# Online Proceedings

## Poster Session 3

**Commons East, Easel 63**

*2:30 PM to 4:00 PM*

**Engineering Novel MAP Kinase Interaction Domains in *Saccharomyces cerevisiae***

*Anna Kus, Senior, Anthropology: Human Evolutionary Biology, Biology (Molecular, Cellular & Developmental)*
*Mentor: Georg Seelig, Electrical Engineering and Computer Science & Engineering*
*Mentor: Arjun Khakhar, Bioengineering*

An organism's ability to sense, interpret, and respond to its environment is an essential requirement of life itself. At the cellular level, this process of connecting signals to behaviors is governed by a diverse set of mechanisms such as mitogen activated protein (MAP) kinase cascades, which are broadly conserved across animals, plants and fungi. Alterations to these connections that arise from evolution or disease can have significant phenotypic effects. MAP kinases transmit signals by colocalizing with a target protein and altering its structure through phosphorylation and thereby producing downstream behavioral changes in the cell. Engineering novel phosphorylation triggered interaction domains will allow MAP kinase signaling networks to be rewired to correct pathological dysfunction or to generate novel responses to environmental signals. We intend to use an engineered protein scaffold with a phosphorylatable motif and an occluded binding motif, which was designed by collaborators in the Baker lab, to create a phosphorylation triggered interaction motif in *Saccharomyces cerevisiae*. By rewiring the *S. cerevisiae* mating MAP kinase cascade to phosphorylate this scaffold and incorporating a yeast three hybrid output, we hope to demonstrate the function of this new class of interaction domains *in vivo*. We hypothesize that upon phosphorylation, the scaffold will undergo a conformational change revealing the previously occluded binding motif, allowing another protein to bind and produce downstream effects. Such novel interaction domains will serve as a "toolbox" to allow the rewiring of MAP kinase cascades in any context in which they naturally occur. This approach could be used to fix pathological miswiring of MAP kinase cascades that contribute to anomalies of development or diseases such as cancer. Additionally, the creation of new connections using these interaction domains could be utilized to engineer organisms or cells with useful functions such as plants with enhanced defensive traits or cancer targeting T-cells.

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**Molecular DNA Classifier Circuit for Disease Diagnostics**

*Robyn Langevin, Junior, Bioengineering*
*Mary Gates Scholar*
*Mentor: Georg Seelig, Electrical Engineering and Computer Science & Engineering*
*Mentor: Randolph Lopez, Bioengineering*

Variation in gene expression can be used as a way to test for or track the progression of large scale diseases. Although existing methods to evaluate expression such as RNA sequencing or microarrays are widely used in medical research, clinical application is limited because of time and cost. By monitoring gene expression levels clinicians could perform earlier diagnosis, evaluate therapeutic efficacy and predict recurrence of disease. Gene profiling by a linear DNA-based molecular circuit to classify samples with varying gene expression patterns would provide a novel approach resulting in a rapid, cost-efficient and reliable alternative to existing gene expression diagnostics. Previous work done on the project shows that multi-stage strand displacement cascades can be engineered to perform catalytic signal amplification with high sensitivity, amplification and specificity. In the Seelig lab, already a linear DNA molecular classifier has been engineered to distinguish between bacterial and viral infections and could correctly label 94.0% and 80.5% samples respectively. Although the previous experimental data supports the mythology of the classifier, it is not an ideal representation of clinical use. For that reason, I am working to scale up the molecular circuit by using RNA derived directly from human cancer cell lines to see if the classifier can robustly identify the originating cell line. I will take amplified RNA from each cell and add it to the classifier. The accuracy of initial binding will be analyzed by a fluorescent readout measured across both channels, corresponding to successful strand displacement. Upon demonstration of rapid, cost-effective and accurate classification of human cancer cell lines I then hope to translate this research into classification of clinical samples with the goal to adapt the current methodology into a point of care diagnostics device.