BCHM 421/422 – 2018/2019

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:

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Sin YY, Baron G, Schulze A, **Funk CD**. Arginase-1 deficiency. J Mol Med (Berl). 2015 Dec;93:1287-96.

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