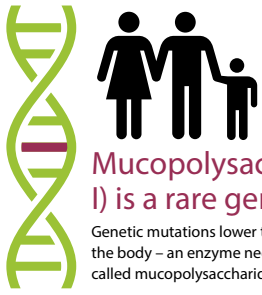


What is Gene Therapy for MPS I?

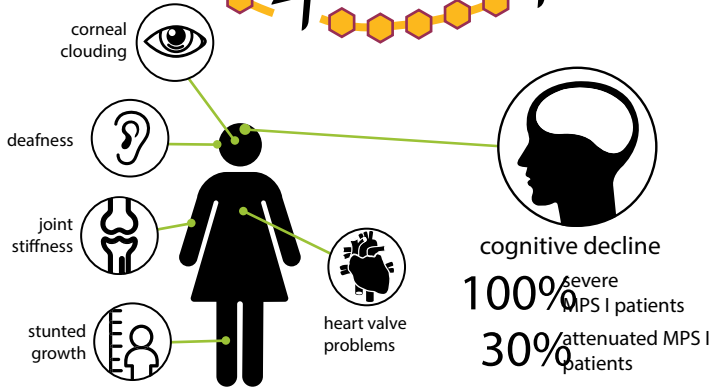
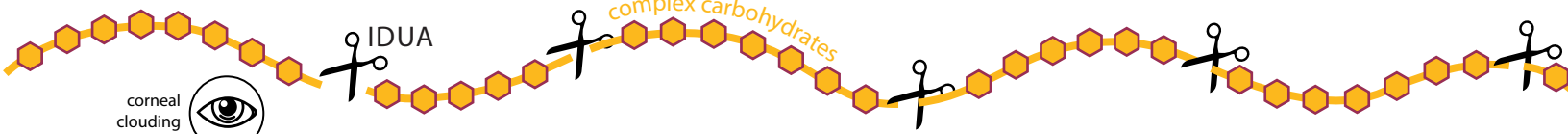
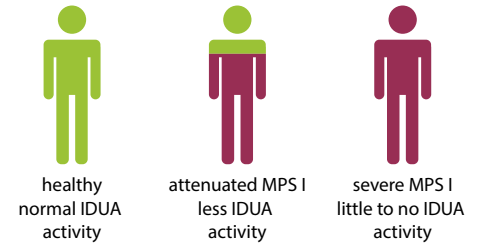


Mucopolysaccharidosis type I (MPS I) is a rare genetic disease

Genetic mutations lower the level of alpha-L-iduronidase (IDUA) activity in the body – an enzyme needed to break down complex carbohydrates called mucopolysaccharides



The lower the level of IDUA activity in the body, the more severe the patient's symptoms



Current treatments fall short

- Hematopoietic stem cell transplantation (HSCT) for severe MPS I**
 - high-risk procedure
 - incomplete correction of cognitive impairment
 - resolution of physical symptoms is also incomplete
- Enzyme replacement therapy (ERT) for attenuated MPS I**
 - delivered through vein
 - no effect in brain; partially alleviates physical symptoms
 - requires ongoing therapy at frequent intervals

HOW CAN GENE THERAPY HELP?

A promising new experimental therapy with the potential to improve cognitive deficits after a one-time treatment. While several approaches to MPS I gene therapy are being developed, intrathecal gene therapy strives to deliver a functional copy of the IDUA gene directly to the brain.

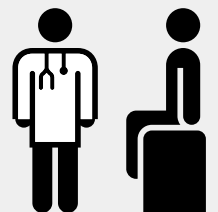
- a normal healthy copy of the IDUA gene is produced
- gene is inserted into a harmless Adeno-Associated Virus (AAV) to create a viral vector
- AAV vector is injected into the cerebrospinal fluid (CSF) that flows through the brain and spinal cord
- some cells take up AAV vector and begin to make functional IDUA, which is released into the CSF
- secreted IDUA can be used by other cells throughout the brain and spinal cord which may improve cognitive function

Safety first



gene therapy has proven relatively safe and effective in animal models of MPS I

What's next?



early clinical trials for MPS I evaluating safety in human subjects are on the horizon