

### “Identifying Promoter Transcription Factor Binding Sites Regulating Expression of Apolipoprotein-E in H4 Neuroglioma Cells”

**Aanand Patel and William Hong, Troy High School, Fullerton, CA – 2008 National Team Finalists**

**Abstract:** Alzheimer’s disease is a neurodegenerative and fatal disease and the 6<sup>th</sup> leading cause of death in the U.S. Though the cause of Alzheimer’s is unknown, the apoE gene has been associated with Alzheimer’s disease. The purpose of this experiment was to narrow down the transcription factor binding sites on the apoE promoter which regulate apoE expression. Segments of the apoE promoter were cloned into the pFRL7 vector, upstream of the Firefly luciferase reporter gene. H4 neuroglioma cells transfected with the vector containing apoE promoter segments were then tested for luminescence. The results showed an increase in expression for the -2114/-1850 base pair region of the apoE promoter, but when the -2114/-1850 region was split into four more constructs, none of them increased expression. To check for the possibility of interacting factors, apoE promoter constructs were tested with variable 5’ ends and fixed 3’ ends. These results showed that the -2054/-1850 region increased expression, and both ends were necessary for the increase, indicating a possible interaction between the two ends of this region. Bioinformatics showed AP-2alphaA as a likely cause of the increased expression.

**Mentor:** Dr. Nilay Patel

### “A Functional Genomic Framework for Chemotherapeutic Drug Improvement and Identification”

**Sajith Wickramasekara and Andrew Guo, North Carolina School of Science and Mathematics, Durham, NC – 2008 National Team Winners**

**Abstract:** Chemotherapeutic drugs function by inducing cytotoxicity in rapidly dividing cells through mitotic impairment or forced apoptosis. It is common for non-cancerous cells to be affected by these drugs, resulting in detrimental side effects. To mediate these undesired responses, we proposed a genomic framework using the eukaryotic yeast *Saccharomyces cerevisiae* deletion collection to identify genes that confer resistance to DNA damaging agents including chemotherapeutic drugs. Based on the genomic conservation of yeast with humans, we determined human orthologs to our yeast targets and verified their roles in mediating cellular response to DNA damage. Our initial genome-wide screen in diploid yeast identified 376 genes that conferred resistance to the widely used G1/S phase chemotherapeutic drug, doxorubicin. A similar haploid yeast screen identified five-fold fewer targets, which, due to a lack of recombination ability in G1 haploids, suggests the presence of a G1/S specific DNA repair network in diploid yeast. To further test our framework we screened the G1 toxin zymocin and identified significant genetic overlap with the genes that mediate doxorubicin resistance, indicating zymocin’s potential as a chemotherapeutic agent. Successful development of our framework has direct application in sensitizing tumors, identifying novel treatments, and building a foundation for personalized medicine.

**Mentor:** Dr. Craig B. Bennett

## **“A Computational Model for Translational Efficiency and Frameshifts in Escherichia coli Using a Genetic Signal Processing Approach”**

**Vivek Bhattacharya, Hao Lian and Daniel Vitek, William G. Enloe High School, Raleigh, NC – 2007  
National Team Finalists**

Abstract: In modern genetics, *E. coli* is used as an expression system to commercially produce proteins. However, sequence-dependent features, such as rare codons and codon bias, have large effects on translational efficiency. To tackle this problem, we proposed a stochastic model to computationally estimate translational efficiency and predict frameshifting, uniting ideas from biological literature and developing two metrics with considerable predictive power for translational efficiency. We ran our model on 4364 sequences from the *E. coli* genome and found over 90% of them to have predicted high yields; moreover, the model predicts ribosomal proteins to translate at even higher rates---both results that concur with experimental evidence. We investigated a set of eight sequences of recombinant bovine growth hormone, and the model correctly determined high or low levels of translation for seven of them. We then examined variations of *prfB*, a gene with a programmed frameshift, and the model grouped these sequences into two general categories of high and low yield, consistent with experimental results. Successful development of a computational model and metrics for translational efficiency implicates itself in optimizing recombinant protein yield in multiple fields, including commercial protein synthesis.

**Mentor:** Dr. Donald L. Bitzer