632, 3607, 1328, 1455, 1913, 1497, 1317, 1951, 1778, 1379, 3768, 4225, 1668, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 571, 1401, 4438, 1895, 1264, 572, 1912, 573, 3939, 4170, 4056, 1271, 1065, 1521, 1221, 1066, 1451, 1654, 1067, 3934, 4080, 4352, 574, 1700, 3739, 1565, 1419, 1811, 3950, 1690, 1397, 3716, 1569, 1465, 1437, 1674, 4337, 1285, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4229, 4292, 4193, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 1729, 4223, 1540, 4455, 1068, 1069, 4512, 1723, 1070, 3750, 3633, 4070, 4104, 4162, 4235, 1863, 4346, 1881, 1071, 1814, 1572, 2418, 575, 4443, 3761, 1346, 1587, 1072, 3592, 576, 1891, 4469, 2430, 1275, 577, 1950, 1963, 4129, 1073, 1296, 1360, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1556, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 2185, 2279, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 2222, 578, 3928, 4295, 3715, 3855, 3609, 1990, 4076, 4175, 3927, 1757, 1650, 4299,

1773, 2004, 1267, 1364, 579, 1462, 1879, 4007, 3729, 3665, 3722, 1691, 1712, 1074, 1624, 1751, 1394, 3924, 3952, 580, 581, 2003, 1343, 2203, 1559, 1250, or 1555.

8. The VP capsid polypeptide of any one of claims 1-5, wherein X^2 of SEQ ID NO: 5014 is K or R.

9. The VP capsid polypeptide of claim 8, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 285, 1626, 299, 3809, 4271, 3844, 1436, 300, 1515, 1617, 3646, 4059, 1431, 1331, 310, 3804, 1363, 1934, 1602, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 1345, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 2772, 3230, 3043, 2922, 3581, 3524, 2869, 2610, 3298, 2775, 3108, 2603, 3614, 2612, 2860, 3187, 3238, 3786, 4385, 3016, 3436, 2876, 2987, 3532, 3438, 3561, 3259, 2663, 2890, 3433, 3071, 3018, 2580, 2755, 3015, 2540, 3398, 2664, 2583, 2830, 2644, 2641, 3513, 2725, 2723, 3338, 3556, 2866, 2514, 2932, 2753, 2862, 2899, 2605, 2989, 3096, 3124, 2985, 2716, 3145, 3017, 2591, 2640, 3033, 1853, 3216, 3316, 3412, 2971, 3256, 3153, 3575, 3339,

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1647, 1475, 3892, 3674, 1739, 3926, 3595, 1943, 3756, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 3781, 1535, 1210, 4492, 4365, 4118, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 4350, 4334, 3821, 1932, 3929, 4171, 1258, 3824, 3631, 4465, 4494, 1320, 1398, 3828, 1204, 1223, 1284, 1685, 3773, 4209, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4327, 4037, 4163, 3918, 4486, 1243, 3933, 4178, 1662, 1643, 4152, 3634, 3617, 4445, 4303, 1370, 3838, 4199, 4284, 1213, 4382, 1399, 1187, 3714, 1828, 4487, 3615, 1842, 1501, 3746, 4018, 4420, 3606, 4121, 3724, 3935, 1941, 4419, 4282, 1955, 1949, 4310, 4488, 1577, 4127, 1288, 1171, 3670, 4052, 3627, 3777, 936, 1371, 3685, 1325, 1940, 380, 4482, 4258, 3812, 1581, 1860, 4124, 4508, 4500, 3652, 3972, 1309, 1630, 1528, 3717, 1217, 3692, 4430, 3764, 4316, 4285, 3645, 3971, 4421, 1172, 4026, 2740, 3125, 3546, 1725, 1206, 3842, 4404, 3690, 3962, 4513, 4340, 4329, 4410, 3703, 4136, 1763, 1487, 3589, 3907, 4153, 2707, 3730, 4426, 4180, 4041, 3923, 4444, 3851, 4429, 4361, 1441, 4394, 4302, 3758, 4510, 3742, 1868, 4077, 1710, 1939, 1335, 1666, 1407, 4187, 1193, 1188, 1196, 1724, 1717, 1200, 1646, 4176, 1232, 1989, 4125, 1741, 1508, 1580, 4060, 4378, 1576, 1212, 1893, 3921, 3585, 1174, 1396, 4061, 4015, 1207, 3698, 3825, 3922, 4021, 4181, 1598, 1916, 1429, 4502, 4231, 1321, 4390, 3693, 3734, 1382, 3684, 1747, 3806, 3896, 3635, 1768, 4025, 3976, 3840, 3963, 4286, 1502, 3836, 4161, 3659, 3743, 4130, 3605, 1385, 1783, 4392, 4328, 1316, 4173, 4265, 1246, 1985, 1629, 1829, 1737, 3826, 1473, 1992, 1883, 1656, 1837, 1914, 1839, 1834, 3984, 4495, 3910, 4160, 3671, 4184, 4132, 4250, 1503, 1237, 1523, 1417, 4063, 1562, 3977, 1971, 1707, 1847, 1792, 3769, 4074, 1534, 4239, 4003, 3915, 1689, 1776, 1599, 1265, 1410, 1823, 1498, 954, 955, 2437, 4139, 1482, 3602, 4434, 3721, 1592, 1825, 1698, 1519, 1352, 4202, 4409, 1977, 1917, 2382, 3675, 1833, 3974, 419, 4309, 4045, 3854, 3682, 2491, 444, 445, 1972, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3873, 3755, 1216, 3599, 3775, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3694, 446, 3985, 3535, 1306, 4084, 3282, 447, 1353, 2168, 3879, 2698, 1894, 1882, 1817, 1880, 490, 1018, 3917, 3616, 4311, 1800, 4473, 4085, 4401, 1310, 3783, 3765, 1538, 3870, 491, 1948, 3699, 1735, 3792, 4290, 2074, 492, 1019, 2012, 1803, 3642, 497, 1322, 1261, 4027, 3478, 3763, 2959, 1293, 2462, 517, 3197, 1595, 3413, 1675, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 3803, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 1449, 2121, 1044, 3720, 4351, 4414, 1673, 3453, 3254, 2501, 1050, 3515, 2219, 1433, 1323, 4301, 1569, 1465, 1437, 1674, 4337, 1285, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938,

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10. The VP capsid polypeptide of any one of claims 1-5, wherein X^3 of SEQ ID NO: 5014 is K or R.

11. The VP capsid polypeptide of claim 10, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 760, 53, 3925, 55, 3654, 56, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 3882, 3713, 1942, 1312, 4501, 76, 77, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891,

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12. The VP capsid polypeptide of any one of claims 1-5, wherein X^4 of SEQ ID NO: 5014 is K or R.

13. The VP capsid polypeptide of claim 12, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 739, 4177, 1289, 15, 743, 3477, 3051, 2982, 2877, 746, 3036, 3426, 3073, 3169, 3362, 2784, 3192, 1638, 25, 1703, 1836, 3660, 30, 32, 752, 1653, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608,

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3574, 3081, 3007, 3568, 3152, 3367, 3358, 3468, 3290, 3550, 3132, 2726, 2879, 3190, 3309, 2613, 2765, 3454, 2851, 2881, 3232, 3458, 3326, 3353, 2927, 3212, 2950, 3376, 3208, 3062, 3612, 3195, 3385, 2686, 2602, 3569, 3123, 2727, 2821, 2636, 2750, 2850, 3050, 2925, 3336, 3540, 2689, 3139, 2526, 3361, 3022, 3427, 3107, 3140, 3371, 3276, 2831, 3501, 2924, 3366, 3199, 3101, 3321, 3499, 2917, 2683, 2800, 2812, 3340, 3227, 3148, 3657, 4446, 1746, 2666, 3246, 3130, 3560, 3236, 2730, 3572, 1607, 3689, 2968, 1457, 1500, 1184, 3450, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 4147, 3002, 2986, 910, 2979, 2542, 4472, 1472, 4057, 4507, 1711, 913, 916, 1594, 4440, 343, 918, 345, 348, 350, 1518, 3728, 3637, 3570, 3429, 2870, 2995, 4338, 3205, 2880, 3261, 1994, 3968, 4291, 4204, 4071, 352, 2820, 3912, 3287, 1218, 1190, 4145, 353, 355, 1782, 928, 3610, 358, 4224, 1918, 1959, 1840, 3736, 4155, 1543, 4049, 1633, 1495, 372, 1873, 1726, 1748, 4411, 4506, 4270, 4156, 3780, 4036, 4030, 4016, 1550, 3899, 1247, 1244, 4140, 3930, 4117, 4189, 4001, 3799, 3643, 3619, 4149, 1313, 3709, 1727, 3893, 1280, 3622, 1784, 3834, 1752, 3979, 4461, 4113, 3817, 4232, 3902, 1857, 1904, 1481, 1516, 3820, 3789, 4252, 4047, 4330, 4082, 4094, 3785, 3687, 4318, 4243, 3866, 1621, 4315, 1192, 1513, 1856, 3324, 2769, 2678, 3296, 375, 1395, 1584, 4093, 3940, 3778, 4374, 4210, 4009, 4264, 4368, 1610, 4194, 4474, 4013, 4266, 1759, 1922, 3663, 1642, 1185, 4356, 3932, 1233, 4212, 3858, 1198, 4192, 3790, 3712, 1969, 934, 1790, 1663, 1336, 3894, 1554, 1494, 1405, 3576, 4314, 3695, 3845, 4511, 3656, 1406, 1596, 4504, 1359, 1734, 3650, 1305, 1208, 1988, 4451, 1282, 4380, 1658, 1452, 1687, 3791, 4491, 4323, 4014, 1304, 1440, 4422, 3861, 1383, 3644, 3691, 4259, 1749, 4216, 1924, 1421, 1387, 3992, 4423, 4253, 1618, 1871, 1256, 3748, 1297, 1586, 1251, 1299, 1954, 3655, 3886, 4278, 4383, 4485, 1392, 3751, 3931, 3986, 3678, 1249, 4353, 4208, 3710, 4238, 4213, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 3954, 4335, 3995, 3582, 4475, 3784, 4470, 4010, 3802, 3941, 4427, 4396, 4348, 3587, 3818, 3864, 3956, 3863, 3731, 3814, 4067, 4354, 3014, 4462, 4246, 4190, 4312, 4023, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4327, 4037, 4163, 3918, 4486, 1243, 3933, 4178, 3627, 3777, 1371, 3685, 1325, 1940, 4482, 4258, 3812, 1581, 1217, 3692, 4430, 3764, 4316, 4285, 3645, 3971, 4421, 1172, 4026, 2740, 3125, 3546, 1725, 1206, 3842, 4404, 3690, 3962, 4513, 4340, 4329, 4410, 3703, 4153, 2707, 3730, 4426, 4180, 4041, 3923, 4444, 3851, 4429, 4361, 1441, 4394, 4302, 3758, 4510, 3742, 1666, 1407, 4187, 1188, 1724, 1646, 4280, 1613, 4006, 1984, 1351, 3653, 3833, 2561, 4442, 3900, 4298, 1203, 4441, 3628, 3725, 937, 4447, 3776, 3658, 4064, 1324, 1367, 3594, 3680, 1300, 1987, 1862, 3998, 1380, 4185, 3686, 3696, 4463, 1350, 4008, 4230, 3853, 4244, 4083, 1546, 3613, 3273, 3452, 3525, 4105, 3835, 1263, 4020, 4144, 1224, 1199, 3667, 2778, 4412, 4407, 1812, 1810, 3823, 1416, 4333, 3146, 4281,

4211, 1979, 1456, 1239, 4167, 3740, 1876, 1388, 1967, 1474, 1471, 4176, 1232, 1989, 4125, 1741, 3585, 1174, 1396, 4061, 4015, 1207, 3698, 3825, 3922, 4021, 4181, 1598, 1916, 1429, 4502, 4231, 1321, 4390, 3693, 3734, 3635, 1768, 4025, 3976, 3840, 3963, 4286, 1502, 3836, 4161, 3659, 3743, 4130, 3605, 1385, 1783, 4392, 3826, 1473, 1883, 1834, 3984, 4495, 3910, 4160, 3671, 4184, 4132, 4250, 1503, 1237, 1523, 1417, 4063, 1562, 3977, 1971, 1707, 3769, 4074, 1534, 4239, 4003, 3915, 1689, 1776, 1410, 1823, 1498, 1329, 386, 3936, 4054, 4260, 4359, 4131, 4297, 4357, 4022, 3770, 4046, 1222, 3953, 4228, 4226, 4277, 1520, 1767, 1466, 1194, 4137, 1908, 1927, 1758, 3772, 3661, 4186, 4174, 1170, 1859, 4183, 1408, 1403, 941, 4033, 3623, 1826, 3719, 1931, 3584, 4004, 3591, 3967, 4168, 3957, 3878, 4165, 4191, 3980, 4058, 4200, 4336, 4322, 3991, 4106, 1641, 1570, 3978, 4154, 1365, 4257, 3846, 4345, 4379, 3603, 1693, 3937, 3801, 4201, 1898, 1845, 1226, 1220, 3745, 3988, 3975, 4236, 4075, 4146, 4256, 4308, 4000, 4148, 3588, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 3727, 4005, 4489, 3982, 4437, 3597, 4342, 3872, 3987, 4490, 3876, 3668, 4300, 4042, 3648, 3996, 3800, 4367, 4099, 1807, 3887, 4428, 1884, 1682, 4364, 4306, 3869, 3600, 3914, 1968, 1670, 3811, 1865, 3961, 1506, 4221, 1376, 1379, 3768, 4225, 945, 394, 1714, 1422, 3618, 4433, 1965, 4471, 954, 4139, 1482, 3721, 1825, 1698, 1519, 1352, 4202, 4409, 1977, 1917, 405, 406, 3889, 413, 962, 418, 3675, 3974, 964, 420, 967, 968, 1897, 1272, 4133, 425, 4141, 430, 3749, 4044, 3590, 1944, 4126, 977, 4400, 1606, 980, 2604, 2895, 3448, 4563, 1692, 4055, 4358, 1664, 4309, 4045, 3854, 3682, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3873, 3755, 1216, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3985, 3535, 1306, 4084, 3282, 447, 1353, 1780, 449, 1485, 453, 1728, 454, 1696, 455, 3116, 1869, 457, 1386, 3879, 2698, 459, 1447, 4425, 1645, 467, 1488, 478, 1604, 1011, 4313, 4073, 4274, 1775, 2000, 2480, 1882, 1817, 1880, 1800, 4473, 3783, 3870, 1948, 3699, 1735, 3792, 4290, 492, 4090, 1019, 1803, 3642, 497, 500, 1333, 1890, 1024, 3608, 1864, 1531, 3636, 1699, 1028, 1366, 1030, 4027, 3478, 3763, 2959, 1293, 517, 3197, 1595, 3413, 2238, 1031, 1448, 1032, 1675, 1797, 3759, 1215, 4122, 3966, 528, 3911, 3289, 1821, 1874, 1037, 536, 1039, 3767, 3683, 540, 541, 1338, 1616, 1901, 1517, 2719, 3803, 4123, 4233, 3129, 3087, 3505, 4158, 1044, 3720, 4351, 4414, 1673, 3453, 3254, 1649, 543, 4240, 3580, 2598, 4062, 2841, 1049, 3515, 1433, 1323, 4301, 1051, 3738, 1270, 3857, 1056, 3662, 1057, 3981, 1063, 568, 570, 3620, 1064, 4002, 3964, 3707, 3666, 1348, 4273, 4497, 1401, 4438, 1895, 1912, 3939, 4170, 4056, 1221, 1654, 1067, 3934, 4080, 4352, 574, 3739, 1565, 3950, 1397, 3716, 1569, 1465, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 4455, 4512, 3750, 3633, 4070, 4104, 4162, 4235, 4346, 1572, 4443, 3761, 1346, 3592, 1891, 4469, 1275, 577, 1963, 4129, 1296, 1360, 3733, 4111, 3993, 4108, 3949, 1556, 1435, 1424,

1830, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 4293, 1827, 3839, 3983, 4395, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1650, 4299, 1773, 2004, 1267, 1364, 4007, 3729, 3665, 3722, 1712, 1751, 3924, 3952, 1343, 4114, 1704, 4448, 1786, 3354, 586, 3432, 2891, 587, 1903, 2077, 1080, 1563, 2274, 595, 2559, 2590, 2738, 4478, 4069, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 1412, 4017, 4477, 1794, 4263, 3072, 2199, 3888, 604, 605, 1368, 3827, 4103, 607, 1571, 1438, 3701, 4389, 4897, 1603, 2154, 1715, 4369, 1652, 1733, 4218, 1798, 621, 1667, 1384, 3700, 1788, 1600, 1102, 1423, 2771, 1339, 3070, 2557, 2795, 2906, 3299, 3118, 4779, 2028, 1614, 1947, 630, 4479, 3766, 1106, 634, 1108, 635, 638, 3706, 3735, 3390, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1585, 3221, 2643, 2739, 3920, 1801, 4279, 2502, 1117, 2965, 2695, 3293, 3264, 2076, 657, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 667, 1133, 1134, 673, 1933, 1731, 1793, 3342, 683, 1146, 687, 3822, 1601, 692, 3905, 1414, 696, 1695, 4115, 701, 1544, 702, 703, 4031, 2010, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 1532, 1493, 1854, 1510, 705, 1153, 4476, 1375, 712, 1245, 715, 4234, 1154, 1314, 4096, 720, 1311, 721, 722, 4217, 726, 3815, 2005, 1964, 1262, 4480, 4294, 1582, 3439, 2833, 4287, 4509, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 1195, 3859, 3807, 4307, 1454, or 1781.

14. The VP capsid polypeptide of any one of claims 1-5, wherein X^5 of SEQ ID NO: 5014 is K or R.

15. The VP capsid polypeptide of claim 14, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4177, 742, 16, 17, 18, 745, 3477, 1548, 2982, 3426, 3073, 3169, 747, 3362, 4942, 23, 28, 2038, 3660, 750, 31, 32, 1640, 34, 37, 4925, 1205, 4288, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3688, 4320, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 1225, 3178, 3006, 3252, 2991, 2642, 2519, 3363, 2633, 42, 755, 44, 756, 46, 1952, 758, 2410, 2551, 3718, 1308, 1230, 3960, 1378, 2589, 3681, 760, 53, 4951, 4591, 762, 3925, 55, 3654, 763, 60, 61, 4086, 1740, 766, 1966, 63, 2041, 64, 769, 770, 2384, 771, 65, 772, 2197, 68, 3816, 69, 2599, 70, 3865, 1549, 3882, 75, 4501, 76, 774, 1413, 776, 3757, 3593, 4043, 4397, 4415, 3754, 1470, 4360, 3945, 2854, 3523,

3669, 1356, 81, 82, 4065, 83, 84, 1294, 87, 3891, 4456, 4040, 1189, 1490, 90, 92, 782, 94, 1831, 1867, 4458, 1936, 100, 792, 2007, 4556, 795, 104, 106, 1849, 2509, 110, 1906, 798, 2359, 2461, 4864, 1344, 116, 120, 121, 803, 1463, 805, 1760, 123, 124, 806, 127, 2085, 130, 132, 809, 1978, 134, 813, 139, 815, 1326, 141, 142, 145, 4816, 1302, 817, 146, 818, 148, 149, 4546, 150, 153, 156, 157, 163, 164, 166, 169, 823, 824, 1483, 175, 177, 178, 179, 826, 827, 182, 183, 829, 184, 185, 190, 191, 192, 2361, 195, 1391, 197, 2223, 201, 202, 4775, 1334, 837, 3901, 3312, 212, 4386, 3028, 213, 1446, 214, 215, 1896, 3490, 217, 219, 223, 225, 2088, 4542, 226, 227, 230, 843, 844, 237, 845, 239, 849, 852, 1536, 854, 244, 245, 248, 855, 251, 253, 255, 257, 858, 860, 262, 863, 4535, 865, 264, 1241, 265, 1477, 267, 867, 1252, 273, 275, 1980, 277, 281, 1892, 879, 1539, 881, 1295, 282, 285, 1626, 2082, 1374, 1620, 4564, 289, 887, 888, 889, 4324, 293, 4138, 296, 3903, 892, 3829, 298, 301, 302, 1589, 4370, 2342, 309, 4059, 310, 1779, 1558, 1552, 317, 320, 898, 321, 2016, 2134, 324, 325, 327, 1635, 4484, 1756, 4609, 332, 4635, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3214, 3163, 2541, 3090, 3097, 3462, 3037, 3419, 2780, 2931, 1276, 2789, 3228, 2657, 3189, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3102, 3466, 3461, 2788, 2660, 3344, 2720, 3379, 2826, 3249, 3527, 4460, 3352, 4319, 3906, 4248, 3804, 1363, 1404, 4349, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 3092, 3459, 3144, 3441, 2802, 3479, 2907, 3512, 3518, 3021, 2871, 3032, 2647, 2945, 3045, 2763, 3313, 3034, 3315, 3541, 2746, 2669, 2524, 3003, 2732, 3166, 3046, 3306, 2873, 3364, 3253, 3215, 3061, 2804, 2722, 2964, 2990, 2836, 4098, 4449, 3173, 2762, 3737, 2628, 3507, 2564, 3031, 2872, 3360, 2658, 2930, 2904, 3244, 3217, 3311, 3445, 2840, 3372, 2958, 3098, 3356, 3456, 3388, 2624, 3207, 2576, 2742, 2665, 2815, 3052, 3421, 2593, 3242, 2535, 2966, 2898, 2858, 2943, 2668, 2798, 3196, 2528, 2713, 3001, 2691, 2948, 2767, 2544, 3302, 2734, 2893, 2592, 2861, 3502, 2969, 2582, 3229, 2676, 2545, 3255, 3330, 2547, 3257, 2882, 3151, 3088, 2883, 3318, 2645, 2733, 2587, 3500, 3008, 2715, 2845, 3183, 2654, 3233, 3267, 2741, 2827, 2704, 3091, 2832, 2736, 3177, 3271, 2835, 2908, 3176, 2947, 3292, 3191, 2517, 3026, 3082, 3392, 3782, 3629, 3578, 3885, 4081, 1764, 1852, 4431, 3241, 3077, 2700, 3147, 2648, 3283,

2829, 3278, 2581, 2536, 4363, 2848, 3410, 2797, 2523, 2520, 2721, 3496, 2571, 3198, 3219, 3030, 2673, 2921, 3837, 3301, 3322, 2705, 3239, 2949, 3369, 3396, 2892, 2897, 2766, 3174, 3297, 2550, 2889, 2933, 2793, 2627, 2677, 3119, 2596, 3226, 3172, 3089, 2868, 2839, 3942, 4222, 1504, 3180, 2813, 2652, 2600, 2816, 3201, 3188, 3270, 2997, 2992, 3009, 3520, 2936, 3275, 3165, 3447, 3131, 3305, 2809, 2792, 2729, 2814, 2619, 3266, 2825, 3066, 2857, 2998, 3064, 2681, 3035, 3279, 2764, 3480, 3127, 2912, 3010, 2607, 3211, 3111, 3909, 4269, 3019, 1415, 3020, 2748, 2646, 2787, 2760, 3158, 3170, 2703, 3494, 3404, 2675, 2749, 3341, 3355, 2594, 3495, 2884, 3516, 3042, 2737, 2923, 3563, 2855, 3476, 2611, 2937, 3383, 2875, 3223, 2878, 1808, 2951, 3519, 2579, 2853, 3387, 3401, 3007, 3568, 3152, 3367, 3358, 336, 3290, 3550, 3309, 2613, 2765, 1355, 2881, 3232, 3458, 3326, 3353, 2927, 3212, 2950, 3376, 3208, 3062, 3612, 3195, 3385, 2686, 1622, 3361, 3022, 3427, 3107, 3140, 3371, 3276, 2831, 3501, 2924, 3366, 3199, 3101, 3321, 3499, 2917, 2683, 1464, 3560, 3236, 2730, 3572, 1607, 909, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 3002, 2338, 4472, 1472, 1529, 4507, 1583, 340, 912, 2013, 913, 2277, 1594, 4440, 917, 343, 344, 345, 346, 350, 351, 4498, 3637, 3570, 3429, 4091, 4338, 3205, 2880, 3261, 3968, 4291, 4204, 4034, 2820, 3912, 3287, 1218, 1190, 4145, 354, 3610, 4224, 1840, 3736, 1770, 4155, 932, 363, 1279, 2156, 1722, 368, 1566, 370, 4967, 372, 1211, 2494, 1726, 1748, 1191, 4039, 4411, 4506, 4270, 4156, 3780, 1550, 3899, 1181, 3919, 1639, 3664, 4189, 4001, 3799, 1240, 1686, 1479, 1307, 1575, 4296, 1665, 3871, 1605, 4408, 4149, 3741, 3893, 1280, 1983, 3979, 3817, 1489, 4214, 3902, 1857, 1904, 3820, 3789, 4252, 4330, 4082, 3785, 3687, 4243, 3704, 4172, 4315, 1192, 2769, 2678, 3296, 2343, 4093, 4453, 3940, 3778, 4374, 4339, 4368, 4194, 4474, 4013, 1771, 1759, 3860, 3832, 1381, 4356, 1233, 4212, 3858, 1198, 3611, 1919, 1819, 3790, 1969, 4247, 1790, 3894, 1554, 3576, 4314, 1851, 1850, 4511, 3656, 3638, 1406, 1443, 1661, 4504, 3831, 4435, 1208, 1988, 3849, 1835, 4380, 4024, 4491, 4323, 4014, 1511, 1981, 1676, 1547, 1383, 3644, 3691, 4259, 1176, 4216, 1924, 1387, 4423, 1256, 4119, 1251, 3990, 4029, 4097, 3890, 3796, 4343, 1202, 4413, 4384, 3808, 3892, 3926, 3756, 4405, 4109, 1210, 4492, 3969, 4436, 3175, 4128, 2970, 1228, 3534, 3437, 3784, 4470, 4010, 4334, 3821, 4171, 3824, 3631, 4494, 1320, 1204, 1223, 1284, 1685, 3760, 3753, 1178, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 3673, 4102, 4100, 4327, 3634, 3617, 4445, 4303, 1370, 3838, 1187, 3615, 3746, 3935, 1941, 4419, 1171, 3670, 3777, 936, 3685, 1325, 1940, 4482, 4258, 3812, 4124, 4508, 4500, 3652, 3972, 1630, 4421, 1172, 4026, 2740, 3125, 3546, 4513, 4340, 1763, 1487, 3589, 3907, 4041, 3851, 4077, 4187, 1193, 1196, 1724, 1717, 1200, 1975, 1613, 4006, 3653, 3833, 1593, 4442, 3900, 4388, 1820, 4317, 4249, 3628, 3794, 4447, 3776, 3658, 1377, 4011, 4272, 3594, 4185, 3686, 3696, 1350, 4230, 3853, 4244, 1909, 3897, 1546, 3273, 3452, 3525, 4105, 3835, 383, 1263, 1492, 3856, 3586, 1175,

4144, 1224, 1199, 3667, 2778, 4412, 1507, 3146, 4281, 1179, 3843, 3740, 1388, 1474, 1342, 1471, 4176, 1741, 1508, 4378, 1212, 4015, 1207, 3698, 3825, 4231, 3806, 3896, 3963, 4286, 3743, 4130, 3605, 4173, 4265, 1246, 1737, 3826, 1473, 1992, 1883, 1656, 3671, 4063, 1847, 4239, 3915, 1265, 1498, 1329, 3874, 4261, 1791, 3579, 4359, 4131, 4297, 4357, 4046, 3788, 4169, 1925, 4228, 4101, 1889, 1369, 4088, 4019, 1194, 3772, 3850, 1315, 1530, 1859, 4183, 1408, 4033, 3623, 1928, 1459, 1765, 4004, 3591, 3967, 4168, 3957, 3878, 3980, 3958, 4051, 3798, 4032, 3991, 4106, 1641, 4464, 3813, 4257, 3846, 4345, 1787, 1214, 4483, 4201, 1220, 3867, 3640, 3916, 1209, 4236, 4075, 4146, 4256, 4308, 4000, 4148, 3588, 3883, 4326, 4092, 4283, 1553, 3805, 4151, 1281, 1681, 4489, 3982, 4437, 3597, 4342, 3987, 3583, 3647, 389, 4304, 3793, 1937, 3996, 3800, 4367, 4099, 1390, 4364, 4306, 1278, 1672, 1542, 1915, 3600, 3948, 3811, 1362, 4276, 1445, 1721, 1632, 3607, 1317, 1778, 1668, 391, 4406, 4341, 1480, 393, 394, 395, 946, 3618, 4433, 1177, 947, 950, 400, 4471, 401, 402, 954, 3602, 4434, 3721, 1825, 4202, 4409, 406, 1631, 1684, 3889, 410, 412, 2352, 1905, 417, 418, 3675, 1833, 3974, 419, 964, 420, 421, 969, 4733, 1272, 971, 423, 3830, 973, 426, 1708, 428, 4141, 3749, 1619, 975, 4044, 3590, 1706, 4400, 979, 2895, 3448, 438, 982, 2433, 983, 442, 3862, 2435, 443, 4309, 4045, 3854, 3682, 444, 445, 4366, 3425, 3231, 3649, 2759, 2724, 3873, 3599, 3775, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 3694, 446, 3985, 3535, 4084, 3282, 988, 2107, 990, 451, 452, 453, 992, 993, 1696, 996, 3116, 1386, 999, 458, 3879, 460, 461, 462, 2339, 1003, 4425, 1645, 1004, 466, 2328, 468, 1231, 1468, 2496, 473, 474, 2108, 1273, 1007, 1744, 1659, 478, 1009, 1012, 4313, 482, 1499, 484, 2513, 2205, 4592, 1458, 4274, 2122, 4905, 4205, 2000, 488, 1894, 3917, 3616, 4311, 4085, 4401, 1310, 3783, 1538, 3870, 1948, 3699, 1735, 3792, 2202, 4090, 2378, 2012, 3642, 1020, 2302, 4665, 4781, 500, 1022, 1023, 4686, 505, 507, 508, 509, 1025, 1732, 1816, 3636, 1028, 516, 1366, 4572, 2489, 1261, 4027, 3763, 2959, 1293, 3197, 1448, 1032, 519, 2420, 522, 3759, 1215, 4122, 1730, 524, 526, 3966, 1035, 527, 528, 529, 530, 531, 1036, 532, 533, 536, 537, 3767, 1929, 1041, 3683, 1043, 4906, 542, 1338, 1796, 4331, 4332, 4466, 3803, 3087, 3505, 1449, 1044, 4414, 3453, 3254, 544, 546, 1045, 547, 4240, 3580, 4680, 549, 550, 2598, 551, 3819, 1259, 4062, 554, 1049, 1050, 1433, 555, 1052, 1053, 3738, 3857, 2089, 1056, 2193, 1257, 1238, 3662, 1059, 1060, 4203, 3981, 1303, 4116, 567, 569, 3620, 4002, 3679, 3707, 4497, 4438, 1264, 3939, 4170, 4056, 1271, 1451, 1654, 3934, 4080, 4352, 574, 3739, 1565, 1419, 3950, 3716, 1465, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4164, 3630, 4229, 4292, 4215, 1729, 4223, 4455, 4512, 3633, 4070, 4104, 4162, 4443, 3761, 1587, 3592, 1891, 4469, 1963, 4129, 1360, 3949, 1861, 4120, 1292, 4293, 3839, 3983, 3928, 4295, 3715, 3855, 3609, 1990, 4007, 3722, 1624, 3924, 3952, 580, 2003, 1343, 582, 4114, 1818, 1704, 4448, 584, 1078, 1786, 585, 1832, 586, 2891, 587, 4936, 1082, 4459, 2113, 590, 2308, 593,

1858, 597, 2738, 4150, 3260, 3481, 4439, 1268, 4050, 3377, 4424, 3492, 1412, 4477, 4263, 3072, 2009, 3888, 3827, 4103, 1438, 609, 610, 611, 3701, 4389, 613, 4369, 617, 1921, 1373, 1870, 4218, 1099, 1702, 4801, 623, 3700, 1788, 625, 4878, 1423, 1339, 3875, 628, 2557, 2906, 2029, 4876, 1103, 631, 4479, 3766, 632, 1104, 1105, 634, 4651, 1108, 1813, 636, 638, 641, 4581, 1112, 2164, 3735, 3390, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 4398, 1269, 3624, 4481, 1432, 3295, 1568, 1766, 2643, 2739, 4760, 1115, 3920, 644, 645, 646, 4279, 3762, 1637, 1509, 2200, 1117, 4780, 2965, 2695, 650, 651, 653, 654, 655, 658, 4035, 2910, 3391, 2808, 3676, 2852, 3284, 3537, 1319, 4467, 1802, 1227, 660, 4812, 2364, 1124, 1125, 665, 4917, 1127, 1129, 1132, 1133, 2236, 673, 4557, 1136, 1139, 678, 4737, 4531, 679, 680, 1144, 681, 4525, 2415, 685, 2445, 3822, 690, 691, 1601, 4621, 3905, 695, 1149, 696, 2027, 2160, 1795, 1372, 4115, 2194, 1920, 4031, 1393, 1277, 1400, 4402, 4157, 4028, 704, 1902, 1510, 4182, 1153, 4476, 2053, 710, 1375, 715, 4096, 717, 1155, 719, 1311, 722, 4217, 1156, 723, 1157, 1627, 4566, 1158, 724, 725, 1953, 1201, 3787, 3747, 1846, 3815, 1822, 1537, 1318, 4294, 733, 734, 3439, 2833, 4505, 4267, 3697, 4112, 2967, 3651, 1805, 1163, 3859, 2275, 737, 1167, 1745, 3807, or 4307.

16. The VP capsid polypeptide of any one of claims 1-5, wherein X^6 of SEQ ID NO: 5014 is K or R.

17. The VP capsid polypeptide of claim 16, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 1308, 3960, 1378, 2994, 3080, 2589, 3681, 51, 760, 762, 3925, 3654, 763, 59, 60, 4086, 1740, 1660, 62, 1966, 63, 2438, 768, 66, 67, 68, 3816, 2599, 2706, 72, 73, 74, 3865, 1549, 1361, 3882, 773, 3713, 1942, 1312, 4501, 76, 1413, 775, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 1356, 4065, 1294, 1484, 85, 86, 3891, 4456, 4040, 4496, 1982,

2001, 1478, 1189, 1490, 1885, 1926, 89, 780, 1180, 92, 781, 782, 783, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 1936, 1590, 98, 99, 789, 790, 1298, 1688, 791, 792, 2007, 102, 103, 104, 105, 107, 108, 1579, 1906, 111, 798, 112, 799, 800, 1444, 801, 114, 115, 1344, 116, 802, 117, 118, 119, 121, 803, 1463, 1760, 806, 126, 128, 807, 129, 131, 808, 133, 1978, 811, 812, 135, 136, 137, 138, 814, 140, 1326, 141, 142, 143, 2344, 816, 1634, 1302, 817, 818, 147, 148, 149, 150, 151, 154, 155, 819, 820, 156, 157, 158, 161, 162, 165, 822, 168, 169, 170, 823, 172, 1651, 173, 1483, 174, 825, 176, 178, 180, 827, 181, 828, 4911, 184, 186, 188, 189, 830, 192, 193, 194, 196, 1391, 198, 199, 200, 201, 202, 203, 205, 832, 206, 834, 207, 208, 209, 210, 835, 836, 1334, 3901, 3312, 2649, 1450, 4386, 3028, 1446, 1522, 3490, 217, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 225, 228, 229, 230, 231, 842, 232, 233, 234, 238, 847, 239, 850, 851, 853, 1536, 240, 241, 242, 243, 244, 245, 247, 250, 251, 254, 255, 857, 256, 258, 259, 859, 260, 861, 862, 864, 263, 2318, 865, 2326, 264, 1241, 266, 1477, 867, 268, 868, 269, 270, 869, 870, 271, 871, 872, 272, 873, 1252, 1591, 875, 274, 275, 276, 876, 877, 277, 278, 280, 1892, 1539, 881, 3601, 3877, 1460, 282, 1799, 284, 1626, 286, 1374, 1620, 1290, 1354, 887, 1956, 889, 292, 4324, 4138, 891, 296, 3903, 297, 3829, 3809, 4271, 3844, 1436, 300, 1617, 1961, 302, 304, 305, 2147, 1589, 4370, 307, 3646, 4059, 1431, 1331, 312, 1779, 313, 896, 1558, 1552, 318, 319, 322, 1958, 323, 324, 901, 1491, 328, 329, 4484, 907, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3414, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 4248, 1557, 3804, 1602, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585,

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2778, 4412, 4407, 3823, 1427, 1507, 1878, 4333, 3146, 4281, 4211, 3843, 1677, 1524, 1525, 1974, 1239, 4167, 3740, 1342, 1471, 4176, 1232, 1989, 4125, 1741, 1580, 4060, 1576, 1212, 3921, 1174, 4061, 4021, 3693, 3734, 1382, 3684, 3806, 3635, 3976, 3840, 4286, 3836, 4161, 3659, 3605, 4392, 4328, 1316, 4173, 4265, 1246, 1629, 1829, 3826, 1992, 1656, 1914, 1839, 3984, 3910, 4160, 4184, 4132, 4250, 1792, 3769, 1534, 4003, 1689, 1599, 1265, 1410, 1823, 1498, 1329, 386, 940, 1655, 3874, 4261, 3626, 3579, 1644, 3936, 4054, 4260, 4297, 4357, 4022, 4046, 1222, 1996, 3788, 3953, 4226, 4277, 4101, 3797, 4019, 3771, 3632, 1402, 4137, 3772, 3661, 4186, 4174, 1170, 3850, 1315, 1611, 1859, 4183, 1403, 4033, 3623, 3596, 1461, 1848, 1173, 1928, 1765, 3719, 3584, 4165, 4191, 3980, 4058, 4200, 4336, 3958, 1260, 4051, 3798, 4032, 1774, 4322, 3991, 4106, 3978, 3965, 4464, 3813, 4154, 1365, 3846, 4345, 4379, 3603, 3937, 3801, 1787, 1214, 4483, 4201, 1845, 1220, 4245, 1347, 3867, 1900, 3640, 3916, 4089, 3745, 3975, 4256, 4308, 4000, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 4005, 4092, 4372, 4283, 3805, 4151, 3982, 3597, 3872, 3987, 4490, 3876, 3668, 4300, 1679, 1242, 3598, 3583, 3647, 4304, 3779, 1907, 4042, 3648, 3996, 3800, 4367, 4099, 1807, 3887, 4428, 1625, 1390, 1884, 1682, 4364, 4306, 3869, 1278, 942, 1505, 1709, 3600, 3914, 3948, 1865, 1716, 3961, 1506, 4221, 1376, 1683, 4276, 1721, 1632, 3607, 1455, 1913, 1497, 1317, 1951, 1778, 3768, 4225, 1668, 390, 4406, 4341, 1480, 1714, 1422, 397, 3618, 4433, 1177, 3898, 398, 950, 400, 1965, 4471, 953, 401, 403, 955, 1482, 3602, 4434, 3721, 1592, 1825, 1698, 1519, 1352, 4409, 1977, 405, 1631, 1684, 409, 3889, 2117, 411, 413, 414, 415, 961, 1905, 416, 963, 3675, 1833, 3974, 965, 970, 1897, 1272, 4133, 3830, 972, 424, 427, 1708, 4141, 3749, 1619, 975, 4044, 3590, 1944, 4126, 1923, 1706, 432, 976, 978, 4400, 1606, 980, 2604, 2895, 436, 3448, 2188, 438, 1692, 442, 3862, 4055, 4358, 2276, 985, 1664, 443, 4309, 4045, 3854, 3682, 1972, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3755, 1216, 3599, 3775, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3694, 3985, 3535, 1306, 4084, 3282, 1780, 448, 990, 991, 1485, 992, 1728, 993, 994, 1696, 997, 3116, 1869, 456, 1386, 1000, 3879, 2698, 460, 1001, 461, 1447, 1002, 1003, 463, 464, 4425, 465, 1004, 466, 469, 1231, 1468, 470, 1005, 476, 1273, 1744, 1488, 1659, 1604, 479, 1013, 1014, 481, 4313, 1499, 1016, 4073, 1777, 485, 4274, 487, 1775, 4205, 1526, 1697, 2000, 488, 1894, 1882, 1817, 1880, 490, 1018, 3917, 3616, 4311, 4473, 4085, 4401, 3783, 3765, 1538, 3870, 491, 3699, 3792, 4290, 494, 2421, 4090, 2012, 1803, 3642, 1322, 1020, 502, 1333, 504, 1890, 507, 3608, 1732, 1864, 1816, 1531, 513, 3636, 514, 1699, 1027, 1366, 4950, 4027, 3478, 2959, 1293, 3197, 1595, 3413, 518, 1032, 1033, 1675, 1797, 2315, 521, 1999, 3759, 1215, 4122, 1730, 3966, 1035, 4973, 528, 3911, 3289, 1821, 530, 532, 1874, 533, 1038, 538, 539, 3767, 1929, 3683, 1338, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 3720, 4351, 4414, 3453, 3254,

1649, 544, 4240, 3580, 1046, 548, 549, 2598, 552, 553, 3819, 1259, 4062, 554, 2841, 3515, 1433, 1323, 4301, 555, 558, 3738, 1567, 559, 1054, 1270, 3857, 2175, 1257, 1238, 3662, 561, 1058, 563, 1061, 4203, 1899, 3981, 1062, 1303, 4116, 1946, 3620, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 1401, 4438, 1895, 1264, 1912, 573, 3939, 4170, 4056, 1271, 1521, 1221, 1451, 3934, 4080, 4352, 1700, 3739, 1419, 1811, 3950, 1690, 3716, 1569, 1437, 1674, 4337, 1285, 4268, 1183, 3881, 3938, 4198, 4416, 4229, 4292, 4193, 4325, 4375, 4432, 4215, 3944, 4195, 4223, 1540, 4455, 4512, 1723, 3750, 4070, 4104, 4235, 1863, 4346, 1881, 1814, 4443, 3761, 1587, 3592, 576, 4469, 1275, 1950, 4129, 1296, 1551, 3733, 4111, 3993, 4108, 1287, 1713, 1556, 1736, 1995, 1705, 1861, 4120, 4417, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 3928, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1757, 4299, 1773, 1364, 1462, 4007, 3729, 3665, 3722, 1691, 1712, 1624, 1751, 1394, 3924, 3952, 581, 2003, 1559, 1250, 1555, 4114, 1818, 1076, 4448, 1078, 1786, 3354, 1832, 3432, 2891, 1903, 4459, 589, 1563, 1084, 591, 592, 594, 595, 1858, 596, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 4439, 3852, 3997, 3847, 4050, 3377, 4424, 4143, 4493, 3492, 1412, 4017, 4477, 1794, 602, 4263, 3072, 2009, 1754, 3888, 603, 604, 1368, 3827, 4103, 1571, 1438, 611, 1093, 612, 1094, 3701, 4389, 614, 615, 1332, 1715, 4369, 1652, 1541, 1921, 1733, 1373, 1870, 619, 4218, 1798, 1702, 1384, 3700, 1788, 1600, 624, 2473, 1423, 2771, 1339, 3875, 3070, 2015, 2557, 2795, 2906, 2103, 3299, 3118, 4576, 1103, 1614, 1947, 631, 4479, 3766, 1107, 635, 1813, 636, 2431, 637, 1109, 639, 3706, 1110, 640, 642, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1568, 1766, 3221, 2643, 2739, 3920, 647, 1801, 4279, 3762, 1637, 1509, 648, 1117, 1119, 2965, 2695, 3293, 4722, 1121, 653, 1122, 3264, 655, 656, 657, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3537, 3994, 1319, 4467, 1623, 660, 1123, 664, 1126, 1128, 1129, 1130, 670, 1527, 671, 1772, 1137, 5005, 1933, 1731, 1793, 3342, 1140, 1141, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 1920, 4999, 1544, 703, 4031, 4305, 1636, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 4028, 3989, 704, 1493, 1902, 1152, 4182, 707, 708, 709, 4476, 1375, 713, 714, 1841, 4234, 1154, 1314, 4096, 718, 719, 720, 2063, 1311, 721, 4217, 1627, 1158, 1953, 1201, 3787, 729, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112,

2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 2423, 1745, 1973, 3807, 4307, 1169, 1454, or 1781.

18. The VP capsid polypeptide of claim 1, wherein X^7 of SEQ ID NO: 5014 is R.

19. The VP capsid polypeptide of claim 18, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 740, 15, 742, 743, 17, 22, 24, 1836, 32, 36, 2450, 39, 752, 753, 1998, 3059, 2519, 757, 48, 1952, 50, 52, 760, 2389, 54, 2346, 58, 4086, 1660, 1966, 768, 2402, 772, 71, 72, 2453, 3882, 775, 1806, 3669, 1356, 2132, 81, 84, 85, 87, 4040, 88, 1885, 782, 783, 784, 785, 94, 788, 2173, 98, 2007, 102, 113, 799, 4848, 1444, 4821, 2329, 115, 119, 2290, 123, 806, 128, 134, 812, 145, 817, 154, 2149, 821, 167, 171, 4596, 183, 830, 191, 194, 2071, 195, 4920, 831, 2223, 207, 3901, 211, 212, 213, 215, 224, 4782, 845, 846, 849, 850, 854, 247, 248, 2245, 255, 261, 264, 265, 1477, 270, 874, 876, 279, 882, 1930, 285, 286, 886, 2119, 2468, 887, 888, 4138, 297, 3844, 302, 893, 307, 308, 2155, 1431, 2312, 900, 1635, 906, 2799, 2128, 2918, 1363, 4251, 2622, 3333, 3474, 3614, 2732, 3166, 3151, 3088, 2883, 3318, 2645, 2733, 3213, 3782, 1844, 2523, 2520, 2997, 2681, 3035, 3279, 2764, 3480, 2787, 1808, 3101, 3689, 4147, 1762, 1976, 340, 1594, 2439, 348, 4498, 1518, 1782, 926, 357, 359, 932, 363, 369, 1873, 3780, 4140, 4001, 3709, 3834, 1752, 4113, 3817, 4232, 1340, 1489, 4214, 3902, 3820, 4330, 1872, 3687, 4318, 375, 4210, 3860, 4212, 3695, 1851, 4504, 1910, 1428, 4323, 4422, 4259, 1176, 3711, 4365, 4383, 3969, 4128, 3802, 3863, 3821, 4171, 3824, 4462, 3760, 3753, 2783, 3880, 3943, 4163, 4178, 4199, 3724, 3670, 4482, 3692, 4430, 4316, 3645, 3690, 3589, 3730, 4426, 3851, 4429, 1335, 1717, 1997, 1975, 4280, 4006, 3900, 4298, 4388, 1341, 1350, 1909, 4412, 4407, 4281, 4167, 1893, 3585, 4015, 1747, 4286, 3826, 1473, 1914, 3984, 4495, 4184, 3977, 1707, 4074, 4003, 3915, 1410, 1498, 940, 4131, 4357, 1925, 1466, 1611, 1530, 4168, 4245, 4075, 3987, 1679, 4306, 3869, 3768, 393, 2265, 3618, 4433, 947, 399, 401, 402, 4139, 1352, 406, 415, 418, 420, 4919, 431, 4044, 976, 433, 434, 435, 442, 3873, 3411, 3985, 987, 1485, 2262, 457, 458, 4425, 466, 467, 468, 1468, 474, 1008, 1012, 1016, 4518, 1697, 490, 3616, 2247, 2302, 499, 500, 501, 509, 2110, 512, 1797, 520, 525, 3966, 1038, 537, 1041, 3683, 2165, 542, 4331, 3129, 1044, 4351, 3453, 1047, 1323, 4301, 557, 3738, 559, 1270, 3857, 1056, 2186, 1057, 1059, 565, 566, 3981, 567, 3620, 4002, 3666, 3939, 1221, 1397, 1437, 4337, 4268, 3938, 4292, 4215, 3750, 3633, 4070, 3592, 1827, 3839, 4395, 3855, 3665, 1624, 2395, 1818, 586, 587, 1903, 1080, 1081, 1082, 589, 1084, 1085, 594, 596, 4439, 3997, 1962, 1087, 4777, 606, 607, 610, 1094, 4389, 1603, 1095, 616, 618, 622, 1104, 4536, 3706, 2481, 3100, 3200, 3621, 4179, 1432, 4381, 643, 1115, 644, 2307, 2477, 652, 657, 658, 3994, 4467, 661, 663, 665, 4600, 1137, 1933, 4840, 1140, 678, 680, 683, 686, 692, 693, 696, 2081, 2280,

698, 1400, 4197, 1532, 1854, 706, 711, 712, 4570, 714, 1841, 1314, 4096, 2249, 726, 1846, 2385, 1318, 733, 3651, 1165, 4839, 4968, 4684, or 1454.

20. The VP capsid polypeptide of claim 1, wherein:

(a) X^3 of SEQ ID NO: 5014 is a basic amino acid residue,

(b) X^6 of SEQ ID NO: 5014 is a basic amino acid residue, or

(c) X^3 of SEQ ID NO: 5014 is a basic amino acid residue and X^6 of SEQ ID NO: 5014 is a basic amino acid residue.

21. The VP capsid polypeptide of claim 20, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 739, 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 45, 756, 46, 48, 1952, 758, 49, 3122, 2551, 3718, 3484, 3577, 759, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 52, 760, 53, 762, 4659, 54, 3925, 55, 3654, 56, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 63, 64, 768, 771, 65, 66, 67, 68, 3816, 2599, 2706, 2399, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 75, 1312, 4501, 76, 77, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 3945, 2854, 3523, 3669, 82, 4065, 83, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 1180, 92, 785, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 103, 794, 795, 104, 105, 106, 1849, 108, 4736, 1579, 110, 1906, 113, 1444, 1344, 116, 802, 117, 118, 2158, 121, 803, 804, 1463, 805, 122, 2058, 124, 125, 127, 4994, 807, 132, 809, 810, 133, 1978, 812, 135, 136, 137, 138, 813, 4673, 140, 815, 1326, 141, 142, 143, 144, 145, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 151, 152, 153, 154, 155, 819, 820, 157, 821, 159, 160, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 180, 826, 827, 181, 828, 182, 183, 4641, 829, 184, 185, 186, 187, 188, 189, 830, 191, 192, 193, 194, 195, 196, 1391, 197, 2223, 200, 201, 202, 203, 204, 205, 832, 833, 206, 834, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 215, 1896, 1522, 3490, 838, 2241, 217, 218, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 226, 227, 230, 231, 842, 232, 233, 235, 844, 236, 237,

2150, 851, 852, 853, 1536, 240, 854, 242, 243, 244, 245, 246, 247, 855, 4634, 249, 250, 251, 252, 253, 254, 255, 857, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 869, 870, 271, 871, 872, 272, 874, 1252, 273, 1591, 275, 1980, 276, 876, 877, 277, 278, 279, 1892, 879, 1539, 880, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 2306, 282, 1799, 283, 1626, 1374, 287, 1620, 1290, 1354, 888, 291, 1956, 889, 292, 4324, 293, 4138, 891, 2224, 3903, 297, 3829, 3809, 4271, 3844, 1436, 1515, 1617, 1961, 304, 306, 1589, 4370, 308, 309, 894, 3646, 4059, 1431, 1331, 4948, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 897, 898, 321, 322, 899, 1958, 2134, 324, 901, 325, 902, 326, 1491, 329, 330, 905, 4484, 1756, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 1888, 4248, 1557, 1363, 1934, 1602, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 1345, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 4166, 4196, 3206, 3328, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 2772, 3230, 3043, 2922, 3581, 3524, 2869, 2610, 3298, 2775, 3108, 2603, 3614, 2612, 2860, 3187, 3238, 3786, 4385, 3016, 3436, 2876, 2987, 3532, 3438, 3561, 3259, 2663, 2890, 3433, 3071, 3018, 2580, 2755, 3015, 2540, 3398, 2664, 2583, 2830, 2644, 2641, 3513, 2725, 2723, 3338, 3556, 2866, 2514, 2932, 2753, 2862, 2899, 2605, 2989, 3096, 3124, 2985, 2716, 3145, 3017, 2591, 2640, 3033, 1853, 3216, 3316, 3412, 2971, 3256, 3153, 3575, 3339, 2915, 2531, 3552, 3475, 3060, 3375, 2756, 3382, 2847, 2859, 3251, 3702, 3423, 2537, 2801, 3076, 2696, 3092, 3459, 3144,

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22. The VP capsid polypeptide of claim 20, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4884, 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 4889, 21, 3192, 4942, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 2450, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368,

2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 759, 50, 1308, 3960, 1378, 2994, 3080, 2589, 3681, 51, 760, 2389, 762, 3925, 3654, 763, 4626, 59, 60, 4086, 1740, 1660, 62, 1966, 63, 2438, 768, 66, 67, 2197, 68, 3816, 2599, 2706, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 1312, 4501, 76, 1413, 775, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 1356, 2132, 4065, 1294, 1484, 85, 86, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 780, 1180, 92, 781, 782, 783, 2356, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 1936, 1590, 98, 99, 789, 790, 1298, 101, 1688, 791, 792, 2007, 102, 103, 104, 105, 107, 108, 1579, 110, 1906, 111, 798, 112, 799, 800, 2461, 1444, 801, 114, 115, 1344, 116, 802, 117, 118, 119, 121, 803, 1463, 1760, 124, 806, 126, 128, 807, 129, 131, 808, 2281, 133, 1978, 811, 812, 135, 136, 137, 138, 814, 140, 1326, 141, 142, 143, 2344, 816, 1634, 1302, 817, 818, 147, 148, 149, 150, 151, 154, 155, 819, 820, 156, 157, 2295, 158, 161, 162, 165, 822, 168, 169, 170, 823, 172, 1651, 173, 1483, 174, 825, 176, 178, 180, 827, 181, 828, 4911, 184, 185, 186, 188, 189, 830, 192, 193, 194, 196, 1391, 197, 198, 199, 200, 201, 202, 203, 4775, 205, 832, 206, 834, 207, 208, 209, 210, 835, 836, 1334, 3901, 3312, 2649, 1450, 4386, 3028, 1446, 2206, 215, 1522, 3490, 217, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 225, 4751, 228, 229, 230, 231, 2448, 842, 232, 233, 4782, 234, 235, 238, 847, 239, 850, 851, 853, 1536, 240, 241, 242, 243, 244, 245, 246, 247, 4923, 4696, 250, 251, 254, 255, 857, 256, 258, 259, 859, 260, 861, 862, 4966, 864, 263, 4970, 2318, 865, 2326, 264, 1241, 266, 1477, 867, 268, 868, 269, 270, 869, 870, 271, 871, 872, 272, 873, 4655, 4972, 1252, 1591, 875, 274, 275, 1980, 276, 876, 877, 2066, 277, 278, 280, 2323, 1892, 1539, 2214, 881, 882, 3601, 3877, 1930, 1460, 282, 1799, 284, 4553, 4772, 1626, 286, 1374, 1620, 1290, 1354, 887, 1956, 889, 4765, 292, 4324, 4138, 891, 296, 3903, 297, 3829, 3809, 4271, 3844, 1436, 300, 1617, 1961, 5010, 302, 304, 305, 2147, 1589, 4370, 307, 3646, 4059, 1431, 1331, 312, 1779, 313, 896, 1558, 1552, 318, 319, 322, 1958, 2454, 323, 324, 901, 1491, 328, 329, 330, 4820, 4484, 1756, 907, 4584, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110,

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23. The VP capsid polypeptide of claim 20, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 35, 36, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 45, 756, 48, 1952, 3122, 2551, 3718, 3484, 3577, 759, 3960, 1378, 2994, 3080, 2589, 3681, 760, 762, 3925, 3654, 60, 4086, 1740, 1660, 62, 1966, 63, 768, 66, 67, 68, 3816, 2599, 2706, 74, 3865, 1549, 1361, 2453, 3882, 3713, 1942, 1312, 4501, 76, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 4065, 1294, 1484, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 1180, 92, 786, 94, 95, 1831, 1867, 4458, 97, 1970, 1936, 1590, 99, 789, 790, 1298,

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1457, 3450, 2577, 2567, 2532, 3415, 2934, 2984, 2568, 4147, 3002, 2986, 2979, 2542, 1762, 4472, 1529, 4057, 1976, 4507, 1583, 1711, 2013, 1594, 4440, 344, 921, 4498, 3728, 3637, 3570, 3429, 4091, 2870, 2995, 4338, 3205, 2880, 3261, 3968, 4291, 4204, 4071, 4034, 1742, 2820, 3912, 3287, 4145, 354, 1782, 927, 3610, 4224, 1918, 1959, 3736, 1770, 931, 4155, 364, 1279, 365, 1543, 367, 4049, 1633, 1722, 369, 1495, 1566, 1211, 1748, 4142, 1434, 1358, 1191, 3732, 4110, 4039, 4411, 4506, 4156, 4036, 4030, 4016, 3899, 1247, 1855, 3919, 1244, 4140, 3930, 4117, 4189, 4001, 3643, 3619, 1240, 1575, 3871, 4135, 4408, 3604, 1274, 3741, 1938, 3709, 3622, 3834, 1983, 1743, 3979, 4461, 4113, 3817, 4232, 4214, 1219, 1486, 1512, 1516, 4047, 4082, 4094, 1574, 1248, 4078, 1872, 1426, 3785, 3687, 4318, 4243, 3866, 3704, 4172, 1513, 1856, 3324, 2769, 2678, 1561, 3296, 377, 1395, 4093, 4453, 3778, 4210, 4009, 4264, 4339, 1738, 4194, 4474, 4013, 4266, 1771, 3860, 3832, 1349, 1381, 3663, 1185, 3932, 3858, 1198, 4192, 3611, 1919, 3790, 3712, 4095, 1887, 4468, 1720, 4247, 2002, 1657, 1336, 3894, 1554, 3576, 4314, 3695, 4362, 1815, 3656, 3638, 4454, 1443, 1661, 1359, 3650, 1648, 3831, 4435, 4451, 1993, 3849, 1718, 4068, 1835, 1425, 1428, 4380, 1658, 1452, 4024, 4072, 3791, 4491, 4323, 4014, 1304, 1511, 1981, 1676, 4422, 3748, 4119, 1297, 1299, 4450, 3990, 4029, 3711, 4344, 1578, 4384, 3892, 3674, 3595, 4405, 3973, 4109, 4159, 3744, 4387, 1960, 4275, 4492, 4365, 4118, 3655, 3886, 4278, 3751, 3678, 4353, 3175, 2970, 1228, 3534, 3437, 3406, 3641, 3639, 4470, 3941, 4348, 3587, 3818, 3814, 4350, 3821, 3929, 3824, 4465, 4494, 1398, 3828, 1284, 3773, 4209, 3014, 3884, 2783, 4038, 3545, 2916, 3112, 2834, 3880, 4399, 4048, 3752, 4207, 1235, 3943, 4355, 4087, 4100, 4163, 4486, 4178, 1643, 4152, 3634, 4445, 4303, 4284, 1213, 4382, 1399, 3714, 4487, 3615, 4018, 4420, 4121, 3724, 4282, 4310, 4488, 4127, 3670, 4052, 4124, 4508, 4500, 3652, 3972, 1309, 1528, 3717, 1217, 2740, 3125, 3546, 3842, 4404, 3690, 3962, 4329, 4410, 3703, 4136, 3589, 3907, 4153, 2707, 4180, 3923, 4444, 4361, 4394, 4302, 3758, 4510, 3742, 1710, 1335, 1997, 1701, 4280, 4006, 1984, 3833, 1593, 2561, 4442, 3900, 4298, 1761, 4388, 1597, 4317, 4249, 1341, 1680, 4441, 3628, 3725, 1945, 937, 4206, 1588, 1439, 3794, 4447, 3776, 3658, 4064, 4011, 4272, 4503, 1367, 3594, 3680, 1300, 1750, 3913, 3774, 1877, 1987, 3998, 1380, 4185, 3686, 3696, 4463, 3853, 4244, 4083, 1909, 3897, 1546, 3613, 3273, 3452, 3525, 1229, 3835, 1234, 3970, 3856, 3586, 1175, 4321, 2778, 4412, 4407, 1810, 3823, 1427, 1507, 1878, 4333, 3146, 4281, 4211, 1179, 3843, 1677, 1524, 1525, 1974, 1239, 4167, 3740, 1342, 4125, 1580, 4060, 1576, 1212, 3921, 1174, 4061, 4021, 3693, 3734, 1382, 3684, 3806, 3635, 3976, 3840, 4286, 3836, 4161, 3659, 3743, 3605, 4392, 4328, 1316, 4173, 4265, 1246, 1629, 1829, 1837, 1914, 1839, 3984, 3910, 4160, 4184, 4132, 4250, 1562, 1847, 1792, 3769, 1534, 4003, 1689, 1599, 1265, 1655, 3874, 4261, 3626, 3579, 1644, 3936, 4054, 4260, 4297, 4357, 4022, 4046, 1222, 1996, 3788, 3953, 4226, 4277, 4101, 3797,

4019, 3771, 3632, 1402, 4137, 3772, 3661, 4186, 4174, 1170, 3850, 1315, 1611, 4033, 3623, 3596, 1461, 1848, 1173, 1928, 1765, 3719, 3584, 3591, 4165, 4191, 3980, 4058, 4200, 4336, 3958, 1260, 4051, 3798, 4032, 1774, 4322, 3991, 4106, 3978, 3965, 4464, 3813, 4154, 1365, 3846, 4345, 4379, 3603, 1693, 3937, 3801, 1787, 1214, 4483, 4201, 1898, 1220, 4245, 1347, 3867, 1900, 3640, 3916, 4089, 3745, 3975, 4256, 4308, 4000, 3868, 4403, 3883, 4326, 4393, 3895, 4237, 3955, 4005, 4092, 4372, 4283, 3805, 4151, 3982, 3597, 3872, 3987, 4490, 3876, 3668, 4300, 1679, 1242, 3598, 3583, 3647, 4304, 3779, 1907, 4042, 3648, 3996, 3800, 4367, 4099, 1807, 3887, 4428, 1625, 1390, 1884, 1682, 4364, 4306, 3869, 1278, 942, 1505, 1542, 1709, 3600, 3914, 3948, 1865, 1716, 3961, 1506, 4221, 1376, 1683, 4276, 1721, 1632, 3607, 1455, 1913, 1497, 1317, 1951, 1778, 3768, 4225, 1668, 390, 4406, 4341, 1480, 1714, 1422, 397, 3618, 4433, 1177, 3898, 398, 950, 400, 1965, 4471, 403, 1482, 3602, 4434, 3721, 1592, 1519, 1352, 4409, 1977, 1631, 1684, 409, 3889, 414, 415, 961, 1905, 416, 963, 3675, 1833, 3974, 965, 970, 1897, 4133, 3830, 972, 424, 427, 1708, 4141, 3749, 1619, 975, 4044, 3590, 1944, 4126, 1923, 1706, 4400, 1606, 2604, 2895, 436, 3448, 1692, 3862, 4055, 4358, 985, 1664, 4045, 3854, 3682, 1972, 2688, 4366, 3425, 3231, 3649, 2759, 2724, 3755, 1216, 3599, 3775, 2754, 2606, 3471, 3234, 2565, 2803, 2562, 2684, 3411, 3405, 2690, 1255, 3694, 3535, 1306, 4084, 3282, 1780, 990, 991, 992, 1728, 994, 1696, 998, 3116, 1869, 456, 1386, 3879, 2698, 1001, 461, 1447, 464, 4425, 1231, 1468, 476, 1273, 1744, 1488, 1659, 1604, 481, 4313, 1499, 1016, 4073, 1777, 4274, 487, 1775, 4205, 1526, 1697, 2000, 1882, 1817, 1880, 490, 1018, 3917, 3616, 4311, 1800, 4473, 4085, 4401, 3783, 3765, 491, 3699, 3792, 4290, 4090, 2012, 1803, 3642, 1322, 502, 1333, 1890, 3608, 1732, 511, 2397, 1864, 1816, 1531, 3636, 1699, 1027, 1366, 4027, 3478, 2959, 3197, 1595, 3413, 518, 1675, 1797, 2315, 1999, 3759, 1215, 4122, 1730, 3966, 3911, 3289, 1821, 530, 1874, 1038, 3767, 1929, 3683, 1338, 1517, 4331, 4332, 4466, 2719, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 3720, 4351, 4414, 3453, 3254, 1649, 544, 4240, 3580, 1046, 2598, 552, 3819, 1259, 4062, 2841, 3515, 4301, 3738, 1567, 1270, 3857, 1257, 1238, 3662, 561, 1058, 1061, 4203, 1899, 3981, 1062, 1303, 4116, 1946, 3620, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 1401, 4438, 1895, 1264, 1912, 3939, 4170, 4056, 1271, 1521, 1221, 1451, 3934, 4080, 4352, 1700, 3739, 1419, 1811, 3950, 1690, 3716, 1437, 1674, 4337, 1285, 4268, 1183, 3881, 3938, 4198, 4416, 4229, 4292, 4193, 4325, 4375, 4432, 4215, 3944, 1409, 4195, 4223, 1540, 1723, 3750, 4070, 4104, 4235, 1863, 4346, 1881, 1814, 4443, 3761, 1346, 1587, 3592, 576, 4469, 1275, 1950, 4129, 1296, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1736, 1995, 1705, 1861, 4120, 4417, 1785, 1236, 4293, 3839, 3983, 4395, 1957, 3928, 4295, 3715, 3855, 3609, 4076, 4175, 3927, 1757, 4299, 1773, 1364, 1462, 4007, 3729, 3665, 3722, 1691, 1624, 1751, 1394, 3924, 3952, 581, 2003, 1559, 1250, 1555,

4114, 1818, 1076, 4448, 1078, 1786, 3354, 1832, 3432, 2891, 1903, 4459, 1563, 591, 594, 598, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 4439, 3852, 3997, 3847, 4050, 3377, 4424, 4143, 4493, 3492, 601, 4017, 4477, 1794, 4263, 3072, 2009, 1754, 1088, 3888, 1368, 3827, 4103, 1571, 1438, 1093, 612, 1094, 3701, 4389, 1332, 1715, 4369, 1652, 1541, 1921, 1733, 1373, 1870, 619, 4218, 1798, 1702, 1384, 3700, 1788, 1600, 624, 2771, 1339, 3875, 3070, 2557, 2795, 2906, 3118, 1614, 1947, 4479, 3766, 635, 1813, 636, 3706, 1110, 640, 1111, 642, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1585, 1766, 3221, 2643, 2739, 3920, 2307, 647, 1801, 4279, 3762, 1637, 1509, 1119, 2965, 2695, 3293, 1121, 1122, 3264, 655, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3994, 1319, 4467, 1623, 664, 1128, 1129, 1130, 670, 1527, 671, 1772, 5005, 1933, 1731, 1793, 3342, 3822, 1601, 3905, 694, 1414, 1795, 1372, 1695, 1866, 4115, 1719, 1920, 1544, 703, 4031, 4305, 1636, 1393, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 1493, 1902, 4182, 707, 708, 4476, 714, 1841, 4234, 1314, 4096, 4217, 1627, 1953, 1201, 3787, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 3705, 1195, 3859, 1164, 1165, 1745, 1973, 1168, 3807, 4307, 1454, or 1781.

24. The VP capsid polypeptide of any one of claims 20-23, wherein the basic residue is selected from the group consisting of K, R, and H.

25. The VP capsid polypeptide of any one of claims 20-24, wherein X^3 of SEQ ID NO: 5014 is K or R.

26. The VP capsid polypeptide of claim 25, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 4177, 1289, 740, 741, 18, 745, 3477, 1548, 3051, 2982, 2877, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 23, 1638, 748, 1703, 1836, 3660, 29, 750, 1640, 33, 34, 35, 36, 37, 38, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485,

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4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4229, 4292, 4193, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 1729, 4223, 1540, 1723, 1070, 3750, 3633, 4070, 4104, 4162, 4235, 1863, 4346, 1881, 1814, 1572, 4443, 3761, 1346, 1587, 1072, 3592, 576, 1891, 4469, 1275, 1950, 1963, 4129, 1296, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1785, 1236, 4293, 3839, 3983, 4395, 1957, 3928, 4295, 3715, 3855, 3609, 1990, 4076, 4175, 3927, 1757, 1650, 4299, 1773, 2004, 1267, 1364, 1462, 1879, 4007, 3729, 3665, 3722, 1691, 1624, 1751, 1394, 3924, 3952, 580, 581, 2003, 1343, 1559, 1250, 1555, 4114, 1818, 1075, 1076, 1077, 1704, 4448, 1078, 1079, 1786, 585, 3354, 1832, 3432, 2891, 2505, 1903, 1081, 1082, 4459, 1083, 1563, 590, 591, 1085, 594, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 599, 3847, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 600, 601, 4017, 4477, 1794, 4263, 3072, 2009, 1754, 1087, 1088, 3888, 1368, 3827, 4103, 606, 1090, 1571, 1091, 1438, 1092, 1093, 612, 1094, 3701, 4389, 613, 1603, 1332, 1715, 4369, 1652, 1096, 617, 1541, 618, 1921, 1733, 1373, 1870, 619, 4218, 1798, 1100, 1702, 1101, 1667, 1384, 623, 3700, 1788, 1600, 624, 626, 2771, 627, 1339, 3875, 628, 629, 3070, 4860, 2557, 2795, 2906, 3118, 1614, 1947, 4479, 3766, 632, 1104, 1105, 633, 1813, 636, 3706, 1110, 640, 1111, 641, 642, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 1114, 1766, 3221, 2643, 2739, 3920, 644, 1116, 645, 646, 647, 1801, 4279, 3762, 1637, 1509, 1119, 2965, 2369, 2695, 3293, 650, 651, 1120, 652, 1121, 3264, 655, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 3994, 1319, 4467, 1802, 1227, 1623, 662, 663, 664, 1124, 1125, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 1135, 672, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 679, 1142, 1143, 681, 1145, 682, 685, 3822, 689, 690, 691, 1147, 1601, 3905, 694, 695, 1414, 1150, 1795, 1372, 1695, 1866, 4115, 1719, 698, 1920, 699, 700, 1544, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 1493, 1854, 1902, 1510, 4182, 706, 707, 708, 4476, 1245, 714, 1841, 4234, 1314, 4096, 717, 1155, 4217, 1156, 723, 1157, 1627, 725, 1159, 1953, 1160, 1201, 727, 3787, 3747, 730, 1846, 3815, 2005, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 734, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1628, 3705, 1195, 3859, 1164, 1165, 1166, 1745, 1973, 1168, 3807, 4307, 1454, or 1781.

27. The VP capsid polypeptide of any one of claims 20-24, wherein X^6 of SEQ ID NO: 5014 is K or R.

28. The VP capsid polypeptide of claim 27, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 4177, 1289, 740, 14, 743, 744, 17, 3477, 1548, 3051, 2982, 2877, 746, 19, 3036, 3426, 3073, 3169, 747, 3362, 2784, 21, 3192, 22, 1638, 748, 24, 749, 27, 1703, 1836, 28, 3660, 29, 750, 1640, 33, 35, 36, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 44, 45, 756, 47, 48, 1952, 3122, 2551, 3718, 3484, 3577, 1308, 3960, 1378, 2994, 3080, 2589, 3681, 51, 760, 762, 3925, 3654, 763, 59, 60, 4086, 1740, 1660, 62, 1966, 63, 2438, 768, 66, 67, 68, 3816, 2599, 2706, 72, 73, 74, 3865, 1549, 1361, 3882, 773, 3713, 1942, 1312, 4501, 76, 1413, 775, 1560, 4289, 3757, 3593, 3908, 4397, 4415, 3723, 3754, 4360, 3945, 2854, 3523, 3669, 1356, 4065, 1294, 1484, 85, 86, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 1490, 1885, 1926, 89, 780, 1180, 92, 781, 782, 783, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 1936, 1590, 98, 99, 789, 790, 1298, 1688, 791, 792, 2007, 102, 103, 104, 105, 107, 108, 1579, 1906, 111, 798, 112, 799, 800, 1444, 801, 114, 115, 1344, 116, 802, 117, 118, 119, 121, 803, 1463, 1760, 806, 126, 128, 807, 129, 131, 808, 133, 1978, 811, 812, 135, 136, 137, 138, 814, 140, 1326, 141, 142, 143, 2344, 816, 1634, 1302, 817, 818, 147, 148, 149, 150, 151, 154, 155, 819, 820, 156, 157, 158, 161, 162, 165, 822, 168, 169, 170, 823, 172, 1651, 173, 1483, 174, 825, 176, 178, 180, 827, 181, 828, 4911, 184, 186, 188, 189, 830, 192, 193, 194, 196, 1391, 198, 199, 200, 201, 202, 203, 205, 832, 206, 834, 207, 208, 209, 210, 835, 836, 1334, 3901, 3312, 2649, 1450, 4386, 3028, 1446, 1522, 3490, 217, 219, 1612, 220, 221, 222, 839, 223, 840, 224, 225, 228, 229, 230, 231, 842, 232, 233, 234, 238, 847, 239, 850, 851, 853, 1536, 240, 241, 242, 243, 244, 245, 247, 250, 251, 254, 255, 857, 256, 258, 259, 859, 260, 861, 862, 864, 263, 2318, 865, 2326, 264, 1241, 266, 1477, 867, 268, 868, 269, 270, 869, 870, 271, 871, 872, 272, 873, 1252, 1591, 875, 274, 275, 276, 876, 877, 277, 278, 280, 1892, 1539, 881, 3601, 3877, 1460, 282, 1799, 284, 1626, 286, 1374, 1620, 1290, 1354, 887, 1956, 889, 292, 4324, 4138, 891, 296, 3903, 297, 3829, 3809, 4271, 3844, 1436, 300, 1617, 1961, 302, 304, 305, 2147, 1589, 4370, 307, 3646, 4059, 1431, 1331, 312, 1779, 313, 896, 1558, 1552, 318, 319, 322, 1958, 323, 324, 901, 1491, 328, 329, 4484, 907, 3536, 2701, 2799, 3332, 3294, 3159, 3069,

2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 3414, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2785, 3249, 3527, 4460, 3352, 2569, 4457, 2011, 4319, 3906, 1533, 1755, 4248, 1557, 3804, 1602, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516, 3113, 2639, 3143, 3044, 2747, 3154, 3280, 3039, 2743, 2902, 3056, 2554, 2522, 3103, 3210, 3434, 2656, 4251, 2588, 3553, 2714, 3078, 3222, 3137, 3357, 2717, 2944, 3012, 3220, 3202, 2811, 3083, 3269, 3566, 2699, 2515, 3023, 2533, 3288, 3075, 3005, 2685, 3058, 2976, 2622, 3333, 3463, 2939, 3521, 3268, 3117, 2626, 2616, 3240, 2570, 3565, 2919, 3157, 2849, 3444, 2631, 3420, 2659, 3325, 3186, 2920, 3258, 3440, 3457, 3310, 2761, 3134, 2621, 3531, 2711, 2774, 2867, 2585, 3155, 2620, 3156, 2844, 3126, 3160, 2909, 3542, 3225, 2887, 3474, 3218, 2744, 2896, 3135, 3424, 3498, 3529, 2661, 2667, 2549, 2819, 2768, 2935, 3182, 2772, 3230, 3043, 2922, 3581, 2869, 2610, 3298, 2775, 3108, 2603, 2612, 2860, 3187, 3238, 3786, 4385, 3016, 3436, 2876, 2987, 3532, 3438, 3561, 3259, 2663, 2890, 3433, 3071, 3018, 2580, 2755, 3015, 2540, 3398, 2664, 2583, 2830, 2644, 2641, 3513, 2725, 2723, 3338, 3556, 2866, 2514, 2932, 2753, 2862, 2899, 2605, 2989, 3096, 3124, 2985, 2716, 3145, 3017, 2591, 2640, 3033, 3316, 3412, 2971, 3256, 3153, 3575, 3339, 2915, 2531, 3552, 3475, 3060, 3375, 2756, 3382, 2847, 2859, 3251, 3702, 3423, 2537, 2801, 3076, 2696, 3459, 3144, 3441, 2802, 3479, 2907, 3512, 3518, 3021, 2871, 3032, 2647, 2945, 3045, 2763, 3313, 3034, 3315, 3541, 2746, 2669, 2524, 3003, 2732, 3166, 3046, 3306, 2873, 3364, 3253, 3215, 3061, 2804, 2722, 2964, 2990, 2836, 3173, 2762, 3737, 2628, 3507, 2564, 3031, 2872, 3360, 2658, 2930, 2904, 3244, 3217, 3311, 3445, 2840, 3372, 2958, 3098, 3356, 3456, 3388, 2624, 3207, 2576, 2742, 2665, 2815, 3052, 3421, 2593, 3242, 2535, 2966, 2898, 2858, 2943, 2668, 2798, 3196, 2528, 2713, 3001, 2691, 2948, 2767, 2544, 3302, 2734, 2893, 2592, 2861, 3502, 2969, 2582, 3229, 2676, 2545, 3255, 3330, 2547, 3257, 2882, 3151, 3088, 2883, 3318, 2645, 2733, 2587, 3500, 3008, 2715, 2845, 3183, 2654, 3233, 3267, 2741, 2827, 2704, 3091, 2832, 2736, 3177, 3271, 2835, 2908, 3176, 2947, 3292, 3191, 2517, 3026, 3082, 3392, 2584, 2712, 3213, 3451, 2634, 3150, 2810, 3303, 2573, 3460,

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3875, 3070, 2015, 2557, 2795, 2906, 2103, 3299, 3118, 4576, 1103, 1614, 1947, 631, 4479, 3766, 1107, 635, 1813, 636, 2431, 637, 1109, 639, 3706, 1110, 640, 642, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 1269, 3095, 1286, 3624, 4481, 3511, 2735, 4381, 3295, 1568, 1766, 3221, 2643, 2739, 3920, 647, 1801, 4279, 3762, 1637, 1509, 648, 1117, 1119, 2965, 2695, 3293, 4722, 1121, 653, 1122, 3264, 655, 656, 657, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 3537, 3994, 1319, 4467, 1623, 660, 1123, 664, 1126, 1128, 1129, 1130, 670, 1527, 671, 1772, 1137, 5005, 1933, 1731, 1793, 3342, 1140, 1141, 687, 3822, 1601, 1148, 693, 3905, 694, 1414, 1149, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 1920, 4999, 1544, 703, 4031, 4305, 1636, 3810, 4452, 3677, 4227, 4402, 4157, 4197, 1337, 1253, 4028, 3989, 704, 1493, 1902, 1152, 4182, 707, 708, 709, 4476, 1375, 713, 714, 1841, 4234, 1154, 1314, 4096, 718, 719, 720, 2063, 1311, 721, 4217, 1627, 1158, 1953, 1201, 3787, 729, 3747, 730, 1846, 3815, 1964, 1822, 1262, 4480, 1537, 1291, 1318, 4294, 1582, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1805, 3705, 1195, 3859, 1164, 1165, 2351, 2423, 1745, 1973, 3807, 4307, 1169, 1454, or 1781.

29. The VP capsid polypeptide of any one of claims 1-28, wherein:

(a) X^3 of SEQ ID NO: 5014 is not D,

(b) X^6 of SEQ ID NO: 5014 is not D, or

(c) X^3 of SEQ ID NO: 5014 is not D and X^6 of SEQ ID NO: 5014 is not D.

30. The VP capsid polypeptide of claim 29, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40,

2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 2167, 52, 760, 53, 2389, 4755, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 2140, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2379, 81, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 4556, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 1579, 110, 1906, 111, 2428, 798, 2075, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4864, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 4533, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 5009, 144, 145, 816, 4654, 2125, 4663, 4810, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 2170, 4809, 4520, 180, 826, 827, 181, 828, 4695, 2130, 4911, 182, 4582, 4873, 2189, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 2114, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 2187, 4914, 4947, 196, 1391, 197, 4534, 4726, 4788, 198, 199, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 2090, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4974, 4790, 4915, 2464, 4567, 4774, 4964, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2393, 2448, 841, 842, 232, 233, 4782, 234, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4696, 855, 4634, 856, 249,

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4611, 2353, 4603, 4762, 4819, 2221, 4636, 4992, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4516, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 2477, 4724, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 2191, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 4714, 4979, 4812, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 4628, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 2275, 1166, 4968, 4912, 2423, 737, 1167, 4989, 4684, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

31. The VP capsid polypeptide of claim 29, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20,

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641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4881, 4837, 4888, 4648, 642, 4548, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 4629, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4603, 4762, 4819, 2221, 4636, 4992, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4516, 4541, 2200, 4580, 4858, 648, 649, 1117, 4780, 4800, 2477, 4724, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 653, 654, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 2191, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 4714, 4979, 4812, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4606, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 4879, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4642, 722, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 2024, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318,

2283, 4976, 4628, 4294, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4835, 2259, 4571, 2275, 1166, 4968, 2250, 2423, 737, 1167, 4989, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

32. The VP capsid polypeptide of claim 29, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 2167, 52, 760, 53, 2389, 4755, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 2140, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 81, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 2356, 784, 785, 786, 94, 95, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 4556, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4691, 107, 2440, 1849, 108, 797, 4736, 2509, 2018, 2227, 4787, 1579, 110, 1906, 111, 2428, 798, 2075, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4864, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 2424, 2058,

2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 4533, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 5009, 144, 145, 816, 4654, 2125, 4663, 4810, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 4809, 4520, 180, 826, 827, 181, 828, 4695, 2130, 4911, 182, 4582, 4873, 2189, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 4914, 4947, 196, 1391, 197, 4534, 4726, 198, 199, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 2090, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4974, 4790, 4915, 2464, 4567, 4774, 4964, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2448, 841, 842, 232, 233, 4782, 234, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4696, 855, 4634, 856, 249, 250, 251, 252, 253, 254, 255, 857, 2115, 2218, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 4966, 863, 864, 263, 4749, 4970, 2296, 2318, 4535, 865, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 268, 868, 269, 4668, 270, 869, 870, 271, 871, 872, 272, 4822, 4709, 873, 4655, 4972, 2317, 874, 1252, 273, 1591, 4975, 875, 274, 2025, 275, 1980, 276, 876, 877, 2066, 277, 278, 279, 4670, 280, 2323, 2288, 2334, 4939, 4689, 281, 878, 2416, 1892, 879, 1539, 2214, 2215, 880, 2327, 881, 882, 4601, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 2306, 884, 282, 1799, 283, 284, 4988, 4871, 4553, 4772, 2260, 1626, 885, 286, 1374, 886, 2119, 2504, 2468, 287, 1620, 1290, 2425, 2482, 4564, 4671, 2282, 288, 1354, 2033, 289, 887, 290, 888, 291, 1956, 2362, 2467, 889, 2357, 4547, 4765, 292, 4794, 2391, 4324, 293, 890, 294, 295, 4138, 891, 2297, 2254, 296, 2224, 3903, 297, 892, 3829, 298, 299, 3809, 4271, 3844, 1436, 300, 1515, 1617, 301, 1961, 4649, 5010, 302, 2060, 303, 304, 305, 2452, 2147, 4574, 4538, 306, 2293, 1589, 893, 4946, 4370, 4841, 2342, 307, 308, 309, 894, 2246, 2155, 3646, 4059, 1431, 1331, 311, 4948, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 317, 2312, 318, 319, 897, 320, 898, 321, 322, 899, 1958, 2022, 2016, 900, 2454, 323, 2427, 2134, 324, 901, 325, 902, 326, 2373, 4803, 2459, 1491, 327, 328, 903, 2463, 2264, 329, 330, 1635, 4820, 905, 331, 4706, 4484, 1756, 906, 907, 4661, 2179, 4584, 4609, 332, 4907, 4635, 4529, 4683, 4561, 333, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037,

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2795, 2906, 2103, 4869, 2029, 3299, 3118, 4932, 4838, 4901, 4908, 4996, 4779, 2377, 4657, 4646, 4875, 4627, 4515, 4876, 4965, 4605, 4576, 2028, 4985, 4799, 4850, 1103, 4757, 4747, 1614, 1947, 2237, 630, 631, 4997, 4618, 4479, 3766, 632, 1104, 1105, 4886, 1106, 2432, 4827, 633, 1107, 4530, 634, 2371, 1108, 4536, 635, 1813, 636, 2431, 4866, 4991, 4814, 4560, 4956, 637, 4555, 1109, 4633, 2213, 638, 639, 3706, 1110, 640, 1111, 641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4881, 4837, 4888, 4648, 642, 4548, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4629, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4607, 4719, 1116, 645, 646, 4611, 2353, 4603, 4762, 4819, 2221, 4636, 4992, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4516, 4541, 2200, 4580, 4858, 648, 649, 2477, 4724, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 653, 654, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 2191, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 4714, 4979, 4812, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4738, 4811, 4570, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627,

2116, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 4628, 4294, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4835, 2259, 2275, 1166, 4968, 2423, 737, 1167, 4989, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

33. The VP capsid polypeptide of any one of claims 1-28, wherein:

(a) X^3 of SEQ ID NO: 5014 is not E,

(b) X^6 of SEQ ID NO: 5014 is not E, or

(c) X^3 of SEQ ID NO: 5014 is not E and X^6 of SEQ ID NO: 5014 is not E.

34. The VP capsid polypeptide of claim 33, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 34, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 2072, 2034, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 52, 760, 53, 2389, 4934, 4951, 761, 4591, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 57, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 2140, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2132, 2379, 81, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 85, 4594, 86, 778, 87,

3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 787, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 4585, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 4556, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 109, 1579, 110, 1906, 111, 2428, 798, 2075, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 123, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 4533, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 5009, 144, 145, 816, 4654, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 2170, 4809, 4520, 180, 826, 827, 181, 828, 4695, 4911, 182, 4582, 4873, 4596, 2020, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 2114, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 2187, 4914, 4947, 196, 1391, 197, 4534, 4726, 4788, 198, 199, 4920, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4953, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 5007, 4542, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2393, 2448, 841, 842, 232, 233, 4782, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 4704, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4923, 2245, 4696, 855, 4634, 856, 249, 250, 251, 252, 253, 254, 255, 857, 2115, 4880, 2218, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 4966, 863, 864, 263, 4749, 4970, 2296, 2318, 865, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 4977, 268, 868, 269, 4668, 5002, 270, 869, 870, 271, 871, 872, 272, 4822, 4709, 873, 4655, 4972, 2392, 874, 1252, 273, 1591, 4975, 875, 274, 2025, 275, 1980, 276, 876, 877, 2066, 277, 278, 279, 4670, 280, 2323, 2288, 2334, 4939, 4689, 281, 878, 1892, 879, 1539, 2214, 2215, 880, 2327, 881, 882, 4601, 883, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 2306, 884, 282, 1799, 283, 284, 4988, 4553, 4772, 4817, 2260, 285, 1626, 2082, 885, 286, 1374, 886, 2119, 2468, 287, 2408, 1620, 1290, 2425, 2482, 4564, 4671, 2282, 288, 2354, 1354, 2033, 289, 887, 290, 888, 291, 1956, 2362, 2467, 889, 2357, 4547, 4765, 292, 4794, 2391, 4324, 293, 890, 294, 295, 4138, 891, 2297, 2254, 296, 2224, 3903, 297, 892, 3829, 298, 299, 3809, 4271,

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2012, 1803, 3642, 497, 1322, 1020, 498, 1021, 2235, 2302, 2488, 4665, 4540, 5006, 499, 2049, 2404, 4685, 500, 501, 1022, 502, 1333, 503, 1023, 4686, 4804, 504, 4727, 505, 506, 4938, 4805, 2065, 1890, 4891, 1024, 507, 508, 509, 1025, 510, 1026, 3608, 1732, 511, 2397, 1864, 1816, 1531, 512, 513, 2451, 3636, 5012, 4892, 514, 1699, 4593, 1027, 4987, 515, 2495, 4660, 1028, 516, 1029, 2409, 1366, 2112, 2178, 2124, 2376, 5011, 4572, 4957, 4789, 4543, 4664, 4678, 2093, 4746, 2489, 4922, 2145, 1030, 4832, 4950, 1261, 4027, 3478, 3763, 2959, 1293, 2462, 517, 3197, 1595, 3413, 2238, 1031, 2228, 1448, 518, 2057, 2305, 2133, 2061, 4526, 4617, 1033, 2429, 2311, 1675, 4785, 1797, 519, 4578, 2271, 2466, 2148, 2420, 520, 4854, 2381, 2315, 2284, 4813, 521, 1034, 522, 523, 1999, 3759, 1215, 4122, 1730, 524, 525, 526, 3966, 4573, 5008, 1035, 527, 4973, 2508, 528, 3911, 529, 3289, 1821, 530, 531, 2426, 1036, 532, 1874, 533, 534, 1037, 535, 1038, 536, 1039, 537, 538, 539, 1040, 3767, 1929, 1041, 1042, 3683, 2100, 4853, 2300, 2165, 540, 541, 1043, 4906, 542, 1338, 2292, 2021, 1616, 1901, 1796, 1517, 4331, 4332, 4466, 2719, 3803, 4123, 4233, 1824, 3129, 3087, 3505, 4158, 4254, 1449, 2121, 1044, 3720, 4351, 4414, 1673, 3453, 3254, 2501, 1649, 543, 544, 545, 546, 1045, 547, 2084, 4240, 3580, 4680, 1046, 548, 2062, 1047, 550, 2598, 551, 552, 553, 3819, 1259, 4062, 1048, 554, 2841, 1049, 1050, 3515, 2219, 1433, 1323, 4301, 555, 556, 1051, 557, 558, 1052, 1053, 3738, 1567, 559, 1054, 1270, 3857, 1055, 2151, 560, 2175, 2089, 1056, 2198, 2193, 1257, 1238, 3662, 561, 2186, 1057, 4637, 562, 1058, 563, 4872, 2097, 564, 1059, 565, 566, 1060, 1061, 2231, 4203, 1899, 3981, 1062, 1303, 4116, 567, 1063, 568, 569, 570, 2367, 1946, 3620, 1064, 1514, 4002, 3679, 3964, 3707, 3666, 1348, 4273, 1804, 4497, 571, 1401, 4438, 1895, 1264, 572, 1912, 573, 3939, 4170, 4056, 1271, 1065, 1521, 1221, 1066, 1451, 1654, 1067, 3934, 4080, 4352, 574, 1700, 3739, 1565, 1419, 1811, 3950, 1690, 1397, 3716, 1569, 1465, 1437, 1674, 4337, 1285, 4268, 1183, 3726, 3881, 4134, 4347, 4012, 3938, 4066, 4198, 4416, 4164, 3630, 4229, 4292, 4193, 4325, 4375, 4371, 4432, 4215, 1753, 3944, 1409, 4195, 1729, 4223, 1540, 4455, 1068, 1069, 4512, 1723, 1070, 3750, 3633, 4070, 4104, 4162, 4235, 1863, 4346, 1881, 1814, 1572, 2418, 575, 4443, 3761, 1346, 1587, 1072, 3592, 576, 1891, 4469, 2430, 1275, 577, 1950, 1963, 4129, 1073, 1296, 1360, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1556, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 2279, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 2222, 578, 3928, 4295, 3715, 3855, 3609, 1990, 4076, 4175, 3927, 1757, 1650, 4299, 1773, 2004, 1267, 1364, 579, 1462, 1879, 4007, 3729, 3665, 3722, 1691, 1712, 1074, 1624, 1751, 1394, 3924, 3952, 580, 581, 2003, 1343, 2203, 1559, 1250, 1555, 2304, 582, 2395, 4114, 1818, 1075, 583, 1076, 1077, 1704, 4448, 584, 4882, 1078, 1079, 1786, 585, 3354, 1832, 586, 3432, 2891, 587, 588, 4583, 2505, 1903, 2077, 4936, 4658, 4830, 2446, 1080, 2278, 1081, 1082, 4459, 1083, 589, 1563, 1084, 2255, 2113, 590, 591, 1085, 2256,

592, 2308, 593, 594, 2274, 595, 4931, 2407, 1858, 596, 597, 598, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 599, 3847, 4993, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 1412, 2455, 600, 2457, 2321, 1086, 601, 4017, 4477, 1794, 2483, 4776, 2291, 602, 4263, 3072, 2009, 2199, 1754, 1087, 1088, 3888, 603, 604, 4777, 2324, 605, 1368, 3827, 4103, 606, 607, 1089, 2220, 4549, 1090, 1571, 1091, 1438, 608, 1092, 609, 610, 611, 1093, 612, 1094, 3701, 4389, 613, 4897, 1603, 614, 1095, 2154, 5000, 615, 616, 2263, 1332, 1715, 4369, 1652, 1096, 617, 1541, 618, 1921, 1733, 1373, 1870, 619, 4218, 1798, 2387, 1097, 1098, 1099, 1100, 620, 1702, 621, 622, 4801, 2398, 2239, 1101, 1667, 1384, 623, 4745, 3700, 1788, 1600, 624, 2098, 625, 4550, 4721, 4960, 4878, 2473, 4792, 4675, 1102, 1423, 626, 2771, 627, 1339, 3875, 628, 629, 3070, 4565, 2118, 4818, 4860, 2557, 2795, 2906, 2103, 4869, 2029, 3299, 3118, 4932, 4838, 4901, 2377, 4657, 4646, 4875, 4627, 4515, 4876, 4965, 4605, 4576, 2028, 4985, 4799, 4850, 1103, 4747, 1614, 1947, 2237, 630, 631, 4618, 4479, 3766, 632, 1104, 1105, 4886, 1106, 2432, 4827, 633, 1107, 4530, 634, 2371, 4651, 1108, 4536, 635, 1813, 636, 2431, 4866, 4991, 4814, 4560, 4956, 637, 4555, 1109, 4941, 4577, 2213, 638, 639, 3706, 1110, 640, 1111, 641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4524, 4881, 4837, 4888, 4648, 642, 4548, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4516, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 2191, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 674, 2456, 4606, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 1139, 677, 4840, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145,

682, 683, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 2512, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 4652, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 4879, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 2414, 718, 1155, 719, 720, 2063, 1311, 4921, 721, 4642, 722, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 730, 731, 2024, 1846, 2507, 2368, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 2275, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

35. The VP capsid polypeptide of claim 33, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 2469, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 35, 36, 37, 4742, 2450, 38, 4925, 39, 751, 752, 2144, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 2167, 52, 760, 53, 2389, 4934, 4951, 4755, 761, 762, 4659,

54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 2438, 2041, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2132, 2379, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 2299, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 787, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 4585, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 109, 1579, 110, 1906, 111, 2428, 798, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4864, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 4791, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 144, 145, 816, 4654, 2125, 4663, 4810, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 2170, 4809, 4520, 180, 826, 827, 181, 828, 4695, 2130, 4911, 182, 4582, 4873, 4596, 2020, 2189, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 2114, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 2187, 4914, 4947, 196, 1391, 197, 4534, 4726, 4788, 198, 199, 4920, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446, 214, 2206, 215, 1896, 1522, 3490, 838, 216, 2090, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4953, 4974, 4790, 4915, 2464, 4567, 4774, 4964, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 5007, 4542, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2393, 2448, 841, 842, 232, 233, 4782, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 4704, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4923, 2245, 4696, 855, 4634, 856, 249, 250, 251, 252, 253, 254, 255, 857, 2115, 4880, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 4966, 863, 864, 263, 4749, 4970, 2296, 2318, 4535, 865, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 4977, 268, 868,

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577, 1950, 1963, 4129, 1073, 1296, 1360, 1551, 3733, 4111, 3993, 4108, 3949, 1287, 1713, 1556, 1736, 1995, 1435, 1424, 1830, 1705, 1861, 1197, 1254, 4120, 1545, 4417, 1469, 1292, 2185, 2279, 1785, 1236, 4293, 1827, 3839, 3983, 4395, 1957, 2222, 578, 3928, 4295, 3715, 3855, 3609, 1990, 4076, 4175, 3927, 1757, 1650, 4299, 1773, 2004, 1267, 1364, 579, 1462, 1879, 4007, 3729, 3665, 3722, 1691, 1712, 1074, 1624, 1751, 1394, 3924, 3952, 580, 581, 2003, 1343, 2203, 1559, 1250, 1555, 582, 2395, 4114, 1818, 1075, 583, 1076, 1077, 1704, 4448, 584, 4882, 1078, 1079, 1786, 585, 3354, 1832, 586, 3432, 2891, 587, 588, 4583, 2505, 1903, 2077, 4936, 4658, 4830, 2446, 1080, 2278, 1081, 1082, 4459, 1083, 589, 1563, 1084, 2255, 2113, 590, 591, 1085, 592, 2308, 593, 594, 2274, 595, 4931, 2407, 1858, 596, 597, 598, 1453, 2559, 2590, 2738, 4478, 4069, 1809, 1327, 4150, 3260, 3481, 3672, 3625, 2008, 4439, 3852, 3997, 1411, 599, 3847, 4993, 1268, 4050, 3377, 4424, 1496, 4143, 4493, 3492, 1962, 1412, 2455, 600, 2457, 1086, 601, 4017, 4477, 1794, 2483, 2291, 602, 4263, 3072, 2009, 2199, 1754, 1087, 1088, 3888, 603, 604, 4777, 2324, 605, 1368, 3827, 4103, 606, 607, 1089, 2220, 4549, 1090, 1571, 1091, 1438, 608, 1092, 609, 2320, 2069, 610, 611, 1093, 612, 1094, 3701, 4389, 613, 4897, 1603, 614, 1095, 5000, 615, 616, 2263, 1332, 1715, 4369, 1652, 1096, 617, 1541, 618, 1921, 1733, 1373, 1870, 619, 4218, 1798, 2387, 1097, 1098, 1099, 1100, 620, 1702, 621, 622, 4801, 4855, 4847, 2398, 2239, 1101, 1667, 1384, 623, 4745, 3700, 1788, 1600, 624, 2098, 625, 4550, 4721, 4960, 4878, 2473, 4792, 4675, 1102, 1423, 626, 2771, 627, 1339, 3875, 628, 629, 3070, 4565, 2118, 2015, 4818, 2557, 2795, 2906, 2103, 4869, 2029, 3299, 3118, 4932, 4838, 4901, 4908, 4996, 4779, 4657, 4646, 4875, 4627, 4515, 4876, 4965, 4605, 4576, 2028, 4985, 4850, 1103, 4757, 4747, 1614, 1947, 2237, 630, 631, 4997, 4618, 4479, 3766, 632, 1104, 1105, 4886, 1106, 2432, 633, 1107, 4530, 634, 2371, 4651, 1108, 4536, 635, 1813, 636, 2431, 4866, 4991, 4814, 4560, 4956, 637, 4555, 1109, 4941, 4577, 4633, 2213, 638, 639, 3706, 1110, 640, 1111, 641, 4581, 4893, 4831, 2481, 4644, 4734, 2190, 4524, 4881, 4837, 4888, 4648, 642, 4807, 4896, 4868, 2374, 1112, 4823, 2164, 1113, 3735, 3390, 1694, 3431, 2838, 3483, 3464, 3848, 2558, 3314, 3086, 3029, 2956, 3517, 2651, 2914, 2680, 2632, 3121, 3100, 3528, 3526, 3084, 4220, 3304, 2846, 1186, 3235, 2903, 3559, 2687, 3409, 3237, 2900, 2999, 3349, 3171, 2752, 3262, 3504, 3047, 4376, 3193, 3430, 2525, 2670, 2911, 3508, 2776, 2697, 3200, 2790, 3323, 2543, 2874, 2614, 3904, 3373, 3054, 2617, 4242, 3621, 2708, 4179, 4398, 3959, 4935, 1269, 3095, 1286, 3624, 4481, 1432, 3511, 2735, 4381, 3295, 1585, 2390, 1568, 1114, 1766, 3221, 2643, 2739, 643, 4735, 4760, 4629, 1115, 4918, 4688, 3920, 644, 4723, 4949, 4748, 4607, 4719, 1116, 645, 646, 4611, 2353, 4645, 4603, 4762, 4819, 2221, 4636, 4992, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 2477, 4724, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944,

1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 4714, 4979, 4812, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 2456, 4606, 4588, 4963, 4851, 4558, 4557, 4697, 4610, 4773, 4687, 4708, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 677, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 2141, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4690, 4859, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4732, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 718, 1155, 719, 720, 2063, 1311, 721, 4642, 722, 4833, 4903, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 2248, 730, 731, 2024, 1846, 2507, 2368, 1162, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 4927, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4628, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

36. The VP capsid polypeptide of claim 33, wherein the 581 to 589 region of the VP capsid polypeptide has a sequence of any one of SEQ ID NOs: 2498, 4884, 738, 739, 4177, 1289, 740, 14, 15, 741, 742, 743, 16, 744, 17, 18, 745, 3477, 1548, 3051, 2982, 2171, 2877, 746, 19, 20, 3036, 3426, 3073, 3169, 747, 2406, 3362, 2784, 4889, 21, 3192, 4942, 22, 23, 1638, 748, 24, 25, 749, 26, 27, 1703, 1836, 28, 2038, 2301, 3660, 29, 750, 30, 31, 32, 2095, 1640, 33, 35, 36, 37,

4742, 2450, 38, 4925, 39, 751, 752, 1653, 1205, 3795, 753, 4288, 4219, 2770, 2962, 4241, 4107, 2718, 3317, 4391, 4053, 3263, 2553, 3947, 2710, 2608, 3467, 2796, 2961, 2529, 3320, 2674, 2635, 3446, 3053, 3250, 3688, 1182, 1998, 4320, 3351, 2655, 3514, 2779, 3194, 3319, 3224, 3281, 3708, 2807, 3562, 3274, 3374, 3013, 3416, 2981, 3065, 2777, 3469, 2977, 2638, 2972, 3059, 2574, 3380, 4262, 3167, 3368, 2781, 3547, 3386, 1225, 2960, 3485, 3370, 3443, 2824, 754, 1467, 3327, 3178, 3006, 3252, 2991, 3470, 2888, 2572, 3418, 2642, 2519, 3363, 40, 2633, 41, 42, 43, 755, 2511, 44, 45, 756, 46, 757, 47, 48, 1952, 758, 2341, 2410, 49, 3122, 2551, 3718, 4806, 2216, 3484, 3577, 759, 2080, 50, 1308, 1230, 3960, 1378, 2994, 3080, 2589, 3681, 51, 4694, 2257, 52, 760, 53, 2389, 4934, 4951, 761, 762, 4659, 54, 2146, 3925, 55, 3654, 2087, 2346, 4766, 4682, 4984, 4744, 56, 763, 764, 4626, 4702, 58, 59, 60, 61, 4086, 1740, 1660, 765, 766, 62, 1966, 2032, 2499, 2332, 767, 63, 2096, 2181, 4913, 64, 768, 769, 770, 2384, 2402, 771, 65, 66, 2111, 67, 772, 2458, 2197, 68, 3816, 69, 2599, 2706, 2497, 70, 2234, 2183, 2399, 71, 4769, 2366, 72, 73, 74, 3865, 1549, 1361, 2453, 3882, 773, 3713, 1942, 75, 1312, 4501, 76, 77, 774, 1413, 775, 776, 78, 1560, 4289, 3757, 79, 3593, 4043, 1806, 3908, 4397, 1615, 4415, 3723, 2006, 3754, 1470, 4360, 80, 3945, 2854, 3523, 3669, 1356, 777, 2132, 2379, 82, 4065, 83, 84, 2030, 1294, 2413, 2064, 1484, 85, 4594, 86, 778, 87, 3891, 4456, 4040, 4496, 1982, 2001, 1478, 1189, 88, 1490, 1885, 1926, 89, 90, 91, 779, 2270, 780, 2161, 1180, 92, 781, 782, 783, 93, 2356, 784, 785, 786, 94, 95, 787, 788, 1831, 1867, 96, 4458, 97, 1970, 4656, 2173, 1936, 2349, 1590, 4585, 98, 99, 100, 789, 790, 1298, 101, 1688, 791, 792, 2007, 2070, 102, 793, 4632, 103, 794, 795, 104, 105, 106, 2229, 796, 4980, 4691, 107, 2440, 1849, 108, 2014, 797, 4736, 2509, 2018, 2227, 4787, 109, 1579, 110, 1906, 111, 2428, 798, 112, 2411, 113, 2359, 799, 4848, 800, 2461, 1444, 2313, 2350, 4579, 4821, 801, 114, 2329, 4834, 115, 1344, 116, 802, 117, 118, 119, 4929, 4677, 120, 2158, 121, 803, 804, 1463, 805, 122, 2139, 2290, 1760, 2465, 2424, 2058, 2230, 124, 4717, 806, 125, 126, 2370, 127, 4521, 128, 4971, 4994, 807, 2085, 129, 130, 131, 132, 4933, 808, 2336, 2026, 2204, 809, 810, 2281, 133, 1978, 134, 811, 812, 135, 136, 137, 138, 813, 814, 139, 4673, 140, 815, 1326, 141, 142, 143, 2344, 4544, 144, 145, 816, 4654, 4816, 1634, 1302, 817, 146, 818, 147, 148, 149, 4546, 150, 151, 152, 153, 154, 155, 819, 820, 156, 2149, 157, 2295, 821, 158, 159, 160, 161, 4631, 2441, 162, 163, 164, 165, 166, 822, 167, 168, 169, 170, 171, 823, 172, 4613, 824, 1651, 173, 1483, 174, 175, 825, 176, 177, 178, 179, 4624, 2170, 4809, 4520, 180, 826, 827, 181, 828, 4695, 4911, 182, 4582, 4873, 4596, 2020, 183, 4641, 829, 184, 185, 2244, 4647, 186, 187, 188, 189, 190, 2114, 830, 191, 192, 193, 194, 2071, 4615, 2361, 195, 4852, 2187, 4914, 4947, 196, 1391, 197, 4534, 4726, 4788, 198, 199, 4920, 831, 2240, 2223, 200, 201, 202, 203, 2106, 2503, 4775, 204, 205, 832, 833, 206, 834, 2232, 2294, 207, 2166, 208, 209, 210, 835, 836, 1334, 837, 3901, 3312, 2649, 1301, 211, 212, 1450, 4386, 3028, 213, 1446,

214, 2206, 215, 1896, 1522, 3490, 838, 216, 2241, 217, 218, 4653, 219, 1612, 220, 221, 222, 839, 223, 4953, 2360, 840, 224, 4928, 4741, 225, 2088, 4751, 5007, 4542, 226, 227, 4890, 4519, 4883, 228, 4786, 229, 230, 231, 2393, 2448, 841, 842, 232, 233, 4782, 234, 4962, 2269, 843, 235, 844, 236, 237, 4930, 845, 846, 238, 847, 4704, 239, 848, 849, 2150, 850, 851, 852, 853, 1536, 240, 854, 241, 242, 243, 244, 245, 246, 247, 248, 4923, 2245, 4696, 855, 4634, 856, 249, 250, 251, 252, 253, 254, 255, 857, 2115, 4880, 256, 257, 258, 259, 858, 859, 260, 261, 860, 861, 862, 262, 4966, 863, 864, 263, 4749, 4970, 2296, 2318, 865, 2326, 264, 1241, 265, 266, 866, 1477, 267, 867, 4977, 268, 868, 269, 4668, 5002, 270, 869, 870, 271, 871, 872, 272, 4822, 4709, 873, 4655, 4972, 2392, 874, 1252, 273, 1591, 4975, 875, 274, 2025, 275, 1980, 276, 876, 877, 2066, 277, 278, 279, 4670, 280, 2323, 2288, 2334, 4689, 281, 878, 1892, 879, 1539, 2214, 2215, 880, 2327, 881, 882, 4601, 883, 1295, 3601, 3877, 1930, 1420, 1678, 1460, 2306, 884, 282, 1799, 283, 284, 4988, 4553, 4772, 4817, 2260, 285, 1626, 2082, 885, 286, 1374, 886, 2119, 2468, 287, 1620, 1290, 2425, 2482, 4671, 2282, 288, 2354, 1354, 2033, 289, 887, 290, 888, 291, 1956, 2467, 889, 2357, 4547, 4765, 292, 4794, 2391, 4324, 890, 294, 295, 4138, 891, 2297, 296, 2224, 3903, 297, 892, 3829, 298, 299, 3809, 4271, 3844, 1436, 300, 1515, 1617, 4701, 2174, 301, 1961, 4649, 5010, 302, 303, 304, 305, 2452, 2147, 306, 2293, 1589, 893, 4370, 4841, 2342, 307, 308, 309, 894, 2246, 2155, 3646, 4059, 1431, 1331, 310, 311, 4836, 4948, 312, 895, 1779, 313, 314, 315, 316, 896, 1558, 1552, 317, 2312, 318, 319, 897, 320, 898, 321, 322, 899, 1958, 2022, 2016, 900, 2454, 323, 2427, 2134, 324, 901, 325, 902, 326, 2373, 4803, 2459, 1491, 327, 328, 903, 2463, 2264, 329, 330, 904, 1635, 4820, 905, 2506, 331, 4706, 2092, 4484, 1756, 906, 907, 4661, 2179, 4584, 332, 4907, 4635, 4529, 4683, 4523, 4561, 333, 2337, 3536, 2701, 2799, 3332, 3294, 3159, 3069, 2637, 3025, 2782, 3247, 3350, 2692, 2586, 3004, 3049, 2694, 2650, 3554, 2983, 3403, 3214, 3163, 2541, 3090, 3097, 3462, 1430, 2941, 3486, 2842, 3558, 3104, 3037, 3419, 2780, 2931, 1276, 2928, 2609, 3068, 3128, 2548, 2538, 2618, 2789, 3228, 2657, 3189, 2128, 2863, 3307, 3300, 2546, 3048, 3543, 2946, 2975, 3346, 3067, 2728, 2955, 3408, 3027, 3094, 3203, 2988, 2751, 2953, 2566, 2578, 2823, 3063, 3335, 3000, 3181, 3011, 3138, 3389, 2805, 3074, 2894, 3149, 2560, 3417, 3265, 3378, 2901, 2837, 2822, 2745, 3473, 3530, 3040, 2597, 3509, 3522, 3161, 2926, 3209, 3105, 3400, 2630, 2905, 2671, 2818, 2806, 2702, 2709, 2400, 3549, 3538, 2534, 2773, 2623, 3491, 3243, 3136, 2693, 3164, 3343, 2918, 2555, 2794, 2679, 3510, 3110, 2672, 3442, 2929, 3184, 3488, 2135, 4763, 3414, 3093, 2996, 3141, 3544, 3102, 2856, 2957, 3466, 3461, 2788, 2660, 3344, 3204, 2720, 3379, 2826, 1789, 2396, 2785, 3249, 3527, 4460, 3352, 2051, 2569, 4457, 2011, 4857, 2163, 4783, 4319, 3906, 1533, 1755, 1888, 4248, 1557, 2153, 3804, 1363, 1934, 1602, 1404, 4188, 1330, 4349, 3337, 3533, 2629, 3038, 2539, 3567, 3291, 3348, 3115, 3359, 2993, 3079, 3506, 2527, 2963, 2938, 2516,

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1116, 645, 646, 4611, 2353, 4645, 4998, 2307, 647, 1801, 4279, 3762, 1637, 1509, 4843, 4797, 4590, 4995, 4541, 2200, 4580, 4858, 648, 649, 2502, 1117, 4780, 4800, 4551, 4674, 1118, 1119, 2965, 2369, 2695, 3293, 650, 651, 4730, 4862, 4722, 4944, 1120, 652, 1121, 4983, 4784, 4877, 4643, 653, 654, 4909, 1122, 3264, 655, 2076, 4849, 656, 657, 2447, 658, 659, 4035, 2910, 3391, 2808, 3099, 2913, 3676, 2852, 3284, 2731, 1609, 2375, 2201, 3537, 3994, 1319, 4467, 1802, 1227, 1623, 660, 4844, 2086, 4770, 2192, 1123, 661, 2364, 662, 663, 664, 1124, 1125, 665, 2487, 4899, 2138, 1126, 666, 667, 4569, 4554, 4917, 2322, 1127, 1128, 1129, 668, 669, 1130, 670, 1131, 1527, 1132, 671, 1772, 2314, 1133, 1134, 2470, 1135, 672, 2236, 4716, 673, 4600, 2196, 2456, 4606, 4910, 2123, 1136, 1137, 2358, 5005, 2208, 4952, 4945, 1933, 1731, 1793, 675, 676, 3342, 1138, 677, 4597, 4870, 1140, 4990, 4954, 4916, 678, 1141, 4737, 4527, 2253, 4531, 679, 1142, 1143, 680, 4771, 1144, 4638, 681, 4705, 4525, 4522, 4898, 2325, 2415, 5004, 1145, 682, 683, 1146, 684, 685, 2445, 686, 687, 4861, 2157, 688, 3822, 689, 690, 4743, 691, 1147, 1601, 692, 1148, 693, 4537, 4825, 4625, 4621, 3905, 694, 695, 1414, 1149, 696, 2027, 2159, 4756, 4793, 4575, 2160, 4828, 4731, 4718, 4802, 4750, 1150, 2081, 2258, 697, 1795, 1372, 1695, 1866, 1151, 4115, 1719, 2280, 4662, 698, 2176, 2194, 2217, 1920, 699, 700, 701, 4999, 1544, 4739, 702, 703, 4031, 4305, 1636, 1393, 2010, 3810, 4452, 3677, 4227, 1277, 1400, 4402, 4157, 4197, 1337, 1253, 1532, 4028, 3989, 2449, 4715, 704, 2050, 1493, 1854, 1902, 1510, 1152, 4824, 705, 2340, 4182, 706, 2442, 2484, 707, 708, 709, 4667, 1153, 2412, 4476, 2053, 710, 1375, 711, 712, 713, 4829, 4738, 4811, 4570, 4961, 1245, 714, 2045, 4707, 715, 2169, 4713, 1841, 4234, 4924, 1154, 1314, 4096, 2023, 716, 717, 4895, 718, 1155, 719, 720, 2063, 1311, 721, 4642, 722, 4885, 4666, 2249, 4217, 1156, 723, 1157, 1627, 2116, 4566, 2287, 1158, 2330, 4826, 4622, 4740, 724, 4700, 725, 1159, 5013, 4894, 726, 2434, 1953, 1160, 1201, 727, 3787, 2046, 1161, 728, 729, 2485, 2044, 4568, 3747, 730, 731, 2024, 1846, 2507, 2368, 2019, 2333, 3815, 2005, 2266, 1964, 2347, 2385, 732, 2177, 2059, 4958, 1822, 4815, 1262, 2094, 4480, 1537, 1291, 2419, 1318, 2283, 4976, 4294, 2486, 4926, 1582, 2162, 733, 4587, 734, 735, 3439, 2833, 4287, 4509, 4505, 4267, 3697, 3272, 4112, 2967, 3651, 1991, 1805, 1628, 3705, 2479, 736, 1195, 4863, 1163, 3859, 1164, 2394, 1165, 2355, 2351, 4679, 4835, 2259, 4839, 4571, 1166, 4968, 2250, 4912, 2423, 737, 1167, 4989, 4684, 4669, 4552, 4612, 2127, 1745, 1973, 4767, 1168, 2273, 2310, 3807, 4307, 1169, 2303, 1454, or 1781.

37. The VP capsid polypeptide of claim 1, wherein X^3, X^6, and X^1 of SEQ ID NO: 5014 are basic amino acid residues.

38. The VP capsid polypeptide of claim 1, wherein X^3, X^6, and X^4 of SEQ ID NO: 5014 are basic amino acid residues.

39. The VP capsid polypeptide of claim 37 or claim 38, wherein X^3, X^6, X^1, and X^4 of SEQ ID NO: 5014 are basic amino acid residues.

40. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region of the VP capsid polypeptide comprises at least two basic amino acid residues and no more than one acidic amino acid residue.

41. The VP capsid polypeptide of claim 1, wherein the VP capsid polypeptide comprises one or more features selected from the group consisting of:

(a) the 581 to 589 region comprises two or more basic amino acid residues,

(b) X^3, X^6, X^1, or X^4 of SEQ ID NO: 5014, or any combination thereof are basic amino acid residues, and

(c) the 581 to 589 region comprises no more than one acidic amino acid residue.

42. The VP capsid polypeptide of claim 41, wherein the VP capsid polypeptide comprises two or more of the features.

43. The VP capsid polypeptide of claim 41, wherein the VP capsid polypeptide comprises three of the features.

44. The VP capsid polypeptide of any one of claims 40-43, wherein the acidic amino acid residue is D or E.

45. The VP capsid polypeptide of any one of claims 37-44, wherein the basic amino acid residues are K, R, or H.

46. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013.

47. The VP capsid polypeptide of claim 46, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 14 – SEQ ID NO: 2013.

48. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a

sequence having at least 85% sequence identity to any one of SEQ ID NO: 2514 – SEQ ID NO: 4513.

49. The VP capsid polypeptide of claim 48, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 2514 – SEQ ID NO: 4513.

50. The VP capsid polypeptide of any one of claims 1-49, wherein the 581 to 589 region confers increased retina tissue tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1.

51. The VP capsid polypeptide of claim 50, wherein the retina tissue tropism is at least 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, or at least 500-fold higher than the wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1.

52. The VP capsid polypeptide of claim 50 or claim 51, wherein the 581 to 589 region further confers increased retinal pigment epithelium tissue tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1.

53. The VP capsid polypeptide of any one of claims 1-52, wherein the 581 to 589 region confers decreased photoreceptor tissue-tropism compared to a wild type AAV5 VP capsid polypeptide of SEQ ID NO: 1.

54. The VP capsid polypeptide of claim 53, wherein the photoreceptor tissue comprises rod photoreceptor cells, cone photoreceptor cells, or a combination thereof.

55. The VP capsid polypeptide of any one of claims 1-54, wherein the VP capsid polypeptide comprises an amino acid sequence at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 97%, at least 98%, at least 98.5%, at least 99%, or at least 99.5% identical to SEQ ID NO: 1.

56. The VP capsid polypeptide of any one of claims 1-55, wherein the VP capsid polypeptide has a sequence of SEQ ID NO: 2, wherein residues 581 to 589 of SEQ ID NO: 2 ($X^1X^2X^3X^4X^5X^6X^7X^8X^9$) correspond to the 581 to 589 region.

57. The VP capsid polypeptide of any one of claims 1-56, wherein the VP capsid polypeptide is capable of assembling into a recombinant viral capsid.

58. The VP capsid polypeptide of any one of claims 1-57, comprising at least one amino acid substitution as compared to each of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, and SEQ ID NO: 8.

59. The VP capsid polypeptide of any one of claims 1-58, wherein the 581 to 589 region comprises a net positive charge at pH 7.4.

60. The VP capsid polypeptide of any one of claims 1-59, wherein the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region relative to a wild type VP capsid polypeptide of SEQ ID NO: 1.

61. The VP capsid polypeptide of any one of claims 1-60, wherein the 581 to 589 region confers on a recombinant viral capsid assembled from the VP capsid polypeptide improved stability compared to a wild type AAV capsid comprising a peptide of SEQ ID NO: 1.

62. The VP capsid polypeptide of any one of claims 1-61, wherein the 581 to 589 region confers lower toxicity upon administration to a subject compared to a wild type VP capsid polypeptide of SEQ ID NO: 1.

63. The VP capsid polypeptide of any one of claims 1-62, wherein the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region that contributes to reduced production of neutralizing antibodies relative to a wild type VP capsid polypeptide of SEQ ID NO: 1.

64. The VP capsid polypeptide of any one of claims 1-63, wherein the VP capsid polypeptide further comprises one or more mutations outside of the 581 to 589 region that improves manufacturability relative to a wild type VP capsid polypeptide of SEQ ID NO: 1.

65. A recombinant viral adeno-associated virus (rAAV) capsid comprising the VP capsid polypeptide of any one of claims 1-64, wherein the rAAV capsid preferentially targets retina tissue.

66. The rAAV capsid of claim 65, further comprising a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region.

67. A recombinant adeno-associated virus (rAAV), comprising the VP capsid polypeptide of any one of claims 1-64 assembled into a recombinant viral capsid and a payload encapsidated by the recombinant viral capsid.

68. The rAAV of claim 67, wherein the rAAV preferentially targets retina tissue.

69. The rAAV of claim 67or claim 68, further comprising a VP2 polypeptide comprising the 581 to 589 region and a VP3 polypeptide comprising the 581 to 589 region.

70. The rAAV of any one of claims 67-69, wherein the payload encodes a therapeutic polynucleotide or a therapeutic peptide.

71. The rAAV of claim 70, wherein the payload encodes a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, or an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof.

72. The rAAV of claim 71, wherein the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA.

73. The rAAV of claim 71, wherein the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor.

74. A pharmaceutical composition comprising the VP capsid polypeptide of any one of claims 1-64, the rAAV capsid of claim 65 or claim 66, or the rAAV of any one of claims 67-73.

75. A method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues.

76. A method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513.

77. A method of delivering a payload to a retina tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of claims 1-64.

78. A method of delivering a payload to a retina tissue of a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues; and

(ii) delivering the payload to the retina tissue.

79. A method of delivering a payload to a retina tissue of a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513; and

(ii) delivering the payload to the retina tissue.

80. A method of delivering a payload to a retina tissue of a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of claims 1-64; and

(ii) delivering the payload to the retina tissue.

81. The method of any one of claims 78-80, comprising administering the rAAV via intravitreal administration.

82. The method of any one of claims 78-80, comprising administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration.

83. The method of any one of claims 75-82, further comprising expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload.

84. The method of any one of claims 75-83, further comprising producing a therapeutic effect upon expression of the payload.

85. The method of claim 84, wherein the therapeutic effect is produced upon administration of from 1 x 10^5 to 5 x 10^{14} rAAVs.

86. The method of claim 84 or claim 85, comprising administering an amount of the rAAV sufficient to produce the therapeutic effect without producing a toxicity in the subject.

87. A method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues.

88. A method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513.

89. A method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of claims 1-64.

90. The method of any one of claims 87-89, further comprising expressing the payload in a retina tissue of the subject.

91. The method of any one of claims 87-90, further comprising producing a therapeutic effect in the subject.

92. A method of treating a condition in a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region comprising at least one substitution

relative to SEQ ID NO: 9, and wherein the 581 to 589 region comprises one or more basic amino acid residues; and

(ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

93. A method of treating a condition in a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 14 – SEQ ID NO: 2013 or SEQ ID NO: 2514 – SEQ ID NO: 4513; and

(ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

94. A method of treating a condition in a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of claims 1-64; and

(ii) expressing the payload in a retina tissue of the subject, thereby treating the condition in the subject.

95. A method of treating a condition in a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises the VP capsid polypeptide of any one of claims 1-64;

(ii) delivering the payload to a retina tissue of the subject; and

(iii) producing a therapeutic effect in the retina tissue, thereby treating the condition.

96. The method of any one of claims 92-95, comprising administering the rAAV via intravitreal administration.

97. The method of any one of claims 92-95, comprising administering the rAAV via subretinal injection, topical mucosal administration, or systemic administration.

98. The method of any one of claims 87-97, wherein the condition is an ocular condition.

99. The method of claim 98, wherein the ocular condition is achromatopsia, macular degeneration, cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis.

100. The method of claim 98 or claim 99, wherein the ocular condition is Stargardt disease.

101. The method of any one of claims 76-100, further comprising delivering the rAAV to a retina tissue with higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1.

102. The method of any one of claims 76-101, further comprising delivering the rAAV to a retina tissue with higher tissue tropism than for photoreceptor tissue.

103. The method of any one of claims 76-102, comprising delivering the rAAV to a retina tissue with at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher tissue tropism than a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1.

104. The method of any one of claims 76-103, comprising administering from 1×10^5 to 5×10^{14} rAAVs.

105. The method of any one of claims 76-104, wherein the payload encodes a therapeutic protein, therapeutic polynucleotide, a guide RNA, a tRNA, a suppressor tRNA, a siRNA, a miRNA, an mRNA, a shRNA, a circular RNA, an antisense oligonucleotide (ASO), a ribozyme, a DNAzyme, an aptamer, or any combination thereof.

106. The method of claim 105, wherein the guide RNA is a CRISPR/Cas guide RNA or an ADAR guide RNA.

107. The method of claim 105, wherein the therapeutic protein is selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I,

ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, and RS1.

108. The method of claim 105, wherein the therapeutic polynucleotide targets an mRNA encoding a protein selected from the group consisting of CNGB3, NOS2A, CFH, CF, C2, C3, CFB, HTRA1/LOC, MMP-9, TIMP-3, SLC16A8, GEMIN4, CYP51A1, RIC1, TAPT1, TAF1A, WDR87, APE1, MIP, Cx50, GJA3, GJA8, CRYAA, CRYBB2, PRX, POLR3B, XRCC1, ZNF350, EPHA2, REP1, CALM2, MPP-7, Optineurin, LOX1, CYP1B1, CAV1/2, MYOC, PITX2, FOXC1, PAX6, LTBP2, Complex I, ND, OPA1, RPE65, FBN1, TGFBR2, MTHFR, MTR, MTRR, HGF, C-MET, UMODL1, MMP-1/2, CBS, IGF-1, UHRF1BP1L, PTPRR, PPFIA2, P4HA2, SERPING1, PEDF, ARMS2-HTRA1, FGD6, ABCG1, LOC387715, CETP, NRL, RDH12, PRPH2 (RDS), RHO, RPGR, SNRNP200, NR2E3, IMPDH1, CRX, HK1, IMPDH2, PRPF3, AGBL5, ABCA1, ABCA4, CRB1, USH2A, NRP1, ND4, RLBP1, PTEN, BAP1, GNAQ, GNA11, DDEF1, SF3B1, EIF1AX, CDKN2A, p14ARF, HERC2/OCA2, VEGF, or RS1.

109. The method of claim 105, wherein the payload encodes a therapeutic polynucleotide targeting ABCA1, ABCA4, or CRB1 or a transgene encoding ABCA1, ABCA4, or CRB1.

110. The method of claim 105, wherein the payload encodes a component of a CRISPR/Cas system, an adenosine deaminase acting on RNA (ADAR) enzyme, a transcriptional activator, or a transcriptional repressor.

111. The method of claim 110, wherein the component of the CRISPR/Cas system comprises a Cas3, a Cas8, a Cas10, a Cas9, a Cas4, a Cas12, a Cas13, a guide RNA, or a combination thereof.

112. The method of claim 110, wherein the ADAR enzyme is ADAR1 or ADAR2.

113. The method of claim 110, wherein the transcriptional activator is VP64.

114. The method of claim 110, wherein the transcriptional repressor is KRAB.

115. The method of any one of claims 105-114, further comprising expressing a therapeutic polypeptide or a therapeutic polynucleotide encoded by the payload.

116. The method of any one of claims 105-115, comprising expressing the therapeutic polypeptide or the therapeutic polynucleotide at a higher level in a retina tissue compared to a wild type AAV5 capsid comprising a peptide of SEQ ID NO: 1.

117. The method of claim 116, comprising expressing the therapeutic polypeptide or the therapeutic polynucleotide in a retina tissue at a level that is at least 3-fold, at least 3.5-fold, at least 4-fold, at least 5-fold, at least 10-fold, at least 20-fold, at least 50-fold, at least 75-fold, at least 100-fold, at least 200-fold, at least 500-fold higher, or at least 1000-fold higher compared to the wild type AAV5 capsid.

118. The method of any one of claims 76-117, comprising producing a toxicity in the subject that is lower than a toxicity produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1.

119. The method of any one of claims 76-118, comprising producing a toxicity in the subject that is lower than a toxicity produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retina tissue.

120. The method of any one of claims 76-119, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1.

121. The method of any one of claims 76-120, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV2 capsids.

122. The method of any one of claims 76-121, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV8 capsids.

123. The method of any one of claims 76-122, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a comparable number of wild type AAV9 capsids.

124. The method of any one of claims 76-123, comprising producing a concentration of neutralizing antibodies in the subject that is lower than a concentration of neutralizing antibodies produced upon administration of a number of wild type AAV5 capsids comprising a VP capsid polypeptide of SEQ ID NO: 1 sufficient to deliver a comparable number of payloads to a retina tissue.

125. The rAAV capsid of claim 65 or 66, the rAAV of any one of claims 67 to 73, or the pharmaceutical composition of claim 74 for use as a medicament.

126. The rAAV capsid of claim 65 or 66, the rAAV of any one of claims 67 to 73, or the pharmaceutical composition of claim 74 for use in a method of treating an ocular condition.

127. The rAAV capsid, rAAV or pharmaceutical composition for use of claim 126, wherein the ocular condition is achromatopsia, macular degeneration, cataracts, choroideraemia, glaucoma, optical neuropathy, Marfan syndrome, myopia, polypoidal choroidal vasculopathy, retinitis pigmentosa, Stargardt disease, Usher syndrome, Leber congenital amaurosis, Leber hereditary optical neuropathy, Uveal melanoma, or X-linked retinoschisis.

128. The rAAV capsid, rAAV or pharmaceutical composition for use of claim 126 or 127, wherein the ocular condition is Stargardt disease.

129. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513.

130. The VP capsid polypeptide of claim 1, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 2014 – SEQ ID NO: 2513.

131. A viral protein (VP) capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 4514 – SEQ ID NO: 5013.

132. The VP capsid polypeptide of claim 3, wherein the 581 to 589 region comprises a sequence of any one of SEQ ID NO: 4514 – SEQ ID NO: 5013.

133. A recombinant viral adeno-associated virus (rAAV) capsid comprising the VP capsid polypeptide of any one of claims 129-132, wherein the rAAV capsid preferentially targets retinal pigment epithelium tissue.

134. A recombinant viral adeno-associated virus (rAAV) capsid comprising the VP capsid polypeptide of any one of claims 129-132, wherein the rAAV capsid preferentially targets choroid tissue.

135. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

136. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

137. A method of delivering a payload to a choroid tissue of a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and

(ii) delivering the payload to the choroid tissue.

138. A method of delivering a payload to a retinal pigment epithelium tissue of a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates the payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and

(ii) delivering the payload to the retinal pigment epithelium tissue.

139. A method of treating a condition in a subject, the method comprising administering a recombinant adeno-associated virus (rAAV) to the subject via intravitreal administration, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013.

140. A method of treating a condition in a subject, the method comprising:

(i) administering a recombinant adeno-associated virus (rAAV) to the subject, wherein the rAAV encapsidates a payload, and wherein the rAAV comprises a VP capsid polypeptide comprising a 581 to 589 region corresponding to residues 581 to 589 of an AAV5 VP1 polypeptide, wherein the 581 to 589 region comprises a sequence having at least 85% sequence identity to any one of SEQ ID NO: 2014 – SEQ ID NO: 2513 or SEQ ID NO: 4514 – SEQ ID NO: 5013; and

(ii) expressing the payload in a retinal pigment epithelium tissue of the subject, thereby treating the condition in the subject.