CLAIMS

1. A method of assaying for presence of a viral infection in a subject comprising:

obtaining a methylation pattern for a set of DNA methylation sites from a sample derived from the subject; and

analyzing the methylation pattern for the set of DNA methylation sites with an infection positive methylation classifier and/or an infection negative methylation classifier,

wherein presence of a viral infection in the subject is indicated when a score derived from the infection positive classifier exceeds a cutoff and/or threshold value indicating the presence of a viral infection.

2. The method of claim 1, wherein the viral infection is a SARS-CoV-2 infection.

3. The method of claim 1 or 2, wherein obtaining the methylation pattern for the set of DNA methylation sites is performed on a methylation bead array.

4. A method for determining likelihood of a viral infection producing acute respiratory distress syndrome in a subject comprising:

obtaining a methylation pattern for a set of DNA methylation sites from a sample derived from the subject; and

analyzing the methylation pattern for the set of DNA methylation sites with an acute respiratory distress syndrome positive methylation classifier and/or an acute respiratory distress syndrome negative methylation classifier,

wherein likelihood the subject will exhibit acute respiratory distress syndrome is indicated when a score derived from the acute respiratory distress syndrome positive classifier exceeds a cutoff and/or threshold value indicating likelihood of a viral infection producing acute respiratory distress syndrome.

5. A method of determining the nature of a viral infection in a subject comprising:

obtaining a methylation pattern for a set of DNA methylation sites from a sample derived from the subject; and

analyzing the methylation pattern for the set of DNA methylation sites with a SARS-CoV-2 positive methylation classifier and/or a SARS-CoV-2 negative methylation classifier,

wherein presence of a SARS-CoV-2 infection in the subject is indicated when a score derived from the SARS-CoV-2 positive methylation classifier exceeds a cutoff and/or threshold value indicating presence of a SARS-CoV-2 infection.

6. The method of any one of claims 1 to 5, wherein the viral infection is a SARS-CoV-2 infection.

7. The method of any one of claims 1-6, wherein the sample is a blood sample from the subject, optionally wherein the subject is a human subject.

8. The method of any one of claims 1-7, wherein obtaining the methylation pattern for the set of DNA methylation sites is performed on a methylation bead array, optionally wherein the methylation bead array comprises a set of genes comprising ANLN, ARID3B, ARID5B, CALHM2, CBX3B2, CD38, CHSY1 CMPK2, DDX60, DTX3L, EPSTI1, FAM38A, FGFRL1, GPX1, GTPBP2, IFI27, IFIT3, IRF7, LINC00428, LINC01429, MX1, OAS1, OAS2, PARP9, PHOSPHO1, PPL, RAB40C, REPD, TNFRSF8, TRIM22, TSEN15, and ZDHHC6, or any subset thereof.

9. The method of any one of claims 1-8, wherein analyzing the methylation pattern for the set of DNA methylation sites with an infection positive methylation classifier and/or an infection negative methylation classifier comprises analyzing methylation of a set of genes comprising ANLN, ARID3B, ARID5B, CALHM2, CBX3B2, CD38, CHSY1 CMPK2, DDX60, DTX3L, EPSTI1, FAM38A, FGFRL1, GPX1, GTPBP2, IFI27, IFIT3, IRF7, LINC00428, LINC01429, MX1, OAS1, OAS2, PARP9, PHOSPHO1, PPL, RAB40C, REPD, TNFRSF8, TRIM22, TSEN15, and ZDHHC6,

or any subset thereof, optionally wherein an acute respiratory distress syndrome positive methylation signature comprises hypomethylation of one or more genes selected from a group consisting of IFR7, ARID5B, ANLN, PARP9, MX1, CBX3P2, EPSTI1, CHSY1, MX1, and GPX1, or any subset thereof, and/or hypermethylation of one or more genes selected from a group consisting of LINC01429, CALHM2, LINC00428, OAS1, RAB40C, TSEN15, PEPD, PPL, ARID3B, ZDHHC6, TNFRSF8, DDX60, OAS2, and FGFRL1, or any subset thereof.

10. A computer-implemented method for executing the method of any one of claims 1–9.

11. A methylation bead array of DNA methylation sites comprising a set of genes comprising ANLN, ARID3B, ARID5B, CALHM2, CBX3B2, CD38, CHSY1 CMPK2, DDX60, DTX3L, EPSTI1, FAM38A, FGFRL1, GPX1, GTPBP2, IFI27, IFIT3, IRF7, LINC00428, LINC01429, MX1, OAS1, OAS2, PARP9, PHOSPHO1, PPL, RAB40C, REPD, TNFRSF8, TRIM22, TSEN15, and ZDHHC6, or any subset thereof.

12. A method of detecting COVID-19 in a subject comprising:

obtaining a methylation pattern for a set of DNA methylation sites from a sample derived from the subject suspected of having COVID-19; and

analyzing the methylation pattern for the set of DNA methylation sites with a SARS-CoV-2 positive methylation classifier and/or a SARS-CoV-2 negative methylation classifier, wherein presence of a SARS-CoV-2 infection in the subject is indicated when a score derived from the SARS-CoV-2 positive methylation classifier exceeds a cutoff and/or threshold value indicating presence of a SARS-CoV-2 infection.

13. The method of claim 12, wherein the sample is a blood sample from the subject, optionally, wherein the subject is a human subject.

14. The method of any one of claims 12–13, wherein obtaining the methylation pattern for the set of DNA methylation sites is performed on a methylation bead array.

15. An array for detecting the presence of a respiratory virus in a sample comprising a plurality of oligonucleotide probes attached to a solid support; wherein the plurality of oligonucleotide probes detect a methylation signature of the sample.

16. An array for determining the clinical outcome of a respiratory viral infection in a patient comprising a plurality of oligonucleotide probes attached to a solid support; wherein the plurality of oligonucleotide probes detect a methylation signature of a sample from the patient.

17. The array of claim 15 or 16, wherein the methylation signature comprises detecting a methylation status of at least one gene selected from the group consisting of: A_24_P561165, AA455656, ABCF1, ACBD5, AGL, AGPAT1, AID, AIF1, AIM2, ANLN, ANKRD28, APE1, APOBEC3G, APOL2, APOL3, APOL6, APPBP2, ARID3B, ARID5B, ASK1, ASPM, ATAT1, ATF2, ATP2C1, B2M, BATF, BATF2, BCL2L14, BRD2, C10orf81, C1orf68, C1R, C1S, C2, C3, C4A, C4B, C5, C6, C6orf136, C6orf15, C7, C8, C9, CALHM2, CALR, CASP1, Caspase-3, Caspase-8, CATSPER2, CATSPER2P1, CATSPERG, CBX3B2, CCDC66, CCHCR1, CCRL1, CD19, CD27-AS1, CD4, CD38, CD40, CD74, CD8, CDKN1A, CELF4, CEP162, CFB, CFH, CFHR1, CFHR2, CFHR3, CFHR4, CHSY1, CHTOP, CIITA, CIITA BX117479, c-Jun, CLIC5, CMPK2, CSNK2B, CTNND1, CTSS ZBP1, CUTA, CX3CL1 A_24_P912985, CXCL10, CXCL11, CXCL2, CYP21A2, DAG1, DDR1, DDX60, DENND2B, DEXI, DTNB, DTX3L, DYSF, E2F5, EGFL8, EHMT2, eIF-2, eIF2B, ELAVL2, EPSTI1, ERP27, ETV7, FADD, FAM26F, FAM38A, FAM49B, FGFRL1 GPX1, FKBP5, FLG, FLG-AS1, FRMD3, FZD5, GAPVD1, GPANK1, GPX5, GTPBP2, GTF2H4, HCG17, HCG18, HCG20, HCG22, HCG24, HCG25, HCG27, HCG4, HCG4B, HCP5, HCP5 NNMT, HLA-A, HLA-B, HLA-C, HLA-DMB, HLA-DOA, HLA-DPA1, HLA-DPB1, HLA-DPB2, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DQB1-AS1, HLA-DRA, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-E, HLA-F, HLA-F-AS1, HLA-G, HLA-H,

HLA-V, HRNR, HSD17B8, HSPA1B, ICAM1, IFI16, IFI27, IFI35, IFI44, IFI44L, IFIH1, IFIT2, IFIT3, IFIT5, IFITM1, IFNL1, IFNL2, IFNL3, IFNL4, IFN-α, IFN-β, IFNγ, IFN-γ, IFN-ε, IFN-κ, IFN-ω, IGH, IGK, IGL, IKK-α, IKK-β, IKK-γ, IKKε, IL-10, IL-11, IL-12, IL12A, IL-13, IL-15, IL-17, IL-18, IL18BP, IL-1ra, IL-1α, IL-1β, IL-2, IL-3, IL-33, IL-36ra, IL-36α, IL-36β, IL-36γ, IL-37, IL-38, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IRF1, IRF3, IRF7, IVL, JAK2, JNK, KCTD16, KDM4C, KIFC1, KPRP, LAP3, LCE1D, LCE1E, LCE2B, LCE2C, LCE2D, LCE3C, LCE4A, LELP1, LGP2, LINC00302, LINC00428, LINC01429, LINC01185, LOC100129636, LOC100294145, LOC100507547, LOC101929006, LOC105375690, LRBA, LST1, LTA, LTBR, LT-α, LY6G6F-LY6G6D, LYRM4-AS1, M27126, MAVS, MCCD1, MDA5, MDC1, MEF2C, MEKK1, MICA, MICA-AS1, MICAB, MICB, MICB-DT, MIR219A1, MIR4479, MKK7, MMP25, MOG, MPIG6B, MSH5, MUCL3, MX1, NA, NAIP, NBPF18P, NELFE, NFKB1, NFKB2, NFKBIA, NLRC3, NLRC4, NLRC5, NLRP1, NLRP10, NLRP11, NLRP12, NLRP13, NLRP14, NLRP2, NLRP3, NLRP4, NLRP5, NLRP6, NLRP7, NLRP8, NLRP9, NLRX1, NMI, NOD1, NOD2, NRCAM, OAS1, OAS2, OR10C1, OR12D2, OR14J1, OR2H1, OR2H2, OR2J1, OR2J2, OSMR, PARP9, PCDH15, PDCD6IPP2, PDIA3, PGLYRP4, PHF1, PHOSPHO1; PKR, PMAIP1, PML, POMC, PPL, PPP1R11, PPP2R5A, PPP6R3, PPT2, PRR3, PRR9, PRRC2A, PRRT1, PSMB8, PSMB8-AS1, PSMB9, PSORS1C1, PSORS1C2, RAB40C, RALYL, REC8, REL, RELA, RELB, REPD TNFRSF8, RIG-1, RING1, RIP, RNAse L, RNF43, RNF5, RNF5P1, RPL13A, RPS18, RPS6KC1, RTP4, RXRB, S100A13, S100A7, S100A8, SAMD9L, SCNN1A, SECTM1, SEPX1, SERPINB7, SERPING1, SHMT1, SKIV2L, SLC44A4, SLCO5A1, SMURF2P1-LRRC37BP1, SNAPC3, SNHG32, SNORD32B, SNX14, SOCS1, SP110, SPRR1A, SPRR1B, SPRR3, SPRR4, SPTLC3, SSTR2, STAT1, STAT4, STOML1, SUN1, SYNGAP1, TAP1, TAP2, TAPBP, TBC1D5, TBK1, TCF19, TGFβ, THRB, TK2, TLR1, TLR10, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TMEM140, TMEM185A, TMEM62, TNF, TNFR1, TNFR2, TNFRSF14, TNFRSF14-AS1, TNFSF10, TNFSF13B, TP53, TPTE2P5, TRA, TRADD, TRAF2, TRAF3, TRB, TRD, TRG, TRIM10, TRIM15, TRIM22, TRIM25, TRIM27, TRIM33, TRIM37, TRIM39, TRIM40, TRIT1, TRPM4, TSBP1, TSBP1-AS1, T TSEN15, UBB, UBE2K, UNG, USP8, VAMP5, VARS2, VEZT, VPS52, WARS, XAF1, XPOT, YY1AP1, ZC3HAV1, ZDHHC6, ZMYND11, ZNF248, ZNF512, ZNF610, and ZNRD1ASP.

18. The array of claim 16 or 17, wherein the plurality of oligonucleotide probes comprises at least one sequence selected from the group consisting of SEQ ID NOS:1–7,831.

19. The array of any one of claims 16 or 17, wherein the plurality of oligonucleotide probes comprises at least one sequence selected from the group consisting of SEQ ID NOS:42, 48, 49, 56, 60, 152, 153, 154, 155, 156, 160, 161, 170, 174, 175, 176, 192, 195, 196, 205, 206, 207, 208, 209, 210, 211, 217, 219, 220, 221, 222, 235, 255, 294, 295, 298, 299, 300, 310, 315, 322, 329, 330, 331, 337, 602, 607, 608, 668, 669, 677, 678, 738, 750, 751, 756, 757, 761, 762, 769, 770, 773, 776, 777, 779, 829, 830, 842, 843, 846, 847, 855, 856, 857, 858, 860, 864, 869, 870, 877, 882, 904, 905, 916, 922, 923, 924, 925, 933, 942, 943, 959, 964, 965, 966, 969, 981, 982, 999, 1000, 1002, 1003, 1004, 1005, 1035, 1036, 1046, 1047, 1048, 1049, 1062, 1063, 1090, 1095, 1096, 1097, 1122, 1123, 1138, 1145, 1146, 1155, 1156, 1158, 1165, 1173, 1174, 1180, 1181, 1185, 1210, 1211, 1216, 1217, 1219, 1220, 1225, 1237, 1238, 1247, 1248, 1249, 1250, 1254, 1255, 1256, 1259, 1260, 1263, 1270, 1271, 1296, 1297, 1308, 1309, 1312, 1314, 1318, 1319, 1326, 1328, 1329, 1342, 1348, 1405, 1406, 1413, 1414, 1415, 1416, 1433, 1434, 1443, 1444, 1465, 1470, 1476, 1485, 1486, 1487, 1508, 1509, 1510, 1514, 1612, 1613, 1620, 1627, 1638, 1639, 1664, 1665, 1666, 1669, 1670, 1676, 1677, 1684, 1685, 1701, 1712, 1719, 1720, 1721, 1722, 1726, 1727, 1731, 1738, 1740, 1747, 1748, 1852, 1853, 1854, 1939, 2072, 2073, 2075, 2088, 2090, 2171, 2193, 2194, 2434, 2435, 2604, 2676, 2678, 2680, 2681, 2756, 2914, 2915, 2919, 2920, 3180, 3243, 3774, 3775, 3994, 3995, 3996, 3998, 3999, 4000, 4020, 4021, 4030, 4031, 4046, 4103, 4171, 4179, 4184, 4187, 4188, 4225, 4236, 4251, 4253, 4257, 4258, 4259, 4262, 4263, 4272, 4276, 4277, 4278, 4292, 4293, 4313, 4314, 4316, 4317, 4318, 4328, 4329, 4330, 4343, 4344, 4345, 4357, 4358, 4376, 4377, 4384, 4389, 4390, 4402, 4408, 4409, 4410, 4411, 4414, 4415, 4416, 4418, 4419, 4421, 4422, 4426, 4427, 4430, 4439, 4453, 4454, 4456, 4457, 4458, 4479, 4487, 4488, 4491, 4492, 4493, 4494, 4500, 4501, 4518, 4519, 4525, 4526, 4539, 4540, 4555, 4562, 4563, 4564, 4584, 4585, 4586, 4589, 4594, 4595, 4596, 4597, 4615, 4617, 4618, 4619, 4620, 4621, 4622, 4627, 4628, 4629, 4630, 4631, 4632, 4657, 4658, 4661, 4662, 4671, 4673, 4689,

4690, 4691, 4697, 4698, 4716, 4717, 4726, 4727, 4728, 4729, 4731, 4747, 4768, 4773, 4774, 4778, 4779, 4780, 4781, 4782, 4783, 4784, 4785, 4968, 4969, 4976, 4977, 4987, 4993, 4994, 4995, 4999, 5005, 5006, 5020, 5025, 5026, 5027, 5035, 5049, 5050, 5055, 5056, 5158, 5164, 5171, 5172, 5173, 5188, 5189, 5190, 5191, 5192, 5193, 5204, 5206, 5208, 5209, 5210, 5211, 5212, 5213, 5214, 5217, 5219, 5220, 5225, 5232, 5233, 5234, 5235, 5238, 5239, 5240, 5241, 5294, 5295, 5296, 5313, 5316, 5327, 5370, 5375, 5376, 5377, 5378, 5379, 5385, 5507, 5508, 5509, 5510, 5511, 5512, 5513, 5514, 5515, 5516, 5517, 5561, 5572, 5573, 5574, 5577, 5578, 5579, 5585, 5586, 5592, 5645, 5646, 5649, 5650, 5656, 5657, 5667, 5672, 5681, 5684, 5695, 5696, 5697, 5698, 5699, 5700, 5701, 5702, 5710, 5711, 5720, 5725, 5728, 5729, 5730, 5743, 5744, 5745, 5748, 5749, 5759, 5760, 5761, 5765, 5766, 5768, 5769, 5772, 5780, 5781, 5782, 5802, 5803, 5804, 5807, 5808, 5809, 5813, 5814, 5816, 5817, 5828, 5829, 5833, 5910, 5914, 5917, 5937, 5941, 5942, 5944, 5945, 5948, 5949, 5963, 6018, 6019, 6023, 6031, 6032, 6033, 6039, 6040, 6043, 6045, 6109, 6110, 6111, 6112, 6113, 6116, 6127, 6128, 6133, 6134, 6137, 6225, 6236, 6242, 6449, 6450, 6451, 6452, 6453, 6454, 6455, 6457, 6458, 6461, 6462, 6463, 6466, 6469, 6470, 6471, 6480, 6481, 6545, 6546, 6547, 6613, 6684, 6685, 6692, 6693, 6694, 6695, 6710, 6711, 6731, 6732, 6741, 6787, 6788, 6805, 6806, 6807, 6828, 6829, 6830, 6831, 6832, 6835, 6836, 6846, 6847, 6848, 6849, 6850, 6862, 6868, 6869, 6870, 6871, 6878, 6879, 6897, 6898, 6899, 6900, 6908, 6909, 6914, 6938, 6939, 6949, 6950, 6951, 6952, 6959, 6960, 6971, 6972, 6973, 6974, 6976, 6979, 7110, 7111, 7112, 7113, 7117, 7118, 7120, 7122, 7124, 7135, 7184, 7185, 7401, 7402, 7404, 7408, 7441, 7442, 7482, 7490, 7491, 7497, 7500, 7503, 7504, 7513, 7514, 7515, 7525, 7526, 7621, 7622, 7623, 7624, 7625, 7626, 7627, 7638, 7649, 7650, 7651, 7652, 7665, 7694, 7704, 7705, 7708, 7716, 7717, 7718, 7726, 7727, 7728, 7729, 7738, 7739, 7740, 7741, 7742, 7743, 7744, 7746, 7747, 7749, 7757, 7770, 7771, 7774, 7775, 7777, 7783, 7788, 7789, 7790, 7791, 7798, 7799, 7803, 7804, 7815, 7816, 7823, 7824, and 7825.

20. The array of claim 16 or 17, wherein the methylation signature comprises detecting a methylation status of at least one gene selected from the group consisting of: ABCF1, ABCF1, AIF1, APOBEC3G, APOL6, B2M, BCL2L14, BRD2,

C2, C6orf136, C6orf15, C7, CALR, CD27-AS1, CD4, CD40, CFB, CFH, CHTOP, CIITA, CSNK2B, CUTA, CYP21A2, DDR1, DEXI, EGFL8, EHMT2, GPANK1, GPX5, GTF2H4, HCG17, HCG18, HCG20, HCG25, HCG27, HCG4, HCG4B, HLA-A, HLA-DPA1, HLA-DPB2, HLA-DQA2, HLA-E, HLA-F, HLA-F-AS1, HLA-G, HLA-V, ICAM1, IFI16, IFI35, IFI44, IFI44L, IFITM1, IVL, KIFC1, KPRP, LCE1D, LCE1E, LCE2C, LELP1, LINC00302, LOC100507547, LOC101929006, LY6G6F-LY6G6D, MICA-AS1, MICB, MICB-DT, MSH5, MX1, NA, NBPF18P, NFKB1, NFKB2, NLRC5, NLRP11, NLRP3, NLRP5, NLRX1, OR2H1, OSMR, PDIA3, PHF1, PML, PPP1R11, PPT2, PRR9, PRRC2A, PSMB8-AS1, PSMB9, PSORS1C1, REC8, REL, RELB, RING1, RNF5, RPS18, RTP4, RXRB, S100A13, SCNN1A, SERPING1, SKIV2L, SLC44A4, SNORD32B, SPRR4, SPTLC3, SYNGAP1, TAP1, TBK1, TCF19, TLR3, TNF, TNFRSF14, TNFSF13B, TRAF2, TRAF3, TRIM15, TRIM27, TRIM39, TSBP1-AS1, TUBB, VARS2, VPS52, XAF1, and ZNRD1ASP.