When metabolism goes awry!
The case of maple syrup urine disease

Maple syrup urine disease (MSUD; branched chain keto acid dehydrogenase (BCKDH) deficiency) is a rare, inherited disorder affecting the breakdown of branched chain amino acids (BCAA; L-isoleucine, L-valine, L-leucine). Incidence is about 1:200,000 live births, but much higher in selected populations (Amish, Mennonites, etc). State screening in newborn bloodspots for leucine levels has been mandated for many years. Treatment consists of dietary protein restriction, a liquid formulation low in branched chain amino acids, or orthotopic liver transplantation (OLT) in some instances. While effective, these interventions remain problematic, since they are either unpalatable, treatment is lifelong, compliance is challenging (especially in adolescents), and immunosuppressive interventions are necessary. Accordingly, our laboratory seeks alternative approaches for long-term treatment of MSUD.

Since OLT is effective, we have sought to treat MSUD mice using hepatocyte transplantation (HTx), using isolated cells with normal BCKDH activity. To provide an engraftment advantage, HTx has been performed in newborn mice, whose livers are rapidly expanding. Thus far, preliminary studies have shown ~3% engraftment of exogenous hepatocytes, transient improvement of blood BCAA levels, enhanced expression of BCKDH activity, and improved body weight and lifespan. Importantly, HTx corrects abnormalities in monoamine (dopamine, serotonin) levels in brain known to be associated with MSUD.