Development of a Novel Encapsulated Non-Viral Cell-Based Therapy for MPS VI

**Introduction**

- Mucopolysaccharidosis type VI (MPS VI, Maroteaux-Lamy syndrome) is caused by a deficiency of the lysosomal enzyme arylsulfatase B (ARSB).
- ARSB deficiency results in incomplete or blocked degradation of glucosaminoglycans (GAGs), which accumulate in the lysosome and disrupt normal cell function.
- Disruption of cell function manifests in symptoms of MPS VI:
  - Short stature, coarse facial features, stiff joints, breathing problems, difficulty walking, hip pain
  - Photo on the right shows rapidly progressing 16yr old male patient

**Hypothesis**

Better outcomes could be achieved with sustained, long-lasting human ARSB (hARSB) levels via administration of hARSB-secreting allogeneic human cells shielded within spheres designed to avoid immune rejection and pericapsular fibrotic overgrowth (PFO) in the patient.

**Methods**

1. Engineer cells to express hARSB
2. Evaluate hARSB secreted from cells
3. Encapsulate hARSB-secreting cells
4. Implant in MPS VI mouse model

**Generation of HL-hARSB Fusion Enzyme**

- National Research Council Canada (NRC) has isolated a class of high affinity sdAbs (V₄Hs) that extends the half-life of a cargo protein in plasma

**Conclusion**

- Native and Half-Life extending V₄H-fused Arylsulfatase B produced by engineered cells show equivalent CS/DS lowering in MPS VI fibroblasts relative to recombinant hARSB treatment.
- MPS VI mice treated for 1 week with an encapsulated cell line secreting hARSB fused to Half-Life extending V₄H showed higher tissue activity when compared to treatment with Native hARSB.
- Treatment of MPS VI mice with an encapsulated cell line secreting active hARSB fused to Half-Life extending V₄H results in significant substrate reduction within 14-28 days of administration.

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