**Maple Syrup Urine Disease (MSUD)** results from the body’s inability to break down three amino acids: valine, leucine, and isoleucine - three amino acids that are regularly found in our food. Initial symptoms lead to the sweet smell of maple syrup in urine, sweat, and ear wax, hence the name: Maple Syrup Urine Disease. Left without treatment for a prolonged period of time, the build up of the three amino acids can cause brain damage, developmental delays, seizure-like spasms, and can even be fatal.1,2 MSUD is more common in populations with substantial history of homozygosity. 3 This inability to process these three amino acids (Branched Chain Amino Acids or BCAAs), leads to irreversible build up in the body and is caused by a defective protein called branched chain alpha-ketoacid dehydrogenase. This proteins has four subunits that compose it: E1α, E1β, E2, and E3.4,5,6,7 The E2 subunit will be the focus of this project. The E2 protein subunit is coded by the DBT gene.1 It is known what mutated genes and proteins lead to this phenotype; but, there is currently a lot of research investigating the different types of variants that lead to the disease, specifically in populations that were not part of original studies. Studies have also looked at mutation effects on the proteins based on computer programming, but not in organisms.3,8,9 *It is currently unknown how different variants in the DBT gene affect the E2 subunit in vivo and its effects on disease manifestation and progression.*

My **objective** is to find the most common variants across diverse populations and characterize the various effects on the E2 subunit. The **long term goal** of this study is to use the information on variant’s effects on the E2 protein to predict disease manifestation and progression in order to develop appropriate treatment plans. I **hypothesize** that deletions in highly conserved regions among species will lead to the most severe effects on the E2 subunit and the most severe disease manifestation. Yeast, *Saccharomyces cerevisiae,* and the mouse, *mus musculus*, will be used in this study. Yeast are best show metabolic processes (MSUD is a metabolic disorder). Mice have high homology to humans and can easily be made transgenic.

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