Supplemental Information

A Humoral Immune Response Alters the Distribution of Enzyme Replacement Therapy in Murine Mucopolysaccharidosis Type I

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Figure S1. Serum anti-rhIDU IgG antibody titers in MPS I mice. MPS I mice were treated with 1.57 mg/kg weekly intravenous rhIDU and assayed at 4-week intervals as described in the materials and methods. Symbols indicate individual mice. Closed symbols: antibody-negative mice. Open symbols: antibody-positive mice.
Figure S2. Inhibition of rhIDU uptake by anti-rhIDU antibodies. The uptake of rhIDU into MPS I human fibroblasts was measured in the presence of serum from antibody-negative mice (black bars) and antibody-positive mice (open bars). Values are expressed as a percentage of the uptake of rhIDU into human MPS I fibroblasts in the presence of pooled serum from naive, untreated MPS I (n = 5) and control (n = 5) mice (dashed line). Error bars represent standard deviation.
Figure S3. Distribution of fluorescent-labeled rhIDU using fluorescence intensity compared to enzymatic activity assay. (A) Bar graphs of whole-organ fluorescence intensity (“Fluor intensity,” black bars) and iduronidase activity (“IDU activity,” open bars) in antibody-negative mice. Values are expressed as the percent difference in group means compared to antibody-positive (“AB positive”) mice. Error bars represent standard deviation. (B-F) Scatterplots and linear regression of fluorescence intensity versus iduronidase activity. Filled symbols: antibody-negative mice. Open circles: antibody-positive mice.
Figure S4. Excretion of free AF680 fluorescent label in urine. (A) False-color image of fluorescence in organs of control mouse (top) and mouse treated with intravenous fluorescent-labeled rhIDU (bottom). Arrow: bladder. (B) Table showing lack of iduronidase activity in urine of treated mice.
Figure S5. Anti-rhIDU staining in liver of rhIDU-treated MPS I mice. Immunohistochemistry was performed with EXPOSE IHC detection kit (Abcam, Cambridge, MA) on 10 μm-thick organ sections with antibody against rhIDU (BP13, donated by BioMarin Pharmaceutical Inc. and used at 1:2000 dilution). Top row: antibody-negative treated MPS I mice (“AB Negative”). Bottom row: antibody-positive treated MPS I mice (“AB Positive”). 20x magnification. Scale bar 100 μm.