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Amino Acid Sequence of Human IDS

Iduronate-2-sulfatase (IDS)

→Signal			→Mature 42kD		
10	20	30	40	50	
MPPPR	TGRGL	LWLGLVLSSV	CVALGSETQA	STTDALNVL	LIIVDDLRRPS
60	70	80	90	100	
LGCYGD	KLVR	SPNIDQLASH	SLLFQNAFAQ	QAVCAPSRVS	FLTGRRPDIT
110	120	130	140	150	
RLYDFNS	YWR	VHAG	FSTIP	QYFKENGYVT	MSVGKVFHPG
160	170	180	190	200	
YSWSFP	PPYHE	SSEKYENTTKT	CRGPD	GELHA	NLLCPVDVLD
210	220	230	240	250	
STEQAI	QLLE	KMKTSASPF	F	LAVGYHKPHI	PFRYPKEFQK
260	270	280	290	300	
PDPEVP	DGLP	EVAYNPWMDI	RQREDVQAL	ISVPYGP	PIPV
310	320	330	340	350	
FASVSY	LDTQ	VGRLLSALDD	LQLA	STIIA	FTSDHGWALG
360	370	380	390	400	
FDVATH	VPLI	FYVPGRTASL	PEAGEKLFY	LDPFDSASQL	MEPGRQSM
410	420	430	440	450	
VELVSL	FPTL	AGLAGLQVPP	RCFVPSFHVE	LCREGKNLLK	HFRFRDLEED
→Mature 14kD					
460	470	480	490	500	
PYLFGN	PREL	IAYSQYPRFS	DIPQWNSDKP	SLKDIKIMGY	SIRTIDYRYT
510	520	530	540	550	
VWVGNE	PDEF	LA	FSDIHAG	ELYFVDS	DPL
			QDHNMY	PSQ	GGDLFQLLMP

Italics = signal sequence (MPPPR TGRGL LWLGLVLSSV CVALG)

■ = N-linked glycosylation sites (GlcNac...)

Boxed = Y-sulfation site (PSSEKYENTTKTCRGPD)

Underscore = amino-terminal sequence of 42kD and 14 kD peptides (Sleat 2005)

C⁸⁴ = formylglycine modificationN²⁸⁰ = M-6-P residue(s)**FIG. 1**

CLUSTAL O(1.2.4) multiple sequence alignment of hIDS to orhologs

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SP|P22304|IDS_HUMAN          MPPPRTRGRGLLWLGVLSSVCVALGSETQANSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|K6ZGI9|K6ZGI9_PANTR      MPPPRTRGRGLPWLGLVLSSVCVALGSETQANSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|K7BKV4|K7BKV4_PANTR      MPPPRTRGRGLPWLGLVLSSVCVALGSETQANSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|H9FTX2|H9FTX2_MACMU      MPTPGSGRGFLWLGLVLSSVCVALGCETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
TR|F7EJG2|F7EJG2_CALJA      MPPPRTRSRCLLLLGLVLGSVCVTLSQAQASSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|U3DTL8|U3DTL8_CALJA      MPPPRPSRCLLLLGLVLGSVCVTLSQAQASSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|G7NRX7|G7NRX7_MACMU      MPTPGSGRGFLWLGLVLSSVCVALGCETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
TR|G7Q1V9|G7Q1V9_MACFA      MPTPGSGRGFLWLGLVLSSVCVALGCETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
TR|H2PX10|H2PX10_PONAB      MPPPRTRGRGLLWLGVLSSVCVALGSETQADSTTDGLNVLLIIIVDDLRLPSLGCYGDKLVR 60
TR|A0A0D9R4D1|A0A0D9R4D1_CHLSB MPTPGSGRGFLWLGLVLSSVCVALGSETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
TR|G1RST8|G1RST8_NOMLE      MSPPRTRQGGLLWLGVLSSVCVAXVTSKPPPSFVDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
UPI0000D9F625               MPTPGSGRGFLWLGLVLSSVCVALGCETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
UPI000274358B               MPPPRTRGRGLLWLGVLSSVCVALGSETQANSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
UPI00027F6FC5               MPTPGSGRGFLWLGLVLSSVCVALGCEMQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
UPI00027FAE03               MPPPRTRGLCLLLLGLVLGSVCVTLSQAQANSTTDALNVLLIIIVDDLRLPSLGCYGDKLVR 60
UPI0003ABBF28               MPTPGSGRGFLWLGLVLSSVCVALGCETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
UPI000533297F               MPTPASGRGFLWLGLVLSSVCVALGSETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
UPI0005F40BD2               MPTPASGRGFLWLGLVLRVVCVALGSETQANSTTDALNILLIIIVDDLRLPSLGCYGDKLVR 60
*   *   .   :   **:***   ***:   .   :   *   .*.***:*****

SP|P22304|IDS_HUMAN          SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|K6ZGI9|K6ZGI9_PANTR      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|K7BKV4|K7BKV4_PANTR      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|H9FTX2|H9FTX2_MACMU      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|F7EJG2|F7EJG2_CALJA      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|U3DTL8|U3DTL8_CALJA      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|G7NRX7|G7NRX7_MACMU      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|G7Q1V9|G7Q1V9_MACFA      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|H2PX10|H2PX10_PONAB      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|A0A0D9R4D1|A0A0D9R4D1_CHLSB SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
TR|G1RST8|G1RST8_NOMLE      SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI0000D9F625               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI000274358B               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI00027F6FC5               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI00027FAE03               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI0003ABBF28               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI000533297F               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
UPI0005F40BD2               SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTRTRYDFNSYWRVHAGNFSTIP 120
*****.***:***:*****   ***:*****

SP|P22304|IDS_HUMAN          QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|K6ZGI9|K6ZGI9_PANTR      QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|K7BKV4|K7BKV4_PANTR      QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|H9FTX2|H9FTX2_MACMU      QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|F7EJG2|F7EJG2_CALJA      QYFKDNGYVTMSVGKVFHFGPISSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|U3DTL8|U3DTL8_CALJA      QYFKDNGYVTMSVGKVFHFGPISSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|G7NRX7|G7NRX7_MACMU      QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|G7Q1V9|G7Q1V9_MACFA      QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|H2PX10|H2PX10_PONAB      QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|A0A0D9R4D1|A0A0D9R4D1_CHLSB QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
TR|G1RST8|G1RST8_NOMLE      QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSXXXXXXKTCRGPDGELHA 180
UPI0000D9F625               QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI000274358B               QYFKENGYVTMSVGKVFHFGPISSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI00027F6FC5               QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI00027FAE03               QYFKDNGYVTMSVGKVFHFGPISSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI0003ABBF28               QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI000533297F               QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
UPI0005F40BD2               QYFKENGYVTMSVGKVFHFGPITSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA 180
*****.*****.***:*****.*****

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FIG. 2

SP P22304 IDS_HUMAN	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLI	360
TR K6ZGI9 K6ZGI9_PANTR	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR K7BKV4 K7BKV4_PANTR	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR H9FTX2 H9FTX2_MACMU	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR F7EJG2 F7EJG2_CALJA	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATRVPLM	360
TR U3DTL8 U3DTL8_CALJA	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATRVPLM	360
TR G7NRX7 G7NRX7_MACMU	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR G7Q1V9 G7Q1V9_MACFA	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR H2PX10 H2PX10_PONAB	FASVSYLDTQVGRLLSTLDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
TR G1RST8 G1RST8_NOMLE	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI0000D9F625	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI000274358B	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI00027F6FC5	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI00027FAE03	FASVSYLDTQVGHLLSALDDLHLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATRVPLM	360
UPI0003ABB28	FASVSYLDTQVGRLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI000533297F	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360
UPI0005F40BD2	FASVSYLDTQVGHLLSALDDLQLANSTIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLM	360

SP P22304 IDS_HUMAN	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR K6ZGI9 K6ZGI9_PANTR	SLKDIKIMGYSIRTIDYRYTVWIGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR K7BKV4 K7BKV4_PANTR	SLKDIKIMGYSIRTIDYRYTVWIGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR H9FTX2 H9FTX2_MACMU	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR F7EJG2 F7EJG2_CALJA	SLKYIKIMGYSIRTVDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR U3DTL8 U3DTL8_CALJA	SLKYIKIMGYSIRTVDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR G7NRX7 G7NRX7_MACMU	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR G7Q1V9 G7Q1V9_MACFA	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR H2PX10 H2PX10_PONAB	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	NLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
TR G1RST8 G1RST8_NOMLE	SLKDIKIMGYSIRTIDYRYTVVWGFSPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI0000D9F625	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI000274358B	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI00027F6FC5	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI00027FAE03	SLKYIKIMGYSIRTVDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI0003ABBF28	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540
UPI000533297F	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPFQDHNMYNDSQ	540
UPI0005F40BD2	SLKDIKIMGYSIRTIDYRYTVVWGFNPDEFLANFSDIHAGELYFVDS	DPLQDHNMYNDSQ	540

FIG. 2 continued

SP P22304 IDS_HUMAN	GGDLFQLLMP	550
TR K6ZGI9 K6ZGI9_PANTR	GGDLFQLLMP	550
TR K7BKV4 K7BKV4_PANTR	GGDLFQLLMP	550
TR H9FTX2 H9FTX2_MACMU	GGDLFQLLMP	550
TR F7EJG2 F7EJG2_CALJA	GGELFQSLMP	550
TR U3DTL8 U3DTL8_CALJA	GGELFQSLMP	550
TR G7NRX7 G7NRX7_MACMU	GGDLLQLLMP	550
TR G7Q1V9 G7Q1V9_MACFA	GGDLFQLLMP	550
TR H2PX10 H2PX10_PONAB	GGDLFQLLMP	550
TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	GGDLFQLLMP	550
TR G1RST8 G1RST8_NOMLE	GGDLFQLLMP	550
UPI0000D9F625	GGDLLQLLMP	550
UPI000274358B	GGDLFQLLMP	550
UPI00027F6FC5	GGDLFQLLMP	550
UPI00027FAE03	GGELFQSLMP	550
UPI0003ABBF28	GGDLFQLLMP	550
UPI000533297F	GGDLFQLLMP	550
UPI0005F40BD2	GGDLFQLLMP	550

**:*:* **

Species Legend:

SP P22304 IDS_HUMAN	[Homo sapiens]
TR K6ZGI9 K6ZGI9_PANTR	[Pan troglodytes (Chimpanzee)]
TR K7BKV4 K7BKV4_PANTR	[Pan troglodytes (Chimpanzee)]
TR H9FTX2 H9FTX2_MACMU	[Macaca mulatta (Rhesus macaque)]
TR F7EJG2 F7EJG2_CALJA	[Callithrix jacchus (White-tufted-ear marmoset)]
TR U3DTL8 U3DTL8_CALJA	[Callithrix jacchus (White-tufted-ear marmoset)]
TR G7NRX7 G7NRX7_MACMU	[Macaca mulatta (Rhesus macaque)]
TR G7Q1V9 G7Q1V9_MACFA	[Macaca fascicularis (Crab-eating macaque; Cynomologous monkey)]
TR H2PX10 H2PX10_PONAB	[Pongo abelii (Sumatran orangutan)]
TR A0A0D9R4D1_CHLSB	[Chlorocebus sabaeus (Green monkey)]
TR G1RST8 G1RST8_NOMLE	[Nomascus leucogenys (Northern white-cheeked gibbon)]
UPI0000D9F625	[Macaca mulatta (Rhesus macaque)]
UPI000274358B	[Pan paniscus (Pygmy chimpanzee; Bonobo)]
UPI00027F6FC5	[Papio Anubis (Olive baboon)]
UPI00027FAE03	[Saimiri boliviensis (Bolivian squirrel monkey)]
UPI0003ABBF28	[Macaca fascicularis (Crab-eating macaque; Cynomologous monkey)]
UPI000533297F	[Rhinopithecus roxellana (Golden snub-nosed monkey; Pygathrix roxellana)]
UPI0005F40BD2	[Colobus angolensis palliatus (Peters' Angolan colobus)]

FIG. 2 continued

hIDS MPS II Variants

L41P (mild); 41X (intermediate); D45N (MPS2); R48P (mild); Y54D (severe); N63D (mild/intermediate); A68E (severe); S71N (mild); S71R (severe); L73F (severe); A79E (mild); A82E (MPS2); A82V (no significant enzyme activity); A85S (severe); A85T (mild to severe forms); P86L (intermediate to severe forms); P86Q (MPS2); P86R (severe); S87N (mild); R88C (severe); R88G (severe); R88H (intermediate/severe form); R88L (severe); R88P (severe – total absence of residual activity); V89F (MPS2); L92P (severe); G94D (mild); R95G (intermediate); R95T (mild); 95X (severe); L102R (mild); Y108C (mild); Y108S (mild); N115Y (MPS2); S117Y (severe); 117X (missing in MPS2; severe form; deleterious mutation); T118I (mild to severe; greatly reduced activity); 118X (missing in MPS2; severe form); P120H (mild); P120R (severe); Q121H (severe); Q121R (severe);	E125V (mild); S132W (severe); G134R (severe); K135N (intermediate); K135R (intermediate); H138D (mild/intermediate); G140V (MPS2; no significant enzyme activity); S143F (MPS2); D148H (intermediate); H159P (severe); 159X (missing in MPS2; intermediate form); P160R (MPS2); N181I (mild); L182P (intermediate); C184F (mild/intermediate); C184W (MPS2); L196S (mild/intermediate); D198G (mild); A205P (intermediate); L221P (intermediate); G224E (severe); Y225D (intermediate); K227M (intermediate); K227Q (severe); P228L (MPS2); P228T (severe); H229R (intermediate/severe); H229Y (severe); P231L (mild); D252N (MPS2); L259P (severe); Y264N (MPS2); N265I (intermediate; deleterious mutation); P266H (mild); P266R (MPS2); D269V (MPS2); Q293H (mild); S299I (mild); D308E (mild); D308N (intermediate); T309A (severe); R313C (MPS2; unknown pathological significance); L314P (severe); S333L (severe);	D334G (severe); D334N (mild); H335R (intermediate); G336E (severe); G336R (severe); W337R (intermediate); L339R (severe); G340D (mild); E341K (severe); H342Y (mild); W345C (mild/severe); A346D (mild/severe); A346V (mild/severe); K347I (MPS2); K347Q (severe); K347T (severe); Y348H (MPS2); S349I (severe); P358R (severe); L403R (intermediate); L410P (MPS2); C422G (mild); C422R (severe); C432Y (severe); E434K (MPS2); Q465P (severe); P467L (severe); R468G (mild/severe); R468L (mild/severe); R468Q (severe/intermediate; greatly reduced activity); R468W (mild/severe); P469H (mild); D478G (mild); D478Y (severe); P480L (mild); P480Q (mild); P480R (severe); I485K (MPS2); I485R (severe); MG488 – 489IA (intermediate); Y490S (intermediate); S491F (mild); W502C (severe); W502S (MPS2); E521K (severe); E521V (severe); Y523C (mild).
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FIG. 3

Human IDS Processing Steps

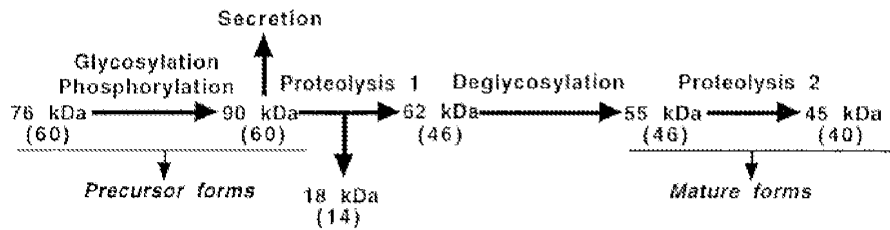


FIG. 7. IDS processing. Molecular mass of deglycosylated polypeptides is indicated in parentheses.

(From, Millat et al., 1997, Exp. Cell. Res. 230: 362-367 (“Millat 1997”) Fig. 7).

FIG. 4

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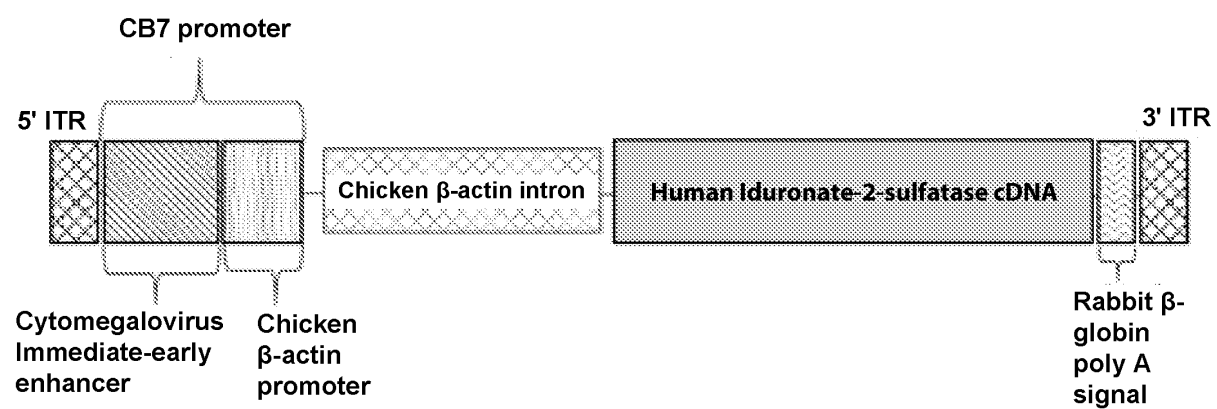


FIG. 5

AAV1	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV2	KGEPVN E ADAAALEHDKAYDR Q LD S GNDPNYLYKNHADADEFQERLKEDTSFGGNLGRAVFQ	120
AAV3-3	KGEPVN E ADAAALEHDKAYDQQLKAGDNPYLYKNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV4-4	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLYKNHADADEFQ R LQGDTSFGGNLGRAVFQ	119
AV5	R GEPVNADEVA R EHDI S NE Q LEAGDNPYLKYNHADADEFQ E KLADDTSFGGNLGKA V FQ	119
AAV6	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV7	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV8	KGEPVNAADAAALEHDKAYDQ Q I Q AGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
hu31	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLYKNHADADEFQERLKEDTSFGGNLGRAVFQ	120
hu32	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLYKNHADADEFQERLKEDTSFGGNLGRAVFQ	120
AAV9	KGEPVNAADAAALEHDKAYDQQLKAGDNPYLYKNHADADEFQERLKEDTSFGGNLGRAVFQ	120
SUBS	R-----E--EV-R---IS-NE--DS-----R-----QK-QD-----K----	
	R R E AG	
	 Q	

VP2₁₃₈→ [---HVR1---

AAV1	AKKR	VLEPLGLVLEE	GAKTAPGKKRPVEQ	SPQ-EPDSSSGIGK	TGQQ	PAKKRLNFGQTGDS	179	
AAV2	AKKR	VLEPLGLVEE	PVKTAPGKKRPVEN	SPV-EPDSSSGTGK	AGQQ	PAKKRLNFGQTGDA	179	
AAV3-3	AKKR	I	LEPLGLVEEAAKTAPGKK	GADVQSPQ-EPDSSSGVGKSGK	Q	PAKKRLNFGQTGDS	179	
AAV4-4	AKKR	VLEPLGLVEE	QAGETAPGKKRLIES	SPQ-QPDSSTGIGK	KGKQ	PAKKLVLFEDE	178	
AV5	AKKR	VLEP	FGLVEE	GAKTAPGKR	RIDHFF-----	KRKARTEDESKPSTSSDA	168	
AAV6	AKKR	VLEP	FGLVEE	GAKTAPGKKRPVEQ	SPQ-EPDSSSGIGK	TGQQ	PAKKRLNFGQTGDS	179
AAV7	AKKR	VLEPLGLVLEE	GAKTAPAKKR	PVEPSPQSPDSS	TGIGKKG	QQ	PAKKRLNFGQTGDS	180
AAV8	AKKR	VLEPLGLVLEE	GAKTAPGKKRPVEP	SPQSPDSS	TGIGKKG	QQ	PAKKRLNFGQTGDS	180
hu31	AKKR	LLLEPLGLVEEAAKTAPGKKRPVEQ	SPQ-EPDSSAGIGKSG	SQ	PAKKL	NFGQTGDT	179	
hu32	AKKR	LLLEPLGLVEEAAKTAPGKKRPVEQ	SPQ-EPDSSAGIGKSG	SQ	PAKKL	NFGQTGDT	179	
AAV9	AKKR	LLLEPLGLVEEAAKTAPGKKRPVEQ	SPQ-EPDSSAGIGKSG	AQ	PAKKRLNFGQTGDT		179	
SUBS	----	V----	F-----	QGGE----	TG-GID	DHF-V-S-----	S-T--KKQARTREKSVPEDE	TGA
	I		PV	A	ALIP	Q	T V T K E D K STSS S	
					E		A S	
							R A	

FIG. 6

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	[HVR2]	VP3₂₀₃→	
AAV1	ESVFD-PQPLGEPPTAAVGPPTMASGGGAPMADNNEGADGVGNASGNWHCDSTWLGD	238	
AAV2	DSVFD-PQPLGQPPAAPSLGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTW	238	
AAV3-3	ESVFD-PQPLGEPPTAAVGPPTMASGGGAPMADNNEGADGVGNSSGNWHCDSTW	238	
AAV4-4	GDGP-----PEGSTSGAMS--DDSEMRAAAGGAAVEGGQGADGVGNASGDWHCDSTW	232	
AV5	EASPSGSQQLQIPAAQPASSLGCADTMSAGGGGLGDNNQGADGVGNASGDWHCDSTW	228	
AAV6	ESVFD-PQPLGEPPTAAVGPPTMASGGGAPMADNNEGADGVGNASGNWHCDSTWLGD	238	
AAV7	ESVFD-PQPLGEPPTAAVGPPTMASGGGAPMADNNEGADGVGNASGNWHCDSTWLGD	239	
AAV8	ESVFD-PQPLGEPPTAAVGPPTMASGGGAPMADNNEGADGVGNSSGNWHCDSTWLGD	239	
hu31	ESVFD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGNSSGNWHCDSTW	238	
hu32	ESVFD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGNSSGNWHCDSTW	238	
AAV9	ESVFD-PQPIGEPPAAPSGVGSMTMASGGGAPVADNNEGADGVGNSSGNWHCDSTW	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	
	[HVR3]		
AAV1	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	297	
AAV2	VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYFDENRFHCHFS	296	
AAV3-3	VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYFDENRFHCHFS	296	
AAV4-4	VTTSTRTWALPTYNNHLYKRLG-----ESLQSNNTYNGFSTPWGYFDENRFHCHFS	287	
AV5	VTKSTRTWALPTYNNHLYKQIS-SVDSNANAYFGYSTPWGYFDENRFHCHFS	287	
AAV6	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	297	
AAV7	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	298	
AAV8	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	299	
hu31	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	298	
hu32	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	298	
AAV9	VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYFDENRFHCHFS	298	
SUBS	-T-K-----V--S---Q-RRLGSGSQSDATQA-T-----S-W-----		
	V	E K AATTEGL S H	
		G V	
		E A	
AAV1	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	357	
AAV2	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	356	
AAV3-3	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	356	
AAV4-4	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	347	
AV5	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	347	
AAV6	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	357	
AAV7	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	358	
AAV8	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	359	
hu31	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	358	
hu32	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	358	
AAV9	QRLINNNWGFPRKRLNFKLFNIQVKEVTNDGVTTIANNLSTVQVFSDEYQLPYVLGS	358	
SUBS	-----M--RAMRV-I-----VQDSTT-----I-I-S-DE-E-----MDA		
		K S QSE E A S	
		S	

FIG. 6 continued

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HVR4

AAV1 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
 AAV2 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
 AAV3-3 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
 AAV4-4 GQEGSLPPFPNDVFMVPQYGYCGLVTGNTSQQQTD RNAFYCLEYFPSQMLRTGNNFEITY 407
 AV5 GTEGCLPAFPQVFTLPQYGYATLNRD--NTENPTERRSSFFCLEYFPSKMLRTGNNFEITY 406
 AAV6 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
 AAV7 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQSVGRSSFYCLEYFPSQMLRTGNNFTFSY 415
 AAV8 AHQGC LPPFPADVFMIPQYGYLT L N N G --- SQAVGRSSFYCLEYFPSQMLRTGNNFQFTY 416
 hu31 AHEGCLPPFPADVFMIPQYGYLT L N D G --- GQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
 hu32 AHEGCLPPFPADVFMIPQYGYLT L N D G --- SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
 AAV9 AHEGCLPPFPADVFMIPQYGYLT L N D G --- 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

HVR5

AAV1 TFEEVPFHSSYAHSQSLDRLMNP LIDQYLYYLNR TQ--NQSGSAQNKD L LFSRGSPAGMSV 473
 AAV2 TFEDVPFHSSYAHSQSLDRLMNP LIDQYLYYLSRTN--TFSGTTTQSNLQFSQAGASDIRD 472
 AAV3-3 TFEDVPFHSSYAHSQSLDRLMNP LIDQYLYYLNR TQ--NQSGSAQNKD L LFSRGSPAGMSV 473
 AAV4-4 SFEKVPFHSSMYAHSQSLDRLMNP LIDQYLGW LQSTTTGTTLNAGTATTNFTKL RPTNFSN 467
 AV5 NFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTN-----NTGGVQFNKNLAGRYAN 459
 AAV6 TFEDVPFHSSYAHSQSLDRLMNP LIDQYLYYLNR TQ--NQSGSAQNKD L LFSRGSPAGMSV 473
 AAV7 SFEDVPFHSSYAHSQSLDRLMNP LIDQYLYYLARTQSNPGGTAGNRELQFYQGGPSTMAE 475
 AAV8 TFEDVPFHSSYAHSQSLDRLMNP LIDQYLYYLSRTQT--TGGTANTQT L GFSQGGPNTMAN 475
 hu31 EFENVPFHSSYAHSQSLDRLMNP LIDQYLYYLSKTINGSG--QNQQT L KFSVAGPSNMMAV 473
 hu32 EFENVPFHSSYAHSQSLDRLMNP LIDQYLYYLSKTINGSG--QNQQT L KFSVAGPSNMMAV 473
 AAV9 EFENVPFHSSYAHSQSLDRLMNP LIDQYLYYLSKTINGSG--QNQQT L KFSVAGPSNMMAV 473
 SUBS T--D-----MF-----A--V-----WGFNR-QTNTS--AGTKRTQ-TQGSAAATFSN
 S E Q S NSTPT TQNSDVN NKNL QGYRD
 N K V TG Q T AE L YRLR TRI L
 A RG G GS E
 ND

HVR6 HVR7 HVR8

AAV1 QFKNWLPGPCYRQQRVSKTKTDN-----NNSNFTWTGASKYNLNGRESIINPGTAMASHK 528
 AAV2 QSRNWLPGPCYRQQRVSKTSADN-----NNSEYSWTGATKYHLNGRDSLVPNGPAMASHK 527
 AAV3-3 QARNWLPGPCYRQQR LSKTANDN-----NNSNFTWTGASKYNLNGRESIINPGTAMASHK 528
 AAV4-4 FAKNWLPGPSIKQQGFSKTANQNYKIPATGSDSLIKYETHSTLDGRWSALTGPMPMATAG 527
 AV5 TYKNWFPGPMPGRTQGWNLGSGVN-----RASVSFAFATTNRMELEGASYQVPPQFNGMTNN 514
 AAV6 QFKNWLPGPCYRQQRVSKTKTDN-----NNSNFTWTGASKYNLNGRESIINPGTAMASHK 528
 AAV7 QAKNWLPGPCFRQQRVSKTLDQN-----NNSNFAWTGATKYHLNGRNSLVNPGVAMATHK 530
 AAV8 QAKNWLPGPCYRQQRVSTTTGQN-----NNSNFAWTGATKYHLNGRNSLVNPGVAMATHK 530
 hu31 QGRNYIPGPSYRQQRVSTTVTQN-----NNSEFAWPGASSWALNGRNSLMNPGPAMASHK 528
 hu32 QGRNYIPGPSYRQQRVSTTVTQN-----NNSEFAWPGASSWALNGRNSLMNPGPAMASHK 528
 AAV9 QGRNYIPGPSYRQQRVSTTVTQN-----NNSEFAWPGASSWALNGRNSLMNPGPAMASHK 528
 SUBS FAK-WL---CIKT-GWNLGSGV-----TG-DSLIKYETHST-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

FIG. 6 continued

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      [-----HVR9-----]
AAV1  DDEDKFFPMSCVMI FGKESA--GASNEALD--NVMITDEEEIKATNPVATERFGTVAVNFQ 585
AAV2  DDEEKFFFPQSGVLI FGKQGS--EKTNVDEIE--KVMITDEEEIIRTNPVATEQYQGSVSTNLQ 584
AAV3-3 DDEEKFFPMSCNLI FGKEGT--TASNAEID--NVMITDEEEIIRTNPVATEQYGTVANLQ 585
AAV4-4 PADSKFS--NSQLIFAGPKQN--GNTATVPG--TLIFTSEEELAAATNATDTDMWGNLPGGDQ 583
AV5    LQGSNTYALENTMI FNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQ 574
AAV6  DDKDKFFPMSCVMI FGKESA--GASNTALD--NVMITDEEEIKATNPVATERFGTVAVNLQ 585
AAV7  DDEDRFFFPSSGVLI FGKTGA--TN-KTTLE--NVLMTNEEEIIRPTNPVATEEYGI VSSNLQ 586
AAV8  DDEERFFFPNGILIFGKQNA--ARDNADYS--DVMLTSEEEIKTTNPVATEEYGI VADNLQ 587
hu31  EGEDRFFFPSSGVLI FGKQGT--GRDNVDAD--KVMITNEEEIKTTNPVATESYQQVATNHQ 585
hu32  EGEDRFFFPSSGVLI FGKQGT--GRDNVDAD--KVMITNEEEIKTTNPVATESYQQVATNHQ 585
AAV9  EGEDRFFFPSSGVLI FGKQGT--GRDNVDAD--KVMITNEEEIKTTNPVATESYQQVATNHQ 585
SUBS  LQGSNTYAMENTMFANPKQN--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

      [---HVR10---]
AAV1  SSSTDPATGVDHAMGALPGMVWQDRDVYLQGPWAKIPHTDGHFHPSPLMGGFGLKNPPP 645
AAV2  RGNRQAATADVNTQGVLPGMVWQDRDVYLQGPWAKIPHTDGHFHPSPLMGGFGLKHPPP 644
AAV3-3 SSNTAPTTGTFVNHQGALPGMVWQDRDVYLQGPWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
AAV4-4 SSSNLETTVDRLTALGAVPGMVWQNRDIYYQGPWAKIPHTDGHFHPSPLIGGFGLKHPPP 643
AV5    SSSTAPATGTYNLQEI VPGSVWMERDVYLQGPWAKIPETGAHFHPSPLMGGFGLKHPPP 634
AAV6  SSSTDPATGVDHVMGALPGMVWQDRDVYLQGPWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
AAV7  AANTAAQTQV VNNQ GALPGMVWQNRDVYLQGPWAKIPHTDGNFHPSPLMGGFGLKHPPP 646
AAV8  QQNTAPQIGTVNSQ GALPGMVWQNRDVYLQGPWAKIPHTDGNFHPSPLMGGFGLKHPPP 647
hu31  SAQAQAQGTGWVQNGILPGMVWQDRDVYLQGPWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
hu32  SAQAQAQGTGWVQNGILPGMVWQDRDVYLQGPWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
AAV9  SAQAQAQGTGWVQNGILPGMVWQDRDVYLQGPWAKIPHTDGNFHPSPLMGGFGMKHPPP 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  QILIKNTPVPANPPAEFSATKEASFITQYSTGQVSVEIEWELQKENS KRWNPEVQYTSNY 705
AAV2  QILIKNTPVPANPSTTFESAKEASFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 704
AAV3-3 QIMIKNTPVPANPPTTFESPAKEASFITQYSTGQVSVEIEWELQKENS KRWNPEIQYTSNY 705
AAV4-4 QIFIKNTPVPANPATTFESTPVNSFITQYSTGQVS VQIDWEIQERS KRWNPEVQFTSNY 703
AV5    MMLIKNTPVPGNI--TSFSDVVFSSFITQYSTGQVTVE MEWELKKENS KRWNPEIQYTNNY 693
AAV6  QILIKNTPVPANPPAEFSATKFAASFITQYSTGQVSVEIEWELQKENS 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

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FIG. 6 continued

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[-----HVR12-----]
AAV1  AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO. 16)
AAV2  NKSNNVDFTVDTNGVYSEPRPIGTRYLTRNL 735 (SEQ ID NO. 17)
AAV3-3 NKSNNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 18)
AAV4-4 GQQNSLLWAFDAAGKYTEPRAIGTRYLTHHL 734 (SEQ ID NO. 19)
AV5    NDPQFVDFAFDSTGEYRTTRPIGTRYLTRPL 724 (SEQ ID NO. 20)
AAV6  AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO. 21)
AAV7  EKQTSVDFEAVDSQGVYSEPRPIGTRYLTRNL 737 (SEQ ID NO. 22)
AAV8  YKSTSVDFAVNTEGVYSEPRPIGTRYLTRNL 738 (SEQ ID NO. 23)
hu31  YKSNNVEEFAVSTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 24)
hu32  YKSNNVEEFAVNTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO. 25)
AAV9  YKSNNVEEFAVNTEGVYSEPRPIGTRYLTRNL 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. 6 continued