

# FYRE First Year Research Experience

Dr. Michael Kennedy is looking for First Year students to become part his research projects through the new FYRE program.

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## FYRE-STEM Sample Projects

### Structural Biology of Regulators of Heterocyst Differentiation in Ancient Cyanobacteria

The goal of this project is to establish a structural understanding of regulation of heterocyst differentiation in filamentous cyanobacteria. The heterocyst is a specialized cell that carries out fixation of atmospheric nitrogen gas and conversion into a usable form of soluble nitrogen, which is needed for continued cell growth and division under conditions of nitrogen starvation. Understanding heterocyst differentiation is significant because it represents the most primitive example of cell differentiation in nature. Photosynthetic cyanobacteria have existed for ~3 billion years and played a pivotal role in the evolution of life on earth. Heterocyst differentiation in ancient filamentous cyanobacteria predates the emergence of multicellular eukaryotic organisms by hundreds of millions of years. Over the last four decades, much has been learned about the proteins that play a role in heterocyst differentiation regulation. This knowledge has emerged from genetic analyses, discovery of phenotypes associated with knocking-out, or mutating certain genes, and from the genome sequencing revolution that has made it possible to compare the proteins present across the several species of cyanobacteria. As powerful as these techniques have been, they have failed to provide the molecular-level biochemical function that each protein plays in orchestrating heterocyst differentiation. The next major advance in understanding the regulation of heterocyst differentiation will come from figuring out the biochemical role that each protein plays. In this project, we will use structural biology techniques to characterize the structure and function of several key players in heterocyst differentiation. The project will involve learning many molecular biology and biochemistry techniques, including gene cloning, bacterial culture and protein purification.

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Sample Projects with Dr. Michael Kennedy

## Metabonomics Study of the Role of Pathogenic Bacteria in a Mouse Model for Nectrotizing Enterocolitis, a Disease that Affects Pre-Term Human Infants

In the preterm infant, NEC causes death of intestinal tissue leading to complications associated with an overall mortality rate of ~26%. Despite more than 55 years since NEC was first recognized, the etiology and pathology of NEC are still not fully understood and there is still no effective treatment to prevent or cure NEC. Progress in understanding the etiology and pathology of NEC could lead to better treatment options, hopefully with more positive morbidity and mortality statistics. In this project, we explore the utility of metabolic profiling to study NEC, using a combination of nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS) based metabonomics. Our metabonomics studies have the potential to provide novel insight into understanding NEC. The specific goals of this project are 1) *to analyze urine, fecal and blood samples from preterm infants at risk for NEC*, and 2) *to continue to develop and utilize a mouse model for NEC that we have developed in our laboratory*.

## A Mouse Model Study to Develop a NMR Method for Early Detection of Pancreatic Cancer

Pancreatic cancer is the fourth leading cause of cancer death in the United States and the most lethal cancer with <5% of patients still living five years after diagnosis. Pancreatic cancer is largely curable if it is detected before the cancer spreads outside the pancreas, but pancreatic cancer is one of the most difficult cancers to detect. There is an urgent need for an effective new method for early detection of pancreatic cancer. What we know about human pancreatic cancer is that it is preceded by precancerous lesions, and some of these lesions go on to form invasive tumors. Our working hypothesis is that precancerous lesions and early stage tumors will release a distinct pattern of small molecules into the pancreatic juice, and that these metabolites should ultimately show up in urine and stool. We predict that this distinct pattern of metabolites will be useful for early detection of pancreatic cancer while the disease is still treatable by surgical resection. The goal of this project is to determine if a metabolic biomarker can be detected in mouse urine or fecal extracts that can be correlated with the emergence and progression of precancerous lesions or early stage tumors. This project will involve working with a mouse model for pancreatic cancer, and the techniques of nuclear magnetic spectroscopy (NMR) and high-performance liquid chromatography- mass spectrometry (LC/MS) will be used for metabonomics analysis.