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Parker, Helen, Ellison, Stuart M, Holley, Rebecca J, O'Leary, Claire, Liao, Aiyin, Asadi, Jalal, Glover, Emily, Ghosh, Arunabha, Jones, Simon, Wilkinson, Fiona L , Brough, David , Pinteaux, Emmanuel, Boutin, Hervé and Bigger, Brian W  (2020) Haematopoietic stem cell gene therapy with IL-1Ra rescues cognitive loss in mucopolysaccharidosis IIIA. *EMBO Molecular Medicine*, 12 (3). e111185 ISSN 1757-4684

DOI: <https://doi.org/10.15252/emmm.201911185>

Publisher: Nature Publishing Group UK

Version: Supplemental Material

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Expanded View Figures

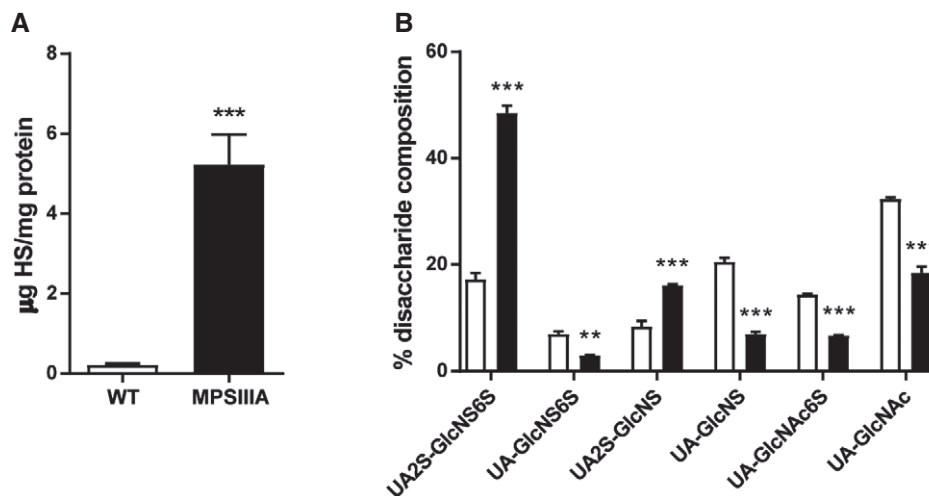


Figure EV1. Heparan sulphate analysis.

A Total relative amounts of HS. Amounts are expressed as $\mu\text{g HS}$ per mg of liver protein and calculated from AMAC fluorescent reads compared to known amounts of HS standards ($n = 3$ GAG samples). Data are expressed as mean \pm STDEV, and data for each cytokine were tested by unpaired t-test; WT versus MPSIII A *** $P < 0.0001$.

B Compositional disaccharide analysis for HS from WT and MPSIII A ($n = 3$ GAG samples). Data are expressed as mean \pm STDEV and were tested by one-way ANOVA with Tukey's post-test; ** $P < 0.01$, *** $P < 0.001$. Symbols above bars are versus WT. Exact P -values are indicated in Appendix Table S7. NAC, *N*-acetylated glucosamine; NS, *N*-sulphated glucosamine; 2S, 2-*O*-sulphate group; 6S, 6-*O*-sulphate group.

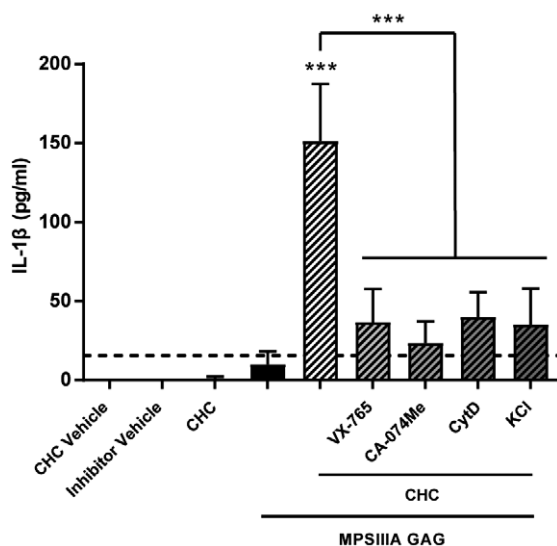


Figure EV2. MPSIII A secondary storage substrates induce secretion of IL-1 β via the NLRP3 inflammasome.

WT-mixed glia were incubated with cholesterol crystals in the presence or absence of caspase-1 inhibitor VX-765 (50 $\mu\text{g/ml}$), cytochalasin D (2 μM), KCl (130 mM) or cathepsin B inhibitor CA-074Me (10 μM). After the incubation, cell culture supernatants were analysed for IL-1 β ($n = 3$ independent experiments each with three intra experimental replicates). Data are expressed as mean \pm STDEV and were tested by one-way ANOVA with Tukey's post-test; *** $P < 0.001$. Symbols above bars are versus MPSIII A GAG alone. Exact P -values are indicated in Appendix Table S7.

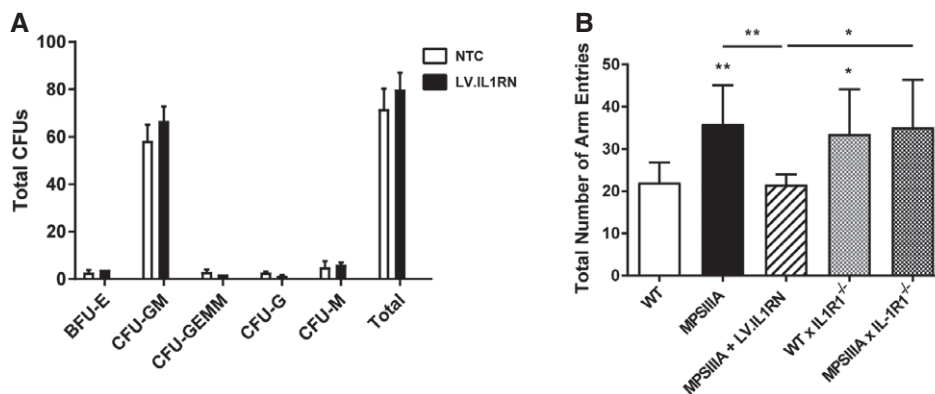


Figure EV3. Further evaluation of LV.IL1RN HSCT safety and efficacy.

A Colony-forming units from lineage-negative-enriched haematopoietic stem cells. Lineage-negative-enriched stem cells were either transduced with LV.CD11b.IL1RN or mock transduced and plated for 14 days in methylcellulose culture medium yielding committed haematopoietic progenitor colonies ($n = 6$ CFU assays). Data are expressed as mean \pm STDEV and were tested by one-way ANOVA with Tukey's post-test.

B Locomotor activity in the Y-maze. The total number of arm entries was assessed as an indicator of explorative behaviour ($n = 10$ mice per group). Data are expressed as mean \pm STDEV and were tested by one-way ANOVA with Tukey's post-test; * $P < 0.05$, ** $P < 0.01$. Symbols above bars are versus WT. Exact P -values are indicated in Appendix Table S7.

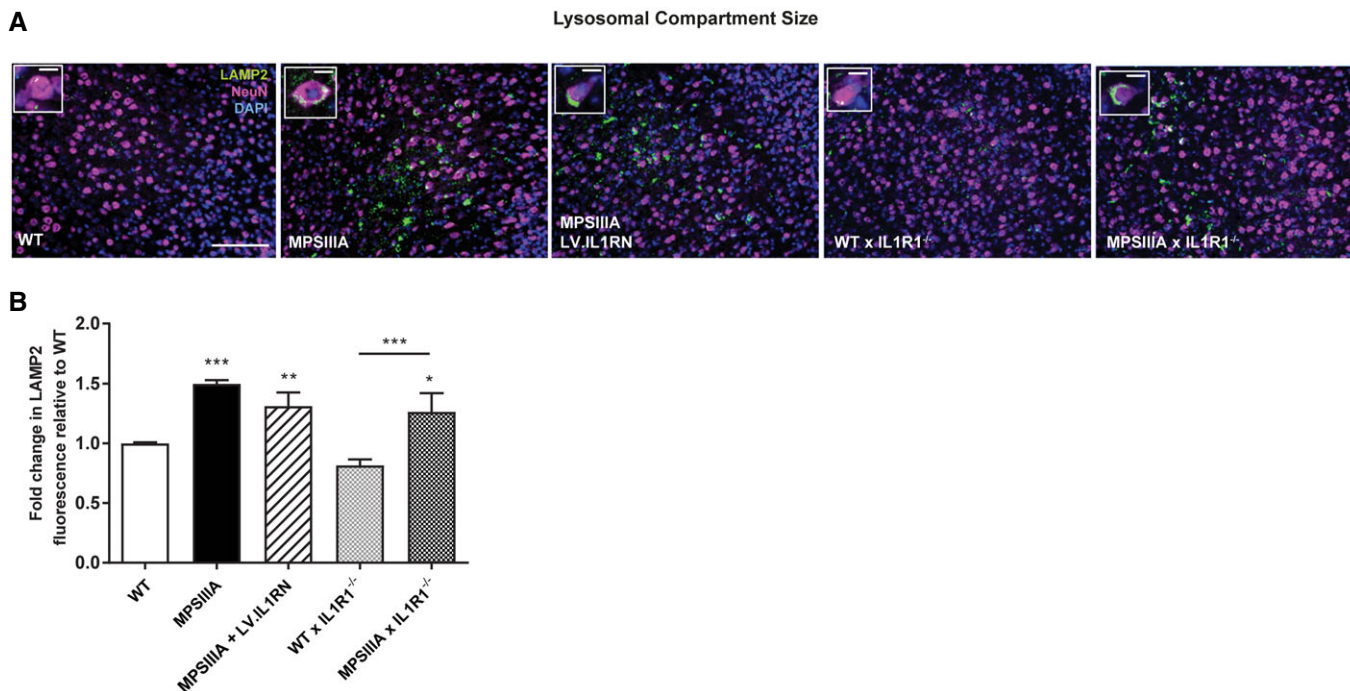


Figure EV4. IL-1 signalling inhibition in MPSIIIA mice has no effect on lysosomal storage.

A Representative images of the cerebral cortex (layers II-V) from control and treated mice stained with LAMP2 (lysosomal size, green)/NeuN (neuronal marker, magenta)/DAPI (nuclear, blue), 20 \times , scale bar: 50 μ m. Inserts, 100 \times , scale bar: 10 μ m.

B Quantification of fluorescence intensity using ImageJ software. Non-linear adjustments were made equally in fluorescent images to reduce background ($n = 4$ mice per group, average of three fields of view per mouse). Data are expressed as mean \pm STDEV and were tested by one-way ANOVA with Tukey's post-test; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Symbols above bars are versus WT. Exact P -values are indicated in Appendix Table S7.