

“SNiPer: Improved SNP genotype calling for Affymetrix 10K GeneChip microarray data”

Anne Lee, Phoenix Country Day School, Paradise Valley, AZ, and Albert Shieh, Chaparral High School, Scottsdale, AZ – 2005-06 National Team Winners

Abstract: High-density nucleotide microarrays have revolutionized our ability to identify the genetic underpinnings of human disease. The first generation of these high-density nucleotide microarrays, designed to measure gene expression, generated an unprecedented amount of highly complex data. New analysis tools were developed and those tools spurred a new field of medical diagnostics. Within the past year, high-density nucleotide microarrays have been developed that can resequence the vast majority of genetic variability between individuals by genotyping between 10,000-500,000 single nucleotide polymorphisms (SNPs). This technology holds the promise of allowing us to find the genetic basis for a number of Mendelian inherited and complex diseases, such as Alzheimer’s disease, autism, and bipolar disorder. Additionally, this technology has and will generate a vast amount of data. Bioinformatics and computer science challenges have only partially been met. We have developed a computational tool that increases the accuracy and genotyping capabilities of the most widely used microarray-based genotyping platform, the Affymetrix array-based GeneChip® Mapping 10K Array. The correct calling of poorly performing SNPs may prove to be key in future linkage studies performed on the 10K GeneChip. It would prove particularly invaluable for those diseases that map to chromosome 19, known to contain a high proportion of poorly performing SNPs.

“The Effect of Foxm1b Inactivation on the Growth of Pancreatic Beta Cells”

Xue Feng, Martin Luther King Magnet High School, Nashville, TN – 2005-06 National Finalist

Abstract: The regulatory hormone insulin is produced by the endocrine beta cells in the Islets of Langerhans of the pancreas. A deficiency of insulin in the circulatory system leads to a form of diabetes. This study determines the effect of the Foxm1b gene on the growth and size of the pancreatic beta cells. Foxm1b is a transcription factor previously found to be critical for the development and regeneration of the liver by regulating the G1/S transition of mitosis. This study further provides evidence that Foxm1b has a similar function in the pancreas. We have inactivated the Foxm1b gene in mice and analyzed changes over time in the proliferation rate and the average area of the pancreatic beta cells. The results show that Foxm1b knockout beta cells tend to proliferate much slower than normal beta cells. The eventual death of older beta cells due to aging and the inability for newer beta cells to replace them lead to a major decrease in the production of insulin in the bloodstream. Based on these findings, we suggest that Type 2, adult-onset diabetes in humans may very well be caused by a mutation in the Foxm1b gene.

“Molecular basis of AnOXIA STRESS survival”

Desh Mohan, Texas Academy of Mathematics and Science – 2005-06 National Finalist

Abstract: Anoxia is a condition of oxidative stress in which there is absolutely no oxygen in the environment. This condition underlies the pathogenesis of several diseases including cardiac, pulmonary, and cerebral dysfunction, and cancerous cells in oxygen-deprived tumors. To better understand this response, we are studying the *Caenorhabditis elegans* nematode. In this study, I examined if (1) gender influences the anoxic stress response in *C. elegans*, and (2) what gender-specific pathways, genes, or molecules may be involved in this response.

I found that gender indeed affects the stress response of the *C. elegans* nematodes to anoxia—males survived anoxic stress much better than their hermaphrodite counterparts. So far, in the search for molecules influencing anoxia, a small heat shock protein, hsp-12.6, was confirmed to be a key factor in anoxia survival. Since, males and hermaphrodites differ in a single X-chromosome, elucidation of potential X-chromosome genes that may impact the anoxia responses emerges as an important future direction of my work. Undoubtedly, unraveling the molecular blueprints for anoxia survival holds the key to how we manage a wide spectrum of human diseases marked by anoxia.

“CpG island methylation of GADD45 α is marker of breast carcinogenesis”

(Lucie) Yueqi Guo and Xianlin Li, the North Carolina School of Science and Mathematics, Durham, NC – 2004-05 National Team Winners

Abstract: GADD45 α is a p53-regulated gene involved in G2/M arrest and possibly apoptosis, suggesting a role in cell growth regulation. In this study, we investigated whether CpG island hypermethylation of GADD45 α is linked to tumor development. Through Northern blotting, the methylation inhibitor 5-azacytidine induced expression of GADD45 α in cancerous (MD468 and MD231) but not normal (DU99) cell lines, suggesting that methylation is cancer-specific. Then, using methylation-specific PCR, we amplified 180-bp products with high GC concentration. The cancer-specificity of methylation in that portion of the gene was seen only weakly. In order to determine sites of consistent methylation in tumor cells, we then used bisulfite sequencing to analyze 1.4kb of the gene. Only three cytosine residues were detected for consistent methylation while normal cell lines exhibited no such patterns. The methylation of these cytosine residues within the CpG island is suggested to occur preferentially in cancer cell lines and is a reliable indicator of carcinogenesis. This presents new markers for the early detection of breast cancer; also, novel therapeutics may target methylation at these cancer-specific sites.

“An Efficient, Functional Telomerase Activity Assay”

H. Mason Hedberg, North Attleboro High School, North Attleboro, MA – 2003-04 National Individual Finalist

Abstract: Telomerase is an enzyme that constructs the telomere during fetal development. The telomere is a DNA-protein complex on chromosomes that allows normal DNA replication and cell division. Telomerase is absent in somatic cells, but is present in 80% of cancer types where it promotes uncontrolled division of cancer cells. This researcher developed a rapid telomerase activity assay that can rank potency among telomerase inhibitors, potential tumor suppressors. It has been named the Telomerase Activity By UV (TABU) assay.

The common assay, Telomerase Repeat Amplification Protocol (TRAP), requires a complex multi-day procedure involving telomerase isolation, PCR amplification, and hazardous reagents. The TABU assay uses telomerase synthesized by *in vitro* gene expression making analysis by UV absorbance possible after a 10 minute incubation. The simple and robust TABU assay was proved using a novel dialysis system, but it is suitable for high-throughput drug discovery campaigns if transferred to a capillary electrophoresis platform.

Mentor: Mr. David Vito

“Somatic *Agrobacterium tumefaciens*-Mediated transformation assays in *Zea mays* (maize) for optimization of *in planta* transformation”

Alexander Yuen and Laurel Benson, Appleton East High School, Appleton, WI – 2003-04 National Team Finalists

Abstract: Optimizing the experimental conditions for the genetic modification, or transformation, of *Zea mays* (maize) will hasten the development of disease and pest resistant crops, synchronize harvest times, and promote greater efficiency of available agrarian resources. This study examined three hypotheses of the somatic transformation of maize leaf cells utilizing *A. tumefaciens* as a bacterial vector: 1) *Zea mays*' immune system will respond to *A. tumefaciens*; 2) varying levels of L-cysteine, ranging from 100mg/L to 400mg/L, will inhibit this immune response to *A. tumefaciens*; and 3) there is a set of optimal experimental conditions (cultivar, *A. tumefaciens* strain, and L-cysteine concentration) involved in the somatic transformation of maize. Results indicate support for all three hypotheses.

This study demonstrates, for the first time, an optimal set of conditions for the somatic transformation of maize. Data from this study support the use of *A. tumefaciens* strain AGL0 (pBU-B35S.IG) suspended in 300 mg/mL of L-cysteine, in either maize cultivars Hi II AxB or B14, for optimization of *in planta* transformation. Moreover, relative to previous transformation rates, there is a seven-fold increase in transformation efficiency. The limitations of these promising findings and suggestions for future applications, are proffered.

Mentor: Ms. Mary McGill

“Identification and High Resolution Mapping of Flowering Time Genes in Rice”

Juliet R. Girard and Roshan D. Prabhu, William L. Dickinson High School, Jersey City, NJ – 2002-03 National Team Winners

Abstract: Genome mapping of rice, combined with breeding and DNA marker assisted selection, can lead to improvement of yield enhancing traits such as days to flowering.

The purpose of this study was to map the quantitative trait locus (QTL) that causes early flowering on chromosome one of *Oryza rufipogon*, to locate candidate genes for the QTL, and develop SNP markers for these genes. This was carried out using an advanced backcross population.

Previously, the elite cultivar Jefferson was crossed with the wild species *O. rufipogon* so that overlapping DNA introgressions existed within the different families of the population.

Polymorphic DNA microsatellite markers were employed to map the location of the QTL.

In order to map the QTL, the marker genotype data was correlated with the phenotype data from each family. The QTL was successfully located. Two regions that underlie the QTL were found.

Three candidate genes were identified within these regions.

Mentors: Michael Cocoran, Dr. Susan McCouch, Dr. Michael Thomson

“Computational Identification of Co-Conserved Genetic Elements in Sequenced Prokaryotic Genomes”

Vlad Codrea, Lyndon B. Johnson High School, Austin, TX – 2002-03 National Individual Finalist

Abstract: There is a pressing need to use bacteria to create medically important products and to stop pathogenic bacteria from producing toxic proteins and metabolites. Manipulation of gene expression can address both of these objectives. Highly co-conserved genetic elements whose leaders exhibit secondary structure may be natural aptamers and the most primitive systems of expressional control lacking protein cofactors. Co-conserved elements were identified by computational comparative genomics using the Python programming language and relational databases. After filtering according to the degree of conservation, 13,562 co-conserved pairs are identified between *E. coli* K12 and 151 other prokaryotic genomes. Out of these, 6,603 pairs are conserved at the level of gene name annotations.

The positive controls, *btuB*, *thiC*, and *thiM*, are all significant matches in the conserved gene name pool. This algorithm may locate possible drug targets in prokaryotic genomes which can be jammed with antisense RNA or designer organic molecules mimicking natural metabolites. Resultant drugs may be effective without disrupting translation and metabolism in higher organisms.

Mentors: Dr. Andrew Ellington, University of Texas at Austin, Tim Fennell, Jay Hesselberth