BC368
Metabolic Disorders Poster Session
Spring 2015

Glycogen Storage Disease Type III: Treatment with Diet and Rapamycin
Nolan Dumont and Brett Sahlberg

Glycogen Storage Disease III (GSDIII; Cori Disease) is a metabolic disorder caused by a defect in glycogen debranching enzyme. It can cause hypoglycemia, hepatomegaly, myopathy and cardiomyopathy. Historically, the standard method of treatment has been symptomatic using diet. Even with minimal treatments available, many patients with GSDIII still live long into adulthood. Rapamycin is a possible future drug therapy for treating GSDIII. It has been shown that rapamycin significantly reduces glycogen *in vivo* in human muscle cells and *in vitro* in dogs.

Mitochondrial Pand(a)monium: Distinguishing Leigh Syndrome from other Defects in Mitochondrial Processes
Leah Harakawa and Justin Lutian

Leigh syndrome (LS) is a neurodegenerative disease that arises from genetic abnormalities that impair mitochondrial function usually in infants and young children. The condition has myriad symptoms, including lactic acidosis and muscle fatigue, which are characteristic of mitochondrial defects in general. To distinguish LS from 'Leigh-like' diseases, patients must exhibit a hallmark symptom: the occurrence of bilateral lesions in MRI scans of the brain, particularly in the basal ganglia, which may look like pandas in some patients. Treatments with any potential for success require knowing which specific enzymes are defective, and can include prescribing biotin and/or coenzyme Q10.

Treating Maple Syrup Urine Disease
Sarah Kletzer, Sophie Suechting, and Ryan Weeks

Maple Syrup Urine Disease (MSUD) is a metabolic disorder characterized by the inability to breakdown branched chain amino acids (BCAA) and the corresponding ketoacids. Usually presenting at birth, the disorder leads to sweet smelling urine, lethargy, coma, and death if left untreated. The most effective treatment includes acute nutrition treatment to monitor BCAA levels and provide a BCAA-less diet, but these treatments often cannot overcome neuropathological effects. Currently, zebrafish are used as a model to better study MSUD and further treatments.

Phenylketonuria: Current Strategies and Future Outlooks for Treatment
Allie Martin and Cameron Matticks

Phenylketonuria (PKU) is one of the most common metabolic disorders in the world affecting 1 in every 10,000 births worldwide. The disorder comes as a result of a deficiency or absence in the activity of phenylalanine hydroxylase (PAH) - which converts phenylalanine to tyrosine leading to accumulation of the former in the bloodstream and brain. The disorder manifests itself most often in decreased intellectual development through childhood but can include seizures. Current treatment for people with PKU include strict dieting to limit the amount of dietary phenylalanine and pharmaceutical supplementation of a critical cofactor, biopterin. Potential future treatment options for PKU include gene therapy, enzyme replacement therapy, and competitive inhibition of phenylalanine transport to the brain.

Acute Intermittent Porphyria

Hunter Moore and Karunya Nathan

Porphyrias result in enzymatic deficiencies of the heme biosynthesis pathway, which predominates in the liver and in erythrocytes. Acute Intermittent Porphyria (AIP) results from a deficiency in porphobinlinogen (PBG) deaminase, an enzyme in the heme biosynthesis pathway, causing the buildup of PBG and 5-aminolaevulinic acid (ALA). AIP is most commonly diagnosed by elevated PBG and ALA urine concentrations. AIP manifests in various neuropsychiatric symptoms that violently elevate in acute attacks, which can be fatal. Acute attacks are thought to be caused by elevated plasma concentrations of ALA, a neurotoxin, which is produced by ALA synthase a rate limiting enzyme in heme synthesis. Regulation of ALA synthase by nuclear receptor coactivator, proliferator-activator receptor γ coactivator 1α (PGC-α) is investigated. PGC-α plays key roles in metabolism and maintaining liver homeostasis. Experimental findings have shown transcription of ALA synthase in the liver to be down regulated by PGC-α in the presence of insulin, presenting mechanism by which glucose infusions quell acute attacks of AIP. Further research into mechanism involving regulation of ALA and ALA synthase can prove useful for future treatment and prevention

Pyruvate Kinase Deficiency: Hemolytic Anemia or Performance Enhancing Capability?

Vania Lopez and Colin Sheehan

Pyruvate kinase deficiency is an inherited disorder that primarily affects red blood cells. Individuals with this deficiency cannot run the final step of glycolysis properly. Red blood cells lack the necessary ATP to survive, so they build-up in the spleen where they are destroyed resulting in a condition known as hemolytic anemia. Since this disorder is inherited, there is no treatment to fix the mutation. However, individuals afflicted with this disorder are able to survive with frequent blood transfusions to replace the damaged red blood cells. Given its key role in glycolysis, researchers at Stanford believe that pyruvate kinase is a key enzyme in muscle fatigue. They have developed an instrument that rapidly cools an athlete's palm while resting, and have shown that performance is greatly increased using the rapid thermal exchanger.

Wilson's Disease: Copper Accumulation due to a Mutation in the ATP7B Gene

Catherine Sharp and Christine Wamsley

This project examines Wilson's disease, a rare autosomal recessive disorder caused by any number of mutations in the ATP7B gene. This condition is characterized by reduced biliary copper excretion and incorporation into the protein ceruloplasmin, resulting in the accumulation of this mineral in the liver and central nervous system. Copper can also deposit in other organs, such as the brain and eyes, and brownish circles in the irises, known as Kayser-Fleischer rings, can sometimes be a sign of the disease. Manifestation of WD varies, but can cause hepatic dysfunction, as well as neurological and psychiatric disorders. Treatment includes chelating agents to remove excess copper and zinc to reduce absorption of copper from the intestinal tract. When all other medical intervention fails, a liver transplant is necessary. Although fatal if left untreated, strict adherence to medication and reduced copper intake can result in a complete halt of the disease's progression and even a reversal of some symptoms.