**Project Outline:** Arginase-1, a Mn^{++} containing enzyme, catalyzes the final step in the urea cycle to produce urea and ornithine. In humans, deficiency/mutation of this enzyme leads to a severe neurological phenotype. In mice, it leads to death within 2 weeks of inactivating the gene. We have been exploring the mechanisms for the species difference, the cause of the neurological sequelae and have explored options for gene editing repair. This project will focus on deciphering relative arginase expression levels in mouse brain vs liver to answer the question “is it loss of arginase-1 in neuronal structures or loss of arginase-1 in liver that is the main contributor to the neurological phenotype?” The examination of a particular inactivating ARG1 patient mutation D232V will also be investigated.

**Supervisor:** Dr. Colin Funk

**Project Title:** Arginase in Health and Disease

**Keywords (3-5):**
1. Urea cycle disorders
2. Hepatocyte
3. Arginase
4. Neurological phenotype

**Project Goals:** Learn more about arginase and the rare genetic disorder of arginase deficiency

**Experimental Approaches:** (i) transfection of cells with arginase constructs; (ii) arginase activity assays and Western blot analysis.

**References:**


Ballantyne LL, Sin YY, Al-Dirbashi OY, Li X, Hurlbut DJ, **Funk CD**. Liver-specific knockout of arginase-1 leads to a profound phenotype similar to inducible whole body arginase-1 deficiency. Mol Genet Metab Rep. 2016 Oct 12;9:54-60.

