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(54) Title: TREATMENT OF MUCOPOLYSACCHARIDOSIS II WITH RECOMBINANT HUMAN IDURONATE-2-SULFATASE (IDS)

(57) Abstract: Compositions and methods are described for the delivery of recombinant human iduronate-2-sulfatase (IDS) produced by human neuronal or glial cells to the cerebrospinal fluid of the central nervous system (CNS) of a human subject diagnosed with mucopolysaccharidosis II (MPS II).

Amino Acid Sequence of Human IDS

Iduronate-2-sulfatase (IDS)

→ Signal → Mature 42kD

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        10         20         30         40         50
MPPPRTGRGL LWLGLVLSSV CVALGSETQA NSTTDALNVL LIVDDLRPS
        60         70         80         90        100
LGCYGDKLVR SPNIDQLASH SLLFQNAFAQ QAVCAPSRVS FLTGRRPDTT
       110        120        130        140        150
RLYDFNSYWR VHAGNFSTIP QYFKENGYVT MSVGKVFHPG ISSNHTDDSP
       160        170        180        190        200
YSWSFPPYHP SSEKYENTKT CRGPDGELHA NLLCPVDVLD VPEGTLPDKQ
       210        220        230        240        250
STEQAIQLLE KMKTSASPFF LAVGYHKPHI PFRYPKEFQK LYPLENITLA
       260        270        280        290        300
PDPEVPDGLP PVAYNPWMDI RQREDVQALN ISVPYGPIPV DFQRKIRQSY
       310        320        330        340        350
FASVSYLDTQ VGRLLSALDD LQLANSTIIA FTSDHGWALG EHGEWAKYSN
       360        370        380        390        400
FDVATHVPLI FYVPGRTASL PEAGEKLFPY LDPFDSASQL MEPGRQSMDL
       410        420        430        440        450
VELVSLFPTL AGLAGLQVPP RCPVPSFHVE LCREGKNLLK HFRFRDLEED
   → Mature 14kD
       460        470        480        490        500
PYLPGNPREL IAYSQYPRPS DIPQWNSDKP SLKDIKIMGY SIRTIDYRYT
       510        520        530        540        550
VWVGFNPDEF LANFSDIHAG ELYFVDSDPL QDHNMYNDSQ GGDLFQLLMP
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Italics = signal sequence (*MPPPRTGRGL LWLGLVLSSV CVALG*)

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

Boxed = Y-sulfation site (PSSEKYENTKTCRGPD)

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

C^{84} = formylglycine modification

N^{280} = M-6-P residue(s)

FIG. 1

[Continued on next page]

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