Tarui Disease - One Letter is All it Takes
Jerreme Jackson 1,3 Letitia Olson 2,3
1 Department of Genome Science and Technology,
2 Department of Biochemistry, Cellular and Molecular Biology, Univ. Tennessee, Knoxville TN 37996,
3 Peer Recipient

What is Tarui disease?
Tarui disease is the least common of the autosomal recessive Glycogen Storage Diseases (GSD). Technically referred to as glycogenosis, this particular GSD is caused by a deficiency in phosphofructokinase-1 and consequently an inability to utilize the body's storage of glycogen. A deficient PFK-1 enzyme results in an overall lack of energy in the muscle tissues, as there is an insufficient amount of ATP to fuel daily activities. This results in rhabdomyolysis (degradation of muscle tissue) in an effort to obtain enough energy to sustain activity. Due to compensatory muscle breakdown, some obvious symptoms of Tarui include small and/or under-developed muscles. Treatments that consist of avoiding strenuous exercise and supplementing the diet with high protein in take, have been found to be helpful(1).

How Does Phosphofructokinase-1 Work?
Phosphofructokinase-1 (PFK1) is an allosteric enzyme that catalyzes what we all know as the "committed" step during glycolysis. During this reaction, fructose 6-phosphate is converted to fructose-1,6 bisphosphate at the expense of one molecule of ATP.

What Mutations Cause This Disease?
Mutations leading to this disease are a G to A substitution at the 5' donor site of intron 5 of the PFK-M gene. This mutation led to a splicing defect: a complete deletion of the preceding exon in the patient's mRNA. The only previously characterized genetic defect in this disease, found in a Japanese patient, was a G to T mutation at the beginning of intron 15 with splicing to a cryptic site within exon 15. Both mutations lead to in-frame deletions, but of different parts of the protein. The differences between the two aberrant proteins may account for clinical differences between various patients (2).

Populations Affected:
Tarui Disease occurs much more often in the Ashkenazi Jew population than in the world population at large. Most of the Jew suffering from this disease have roots in Poland and Russia. Other Populations that Tarui predominates in are those of Japanese, Swedish, and French Canadian ancestry (3) (4).

Phenotypes of Tarui:
Muscle PFK-1 deficiency, technically referred to as glycogenosis, is inherited in an autosomal recessive manner. Patients clinically diagnosed with a deficiency in the muscle isoform of PFK-1 show an increased intolerance to exercise and muscle cramping. In addition to this the urine may take on a red shade caused by the break down of muscle tissues (hemolysis). It is important to note that all PFK-1 deficient individuals do not seek medical attention, which is due in part to mild symptoms.

Conlusions:
People who suspect they may be suffering from this disease may want to undergo genetic testing. Also couples who may have a family history of this disorder may want to be tested to determine the possibility of passing this disorder on to their children.

Future Directions:
Investigate Disease in Spider Monkeys

References
1. http://www.agsd.org.uk/

Acknowledgements
Funding for this workshop was provided by a PEER Training Grant through NIH (1LR25GM086761-01)