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

affects 1 in 100,000

HOW CAN GENE THERAPY HELP?

Current treatments fall short

1. Hematopoietic stem cell transplantation (HSCT) for severe MPS I
   - high-risk procedure
   - incomplete correction of cognitive impairment
   - resolution of physical symptoms is also incomplete

2. 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

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

Safety first

What’s next?

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

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.

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

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

Healthy normal IDUA activity
Attenuated MPS I less IDUA activity
Severe MPS I little to no IDUA activity

IDUA complex carbohydrates

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

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

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

Penn Medicine