

“Development of a Urine Test for the Early Detection of Cancer”**Benjamin Song and Quan Chen, Methacton High School, Eagleville, PA – 2009 National Team Finalists**

Abstract: Although the success of cancer treatment often depends on the early detection of cancer, screening is hindered by low compliance rates for certain invasive screening tests. Previous studies have demonstrated that human urine contains circulation-derived low MW DNA (<300 bp) and that low MW urine DNA can be used to detect cancer-specific genetic and epigenetic alterations. To explore the potential to develop a urine test for cancer screening, we designed PCR-based assays for a known colon cancer epigenetic marker, the aberrant hypermethylation of the vimentin gene (mVIM) and tested its suitability for use with short, fragmented, and circulation-derived low MW urine DNA. It was found that a PCR based assay with a target size of 40 bp could be used for detecting mVIM in low MW DNA and a shorter amplicon could detect mVIM with a higher sensitivity. A blinded concordance study was performed. mVIM was detected in 75% (15/20) of urine samples from patients diagnosed with CRC and 0% (0/10) of urine from healthy controls, and there was a 60% concordance in detecting mVIM between the CRC tissues and corresponding urine samples. This data demonstrates the promising potential of developing a urine test for cancer screening.

Mentor: Dr. Ying-Hsiu Su**“Comparison of Gadolinium Molecular Imaging Probes and Manganese Imaging Probes for the Detection of Atherosclerotic Plaque by Magnetic Resonance Imaging”****Eugenia Volkova, John Jay Senior High School, Cross River, NY and Alexander Saeboe, Somers Central High School, Lincolndale, NY – 2008 National Team Finalists**

Abstract: The current clinical contrast agent standard for MR imaging is a Gadolinium based imaging probe, however current research has proven that Gadolinium undergoes transmetalation and as a result can cause severe to fatal complications and has done so in many cases. As a result there is a pressing requirement to discover another Nanoparticle on which to base MR contrast agents on. The aim of the current study was to assess the degree to which Gadolinium experiences transmetalation, as well as to assess the feasibility of Manganese as a replacement for Gadolinium, using the micelles bound to an IK-17 antibody as a targeting moiety. Micelles were prepared and characterized with respect to size, efficacy, binding, and uptake in macrophages. MRI was performed on ex-vivo aorta obtained from apolipoprotein deficient mice over a 72-hour interval after micelle injection. All micelles exhibited sizes similar to that of high-density lipoproteins (<15nm). The results of these MRI scans revealed that the CNR (contrast to Noise Ratio) of Manganese was equivalent to that of Gadolinium. Flow Cytometry was used in order to determine the toxicity and as a result the amount of transmetalation. Gadolinium showed signs of high levels of transmetalation and thus much more toxic.

Mentor: Dr. Karen Briley-Saeboe

“Inhibition of Bax/Bak Activation by Mitochondrial Fusion: A Novel Mechanism to Block Programmed Cell Death”

James Meixiong, Lakeside High School, Evans, GA – 2008 National Individual Finalist

Abstract: Programmed cell death or apoptosis occurs to regulate and upkeep human development, anti-viral defense and maintenance of tissues. Yet despite its fundamental importance, many of the processes leading up to and occurring during apoptosis are not well understood. Recent studies suggest a key role of mitochondria in apoptosis. Mitochondrial apoptosis is largely regulated by Bcl-2 proteins; however, the role of mitochondrial dynamics in apoptosis has not been determined and is thought to be a passive process. I propose that mitochondrial dynamics is actively regulated and serve to stimulate Bax and Bak activation. Specifically, my hypothesis is that enhanced mitochondrial fusion inhibits Bax/Bak activation while mitochondrial fragmentation elevates it. I took two approaches to test this hypothesis. The first was to promote mitochondrial fusion by over-expressing mitofusin1 or mitofusin 2. The second was to inhibit mitochondrial fragmentation or fission by over-expressing DN-Drp-1, a dominant negative mutant of the fission protein Drp-1. Both approaches led to less activation of Bax/Bak and less release of cytochrome C. Finally, I showed that Bax integration into mitochondria membranes (and Bax activation) was increased more in mitofusin KO MEFs than in wild type MEFs. These results suggest that altering mitochondrial dynamics could change Bax and Bak function (activity and membrane integration). This project also identifies potential targets for future pharmaceutical studies that could target mitochondria dynamics in order to regulate Bax/Bak activation and subsequent apoptotic related diseases including cancer and degenerative disorders.

Mentor: Dr. Craig Brooks