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Human Alpha-L-iduronidase (huIDUA)

Signal		Alpha-L-iduronidase		
10	20	30	40	50
MRPLRPRAAL	LALLASLLAA	PPVAPAEAPH	LVHVDAARAL	WPLRRFWRST
60	70	80	90	100
GFCPPLPHSQ	ADQYVLSWDQ	QLNLAYVGAV	PHRGIKQVRT	HWLLELVTR
110	120	130	140	150
GSTGRGLSYN	FTHLDGYL DL	LRENQLLP GF	ELMGSASGHF	TDFEDKQQVF
160	170	180	190	200
EWKDLVSSLA	RRYIGRYGLA	HVSKWNFETW	NEPDHHDFDN	VSMTMQGFLN
210	220	230	240	250
YYDACSEGLR	AASPALRLGG	PGDSFHTPPR	SPLSWGLLRH	CHDGTNFFTG
260	270	280	290	300
EAGVRLDYIS	LHRKGARSSI	SILEQEKVVA	QQIRQLFPKF	ADTPIYNDEA
310	320	330	340	350
DPLVGWSLPQ	PWRADVTYAA	MVVKVIAQHQ	NLLLANNTTSA	FPYALLSNDN
<i>N-372 req'd for binding & activity</i>				
360	370	380	390	400
AFLSYHPPHF	AQRTLTARFQ	VNNTRPPHVQ	LLRKPVL TAM	GLLALLDEEQ
410	420	430	440	450
LWAEVSQAGT	VLDSNHTVGV	LASAH RPQGP	ADAWRAAVLI	YASDDTRAHP
460	470	480	490	500
NRSVAVT LRL	RGVPPGPGLV	YVTRYLDNGL	CSPDGEWRRL	GRPVFPTAEQ
Disulfide				
510	520	530	540	550
FRRMRAAEDP	VAAAPRPLPA	GGRLTLRPAL	RLPSLLL VHV	CARPEKPPGQ
Bond				
560	570	580	590	600
VTRLRALPLT	QGQLVLVWSD	EHVGSKCLWT	YEIQFSQDGK	AYTPVSRKPS
610	620	630	640	650
TFNLFVFSPD	TGAVSGSYRV	RALDYWARPG	PFSDPVPYLE	VPVPRGPPSP

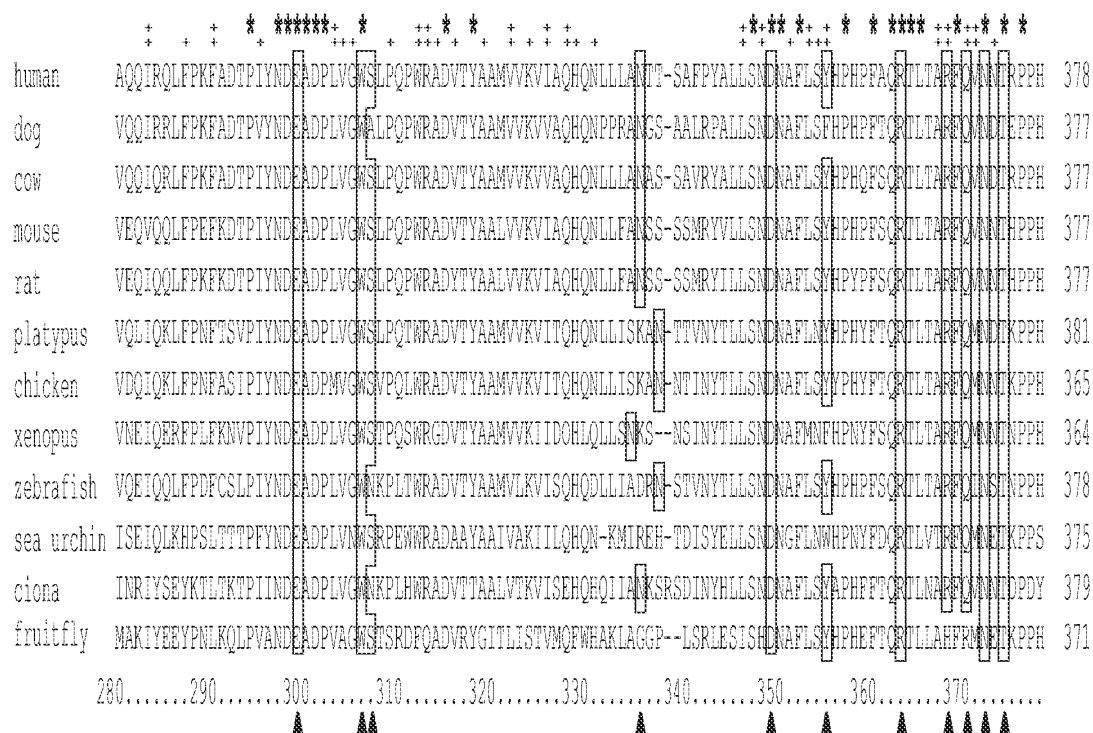
GNP

N = N-linked glycosylation site (GlcNac...)Y = Y-sulfation siteC = Disulfide Bond

FIG. 1

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human	P---	653
dog	CERC	655
cow	----	643
mouse	----	643
rat	----	643
platypus	----	647
chicken	----	630
xenopus	----	630

FIG. 2 continued

Mutation	RMSD (Å)	Number of affected atoms		ASA (Å ²)	Phenotype	Reference	Clinical form	Mut
		Main chain	Side chain					
G51D	0.114	256	293	0	Severe	[22]	Hurler	W402X
A75T	0.037	35	36	1.9	Severe	[23]	Hurler	Not Available
T103P	0.017	6	8	57	Severe	[24]	Hurler	Not Available
A160D	0.069	65	79	1.6	Severe	[25]	Severe	A160D
F177S	0.017	4	8	4.8	Severe	[26]	Hurler	F177S
E178K	0.124	244	338	0.3	Severe	[25]	Severe	c.134-145del2
T179R	0.137	316	356	0.4	Severe	[27]	Hurler	T179R
E182K	0.261	809	991	27.4	Severe	[28]	Severe	W402X
E182D	0.017	0	4	27.4	Severe	[27]	Hurler	C53X
P183R	0.184	380	410	0.1	Severe	[25]	Severe	A327P
G208V	0.094	129	143	0	Severe	[29]	Hurler	G208V
G208D	0.068	66	89	0	Severe	[30]	Hurler	Q70X
L218P	0.040	28	38	0.5	Severe	[22]	Hurler	W402X
L237R	0.096	148	180	0.1	Severe	[27]	Hurler	c.973.4GNA
L238R	0.068	109	105	0.5	Severe	[27]	Hurler	c.883.dupC
I270S	0.009	0	5	44.7	Severe	[31]	Hurler	R628X
D315Y	0.075	120	147	8.6	Severe	[30]	Hurler	Q70X
A327P	0.031	15	12	0	Severe	[22]	Hurler	W402X
D349N	0.038	32	57	7.4	Severe	[32]	Severe	Q70X
R363C	0.074	118	144	14.5	Severe	[33]	Hurler/Scheie ^b	F602I
T366P	0.034	22	29	0.3	Severe	[34]	Hurler	T366P
P385R	0.125	246	239	1	Severe	[24]	Hurler	A327P
T388R	0.155	343	406	2.9	Severe	[35]	Hurler	W402X
R489P	0.047	28	37	164.5	Severe	[22]	Hurler	W402X
P533L	0.177	341	341	1.3	Severe	[36]	Severe	Q70X
V620F	0.078	150	153	0.7	Severe	[37]	Hurler	V620F
R628P	0.107	119	134	58	Severe	[38]	Severe	A327P
P533R	0.140	300	279	1.3	Severe-intermediate	[39,24]	Hurler/Hurler/Scheie	P533R
H33P	0.059	83	96	73.9	Intermediate	[27]	Hurler/Scheie	c.1402+2TNG
A75P	0.039	32	28	1.9	Intermediate	[36]	Intermediate	Q70X
H82P	0.051	50	70	70.7	Intermediate	[40]	Intermediate	W402X
L238Q	0.015	0	10	0.5	Intermediate	[33]	Hurler/Scheie	W402X
G265R	0.144	238	271	1.7	Intermediate	[33]	Hurler/Scheie	W402X
L346R	0.066	101	147	2.9	Intermediate	[41]	Hurler/Scheie	L346R
R363H	0.029	20	48	14.5	Intermediate	[42]	Hurler/Scheie	c.1190-1GNA
T364M	0.069	76	91	0	Intermediate	[43]	Hurler/Scheie	T364M
A436P	0.052	63	39	3.2	Intermediate	[24]	Hurler/Scheie	A436P
P496L	0.055	52	53	0.1	Intermediate	[44]	Hurler/Scheie	A75T
L535F	0.055	48	69	0	Intermediate	[24]	Hurler/Scheie	W402X
F602I	0.006	0	1	2.6	Intermediate	[33]	Hurler/Scheie ^b	R363C
R619G	0.010	3	8	60.5	Intermediate	[45]	Hurler/Scheie	R619G
L490P	0.082	40	67	24.1	Attenuated-intermediate	[44,24]	Hurler/Scheie,Scheie	L490P
Y76C	0.018	14	12	0	Attenuated	[24]	Scheie	Q70X
R89Q	0.048	79	124	0	Attenuated	[32]	Mild	W402X
D203N	0.024	14	16	0	Attenuated	[46]	Scheie	Q60X
C205Y	0.000	1	0	0.8	Attenuated	[29]	Scheie	Y167X
H240R	0.051	59	73	10.5	Attenuated	[29]	Scheie	W402X
E276K	0.143	449	558	3.5	Attenuated	[47,48]	Scheie	E276K
A319V	0.082	129	109	0	Attenuated	[29]	Scheie	A319V
N348K	0.095	175	213	11.6	Attenuated	[24]	Scheie	c.1727+5GNC

FIG. 3

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N350I	0.038	40	34	3.8	Attenuated	[38]	Slow progression	c.134-145del12
T374N	0.023	17	18	43	Attenuated	[49]	Attenuated	c.252insC
Q380R	0.114	179	199	0	Attenuated	[32]	Mild	R628P
R383H	0.042	34	61	0.1	Attenuated	[50]	Attenuated	R383H
R492P	0.051	13	34	153.4	Attenuated	[44]	Scheie	Q70X
L578Q	0.007	1	4	0.7	Attenuated	[51]	Scheie	P533R
S633L	0.050	51	69	7.9	Attenuated	[29]	Scheie	R633L

The mutations localized in the Ig-like domain and adjacent region are shown in bold/shaded.

^a Description of the clinical form of the patients is according to the original papers.

^b An expression study revealed that F602I-IDUA exhibited residual enzyme activity, but not in the case of R363C-IDUA[34].

FIG. 3 continued

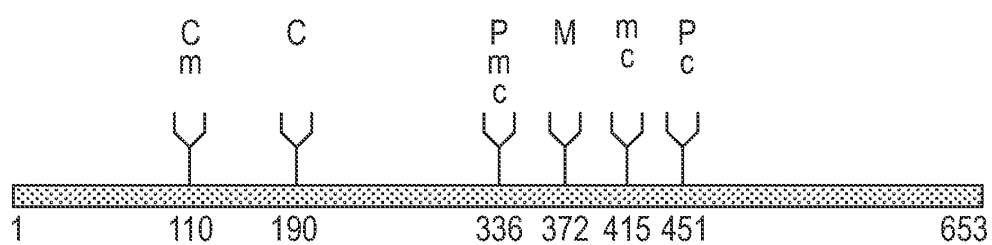


FIG. 4

VP1₁-736→

AAV1 MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
 AAV2 MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
 AAV3-3 MAADGYLPDWLEDNLSEGIREWWALKPGVPQPKANQQHQDNRRGLVLPGYKYLGPNGLD 60
 AAV4-4 -MTDGYLPDWLEDNLSEGIREWWALQPGAPKPKANQQHQDNARGLVLPGYKYLGPNGLD 59
 AV5 MSFVDHPPDWLEE-VGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPNGLD 59
 AAV6 MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
 AAV7 MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
 AAV8 MAADGYLPDWLEDNLSEGIREWWALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
 hu31 MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPKPAERHKDDSRGLVLPGYKYLGPNGLD 60
 hu32 MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPKPAERHKDDSRGLVLPGYKYLGPNGLD 60
 AAV9 MAADGYLPDWLEDNLSEGIREWWDLKPGAPQPKANQQHQDNARGLVLPGYKYLGPNGLD 60
 SUBS -STVDHP-----ETVG--V-QFLK-QA-P-K--PAERKK-DG-----N----F-----
 MF L D E V P QS
 G Q R

AAV1 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFFQERLQEDTSFGGNLGRAVFQ 120
 AAV2 KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEEFQERLKEDTSFGGNLGRAVFQ 120
 AAV3-3 KGEPVNEADAAALEHDKAYDQQLKAGDNPYLKYNHADAEEFQERLQEDTSFGGNLGRAVFQ 120
 AAV4-4 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEEFQERLQEDTSFGGNLGRAVFQ 120
 AV5 RGEFVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEEFQERLQEDTSFGGNLGRAVFQ 119
 AAV6 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFFQERLQEDTSFGGNLGRAVFQ 120
 AAV7 KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFFQERLQEDTSFGGNLGRAVFQ 120
 AAV8 KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFFQERLQEDTSFGGNLGRAVFQ 120
 hu31 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEEFQERLKEDTSFGGNLGRAVFQ 120
 hu32 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEEFQERLKEDTSFGGNLGRAVFQ 120
 AAV9 KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEEFQERLKEDTSFGGNLGRAVFQ 120
 SUBS R-----E--EV-R--IS-NE--DS-----R-----QK-QD-----K-----
 R R E AG
 Q

FIG. 5

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VP2₁₃₈ → **---HVR1---**

AAV1 AKKRVLEPLGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGKTGQQPAKKRLNFGQTGDS 179

AAV2 AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPV-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179

AAV3-3 AKKRILEPLGLVEEAAKTAPGKKGAVDQSPQ-EPDSSSGVGKSGKQPARKRLNFGQTGDS 179

AAV4-4 AKKRVLEPLGLVEQAGETAPGKKRPLIESPQ-QPDSSTGIGKKGKQPAKKKLVEDETGA 178

AV5 AKKRVLEPFGLVEEGAKTAPTGKRIDDHFP-----KRKKARTEEDSKPSTSSDA 168

AAV6 AKKRVLEPFGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGKTGQQPAKKRLNFGQTGDS 179

AAV7 AKKRVLEPLGLVEEGAKTAPAKKRPVEPSPQSPDSSTGIGKKGQQPARKRLNFGQTGDS 180

AAV8 AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQSPDSSTGIGKKGQQPAKKKLNFGQTGDS 180

hu31 AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGSQPAKKKLNFGQTGDT 179

hu32 AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGSQPAKKKLNFGQTGDT 179

AAV9 AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGAQPARKRLNFGQTGDT 179

SUBS ----V---F---QGGE---TG-GIDDFH-V-S----S-T--KKQARTREKSVPEDETGA

I PV A ALIP Q T V T K E D K STSS S

E A S

R A

---HVR2--- VP3₂₀₃ →

AAV1 ESVPD-PQPLGEPPATPAAVGPTTMASSGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 238

AAV2 DSVPD-PQPLGQPPAAPSGLGNTMTATGSGAPMADNNEGADGVGNSSGNWHCDSTWVGDR 238

AAV3-3 ESVPD-PQPLGEPPAAPSTLGSNTMASGGGAPMADNNEGADGVGNSSGNWHCDSQWLGD 238

AAV4-4 GDGP-----PEGSTSGAMS---DDSEMRAAAGGAAVEGGQGADGVGNASGDWHCDSTWSEGH 238

AV5 EAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQADGVGNASGDWHCDSTWVGDR 238

AAV6 ESVPD-PQPLGEPPATPAAVGPTTMASSGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 238

AAV7 ESVPD-PQPLGEPPAAPSSVSGSTVAAGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 238

AAV8 ESVPD-PQPLGEPPAAPSGVGPNMTAAAGGGAPMADNNEGADGVGSSGNWHCDSTWLGDR 238

hu31 ESVPD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGSSGNWHCDSQWLGD 238

hu32 ESVPD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGSSGNWHCDSQWLGD 238

AAV9 ESVPD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGSSGNWHCDSQWLGD 238

SUBS GDG-S-S-QLQQTSGTMSLDPNEVRAAA-GAMGEGGQ-----NA--D-----T-MEGH

DA E S AQPATA AG ST S LV S

I DT A

TD

S

FIG. 5 continued

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HVR3
| |

AAV1 VITTSTRTWALPTYNNHLYKQIS--SASTGASNDNHYFGYSTPWGYFDENRFHCHFSPRDW 297
 AAV2 VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYFDENRFHCHFSPRDW 296
 AAV3-3 VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYFDENRFHCHFSPRDW 296
 AAV4-4 VTTTSTRTWVLPPTYNNHLYKRLG-----ESLQSNITYNGYSTPWGYFDENRFHCHFSPRDW 287
 AV5 VVTKSTRTWVLP SYNNHQYREIKS-GSVDGSNANAYFGYSTPWGYFDENRFHSHWSPRDW 287
 AAV6 VITTSTRTWALPTYNNHLYKQISSAST-GASNDNHYFGYSTPWGYFDENRFHCHFSPRDW 297
 AAV7 VITTSTRTWALPTYNNHLYKQISS-ETAGATNDNTYFGYSTPWGYFDENRFHCHFSPRDW 298
 AAV8 VITTSTRTWALPTYNNHLYKQISNGTSGGATNDNTYFGYSTPWGYFDENRFHCHFSPRDW 299
 hu31 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDENRFHCHFSPRDW 298
 hu32 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDENRFHCHFSPRDW 298
 AAV9 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDENRFHCHFSPRDW 298
 SUBS -T-K-----V-S-----Q-RRLGSGSQSDATQA-T-----S-W-----
 V E K AATTEGL S H
 G V
 E A

AAV1 QRLINNNWGFPRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDSSEYQLPYVLGS 357
 AAV2 QRLINNNWGFPRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFSDEYQLPYVLGS 356
 AAV3-3 QRLINNNWGFPRPKLSFKLFNIQVRGVTQNDGTTTIANNLTSTVQVFTDSSEYQLPYVLGS 356
 AAV4-4 QRLINNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQIFADSSYELPYVMDA 347
 AV5 QRLINNYWGFPRPSLRVKIFNIQVKEVTVDQDSTTTIANNLTSTVQVFTDDDYQLPYVVG N 347
 AAV6 QRLINNYWGFPRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDSSEYQLPYVLGS 357
 AAV7 QRLINNNWGFPRPKLRFKLFNIQVKEVTTNDGVTTIANNLTSTIQVFSDSSEYQLPYVLGS 358
 AAV8 QRLINNNWGFPRPKLSFKLFNIQVKEVTQNECTKTIANNLTSTIQVFTDSSEYQLPYVLGS 359
 hu31 QRLINNNWGFPRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS 358
 hu32 QRLINNNWGFPRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS 358
 AAV9 QRLINNNWGFPRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS 358
 SUBS -----M--RAMRV-I-----VQDSTT-----I-I-S-DE-E-----MDA
 K S QSE E A S
 S

FIG. 5 continued

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HVR4

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AAV1  AHQGC LPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV2  AHQGC LPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
AAV3-3 AHQGC LPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
AAV4-4 GQEGSLPPFPNDVFMVPQYGYCGLVTGNTSQQQTDRNAFYCLEYFPSQMLRTGNNFEITY 407
AV5    GTEGCLPAFPQVFTLPQYGYATLNRD-NTENPTERRSSFFCLEYFPSKMLRTGNNFEITY 406
AAV6  AHQGC LPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV7  AHQGC LPPFPADVFMIPQYGYLTLNNG---SQSVGRSSFYCLEYFPSQMLRTGNNFEFSY 415
AAV8  AHQGC LPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFTY 416
hu31  AHEGCLPPFPADVFMIPQYGYLTLNDG---GQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
hu32  AHEGCLPPFPADVFMIPQYGYLTLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
AAV9  AHEGCLPPFPADVFMIPQYGYLTLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
SUBS  GQQ-S--A--PQ--TL-----CG-VND---GNPTD-NA-F-----EIT-
      T      N   V   A   T   Q Q E      T
                R   E S

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HVR5

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AAV1  TFEEVPPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQ-NQSGSAQNKDLLFSRGSPAGMSV 473
AAV2  TFEDVPPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTN-TPSGTTTQSRLLQFSQAGASDIRD 472
AAV3-3 TFEDVPPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQGTTS GTTNQSRLLFSQAGPQSM SL 473
AAV4-4 SFEKVPFHSSMYAHSQSLDRLMNPLIDQYLWGLQSTTTGTTLNAGTATTNFTKL RPTNFSN 467
AV5    NFEEVPPFHSSFAPSQNLFKLANPLVDQYLYRFVSTN-----NTGGVQFNKNLAGRYAN 459
AAV6  TFEDVPPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQ-NQSGSAQNKDLLFSRGSPAGMSV 473
AAV7  SFEDVPPFHSSYAHSQSLDRLMNPLIDQYLYYLARTQSNPGGTAGNRELQFYQGGPSTMAE 475
AAV8  TFEDVPPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQT-TGGTANTQTLGFSQGGPNTMAN 475
hu31  EFENVPPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTINGSG--QNQOTLKFSVAGPSNMAV 473
hu32  EFENVPPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTINGSG--QNQOTLKFSVAGPSNMAV 473
AAV9  EFENVPPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTINGSG--QNQOTLKFSVAGPSNMAV 473
SUBS  T--D-----MF-----A--V----WGFNR-QTNTS--AGTKRTQ-TQGSAA TFSN
      S E                      QS NSTPT  TQNSDVN NKNL QGYRD
      N K                      V  TG Q    T AE L YRLR TRI L
                        A                RG G      GS E
                                ND

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FIG. 5 continued

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				[HVR6]		[HVR7]		[HVR8]	
AAV1	QPKNWLP	GP	CYRQ	RVSKTKTDN	-----	NNSNFTWTG	ASKYNLNGRES	IINPGTAMASHK	528
AAV2	QSRNWLP	GP	CYRQ	RVSKTSADN	-----	NNSEYSWTG	ATKYHLNGRDSL	VNPGPAMASHK	527
AAV3-3	QARNWLP	GP	CYRQ	RLSKTANDN	-----	NNSNFPWTA	ASKYHLNGRDSL	VNPGPAMASHK	528
AAV4-4	FKKNWLP	GP	SIKQQG	FSKTANQNYKIPATG	SDSLIKYETHSTLDGRWSALT	PGPPMATAG			527
AV5	TYKNWLP	GP	MGRTQ	GWNLGSGVN	-----	RASVS	AFATTNRMELEG	ASYQVPPQNGMTNN	514
AAV6	QPKNWLP	GP	CYRQ	RVSKTKTDN	-----	NNSNFTWTG	ASKYNLNGRES	IINPGTAMASHK	528
AAV7	QAKNWLP	GP	CFRQ	RVSKTLDQN	-----	NNSNFAWTG	ATKYHLNGRNSL	VNPGVAMATHK	530
AAV8	QAKNWLP	GP	CYRQ	RVSTTTGQN	-----	NNSNFAWTG	ATKYHLNGRNSL	ANPGIAMATHK	530
hu31	QGRNYIP	GPSYRQ	RVSTTTVTQN	-----	NNSEFAWPG	ASSWALNGRNSL	MNPGPAMASHK		528
hu32	QGRNYIP	GPSYRQ	RVSTTTVTQN	-----	NNSEFAWPG	ASSWALNGRNSL	MNPGPAMASHK		528
AAV9	QGRNYIP	GPSYRQ	RVSTTTVTQN	-----	NNSEFAWPG	ASSWALNGRNSL	MNPGPAMASHK		528
SUBS	FAK-WL---	CIKT-GWNLGSGV	-----	TG-DSLIK	YETHST-D-ASYQVP-QTPGMTAG				
	TP	F	MG	F K AND		RA	NYTFATTNRME	E D ALT VN NN	
	K		F	L KA		V P	TAG KYN	W II I	
	Y			LD		S	H	E A	
	S			T					

				[----- HVR8 -----]		[---]
AAV1	DDEDKFFP	MSGVMIFG	KESA--	GASNTALD-NVMITDEEEIKATNPVATER	REFGTAVAVNFQ	585
AAV2	DDEEKFFP	QSGVLIFG	KQGS--	EKTNV DIE-KVMITDEEEIRTTNPVATE	QYGSVSTNLQ	584
AAV3-3	DDEEKFFP	MHCNLI	FGKEGT--	TASNAELD-NVMITDEEEIRTTNPVATE	QYGTVANNLQ	585
AAV4-4	PADSKFS-	NSQLIFAG	PKQN--	GNTATVPG-TLIFTSEEELAATNATD	TDMWGNLPGGDQ	583
AV5	LQGSNTY	ALENTMI	FNSQ	PANPGTTATYLEGNMLITSE	SETQPVNRVAYNVGQMATNNQ	583
AAV6	DDKDKFFP	MSGVMIFG	KESA--	GASNTALD-NVMITDEEEIKATNPVATER	REFGTAVAVNLQ	585
AAV7	DDEDKFFP	SSGVLIFG	KTGA--	TN-KTTLE-NVLMTNEEEIRPTNPVATE	EYGIVSSNLQ	586
AAV8	DDEERFFP	SNGLIFG	KQNA--	ARDNADYS-DVMLTSEEEIKTTNPVATE	EYGIVADNLQ	587
hu31	EGEDRFFP	PLSGSLIFG	KQGT--	GRDNVDAD-KVMITNEEEIKTTNPVATESY	GQVATNHQ	585
hu32	EGEDRFFP	PLSGSLIFG	KQGT--	GRDNVDAD-KVMITNEEEIKTTNPVATESY	GQVATNHQ	585
AAV9	EGEDRFFP	PLSGSLIFG	KQGT--	GRDNVDAD-KVMITNEEEIKTTNPVATESY	GQVATNHQ	585
SUBS	LQGSNTY	AMENTMFAN	PKQN--	TNTATVPG-TLIF-S-S-TQPV-ATDYDMW-NLPGGD-		
	PADEK S	QHQLI	SESA	EASKAALE-NMLM D	RA R NVF TMSN L	
	DDK	NN V	TPS	AK KTY L	A QG I V N	
		S I	N	EI	E S S F	
		N		Y	R D	

FIG. 5 continued

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[---HVR10---]
 AAV1 SSSTDPATGDVHAMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKNPPP 645
 AAV2 RGNRQAATADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 644
 AAV3-3 SSNTAPTGTVNHQALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
 AAV4-4 SNSNLPTVDRLTALGAVPGMVWQNRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKHPPP 643
 AV5 SSTTAPATGTYNLQEI VPGSVWMERDVYLQGPIWAKIPETGAHFHPSPLMGGFGLKHPPP 634
 AAV6 SSSTDPATGDVHVMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
 AAV7 AANTAAQTQVNNQALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPP 646
 AAV8 QQNTAPQIGTVNSQALPGMVWQNRDVYLQGPIWAKIPGTDGNFHPSPLMGGFGLKHPPP 647
 hu31 SAQAQAQTGWVQNGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
 hu32 SAQAQAQTGWVQNGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
 AAV9 SAQAQAQTGWVQNGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
 SUBS RNSNLPTVDRLTALEAV--S--ME--I-----E-GAH-----AI----L-N---
 ASNTA AIADYHTM V N
 QGTRD QT NH
 Q V L
 V
 S

[---HVR11---]
 AAV1 QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENS KRWNPEVQYTSNY 705
 AAV2 QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 704
 AAV3-3 QIMIKNTPVPANPPTTFSPAKFASFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 705
 AAV4-4 QIFIKNTPVPANPATTFSSSTPVNSFITQYSTGQVSVQIDWEIQERSKRWNPEVQFISNY 703
 AV5 MMLIKNTPVPGNI-TSFSQVPSFITQYSTGQVTVEMEWELKKENS KRWNPEIQYTNNY 693
 AAV6 QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENS KRWNPEVQYTSNY 705
 AAV7 QILIKNTPVPANPPEVFTPAKFASFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNF 706
 AAV8 QILIKNTPVPADPPTTFNQSKLNSFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 707
 hu31 QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 705
 hu32 QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 705
 AAV9 QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 705
 SUBS MMM-----G-IAAE-SDVPVS-----QMD--IK--R-----V-----
 F SET TAA FA
 S PT
 V QS
 S

FIG. 5 continued

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      [----HVR12----]
AAV1  AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO. 16)
AAV2  NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 735 (SEQ ID NO. 17)
AAV3-3 NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 18)
AAV4-4 GQQNSLLWAPDAAGKYTEPRAIGTRYLTHHL 734 (SEQ ID NO. 19)
AV5    NDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL 724 (SEQ ID NO. 20)
AAV6  AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO. 21)
AAV7  EKQTGVDFAVDSQGVYSEPRPIGTRYLTRNL 737 (SEQ ID NO. 22)
AAV8  YKSTSVDFAVNTEGVYSEPRPIGTRYLTRNL 738 (SEQ ID NO. 23)
hu31   YKSNNVEFAVSTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 24)
hu32   YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 25)
AAV9   YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 26)
SUBS   GQQVSLWTPDAA-K-RTT-A-----HP-
      NDPQF D   SSN E T           H
      A  TG      NQ L
      E  A       T

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FIG. 5 continued

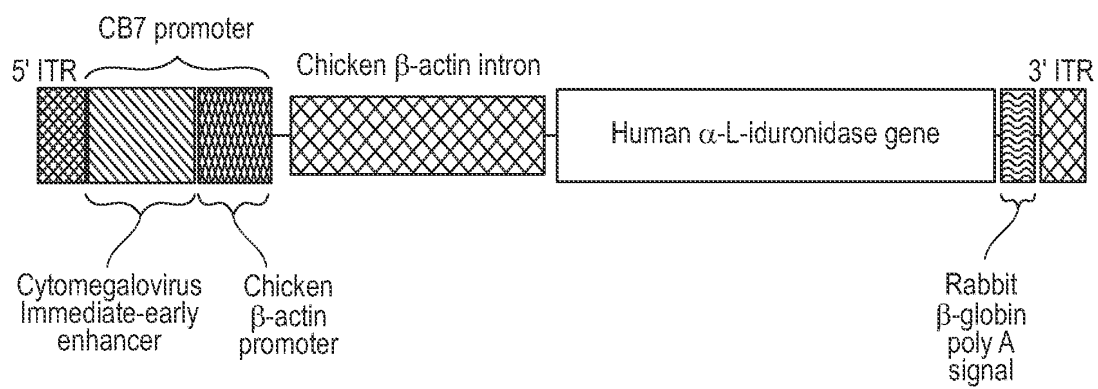


FIG. 6