Maple Syrup Urine Disease (MSUD) is a rare genetic disease that leads to a buildup of the branched-chain amino acids (BCAAs) in the blood and urine. Genetic mutations to one or more of the following genes prevents formation of a complex that is essential for breaking down the amino acids, leucine, isoleucine, and valine (the BCAAs):

- BCKDHA
- BCKDHB
- DBT

Experimental, molecular therapies, including delivery of messenger RNA (mRNA) and AAV gene therapy strive to overcome the genetic mutation(s) causing MSUD in different ways. Current treatments have limitations:

- Monitoring and Diet Control: MSUD patients must constantly monitor the chemistry of their blood and urine, and carefully control their diet for management of BCAA levels.
- Liver Transplant: Limited availability, high risk

Potential New Therapies for MSUD

1. A normal healthy copy of the gene(s) containing a mutation is produced and is inserted into either a harmless viral vector or a lipid nanoparticle containing an mRNA.

2. AAV vector is delivered to the patient’s body through the circulatory system with a one-time intravenous injection.

3. Liver cells (hepatocytes) take up vector and begin to express functional copies of the affected gene.

4. Functional proteins are produced and can break down the BCAAs and prevent a toxic build up of these amino acids and their by-products, lowering levels in the blood.

Safety First

Gene therapy has proven relatively safe and effective in animal models of MSUD.

What’s next?

Early clinical trials for MSUD evaluating safety in human subjects are next.