Applicant: Name

Department: Biological Engineering

Lab: PI

Supervisor: Supervisor

Project Title: Digital RNA Circuits for Detection and Destruction of Pancreatic Ductal Adenocarcinoma

"Synthetic Biology is the design and construction of new biological entities such as enzymes, genetic circuits, and cells or the redesign of existing biological systems," according to the Synthetic Biology Engineering Research Center, a group of partnership of five universities, including MIT. Essentially, synthetic biology is the process of breaking down biology into parts such as ribosome binding sites, genes and promoters, combining these parts to make devices such as switches and AND gates, combining devices to make systems such as cell type classifiers and inserting these systems into chassis like mammalian and bacterial cells. Synthetic biology closely mirrors electrical engineering and has many practical uses in fields such as manufacturing using microbial biochemical synthesis, health and medicine with cancer therapeutics and artificial tissue homeostasis, and information processing with cellular computing. The limits to synthetic biology are essentially endless.

The International Genetically Engineered Machines (iGEM) competition is an undergraduate research competition in synthetic biology. Teams are given kits of standardized biological parts and are allowed to create new parts and add these parts to the Registry of Standard Biological Parts. The end goal is to design and build an interesting synthetic biological system to improve on some quality of life. For example,

MIT's 2011 iGEM project "Tissues By Design" focused on tissue self-construction to result in specific patterns of cell differentiation. About 180 teams compete from around the world and present their projects at regional iGEM jamborees. The top teams from regionals will go on to World's held at MIT in November.

This spring and this summer, I and 13 other MIT undergraduates will be participating in the iGEM competition under the supervision of faculty advisors: Peter Carr, Narendra Maheshri, Roger Kamm, Natalie Kuldell, Timothy Lu, Ron Weiss, Jonathan Babb and many graduate student mentors. This spring, I will be specifically working about six hours per week with Dr. Jonathan Babb in the Weiss Lab in the Synthetic Biology Center NE47 Room 215.

Throughout the spring semester, specifically, in preparation for summer, I will be attending weekly planning meetings with the team in order to brainstorm ideas for our project, training on many specific lab protocols and beginning work on our iGEM project once the idea is formulated. While training, I will be using equipment such as the FACS (Fluorescence-activated cell sorter), Tecan Liquid handler, incubator and microbiology workspace. I will be utilizing biological techniques such as Gateway Cloning, Gibson Assembly, minipreps, PCR, restriction digest, sequencing etc. I will also be using a liquid handling robot in the Weiss lab to automate various DNA assembly techniques.

Although our team's project idea has not been finalized, I am extremely interested in pursuing cancer therapeutic applications of synthetic biology, specifically for pancreatic ductal adenocarcinoma (PDAC). PDAC is one of the deadliest forms of cancer, with a less than 20% five year survival rate, in part because the pancreas is difficult to reach for treatment and the cells produce a certain protein, Mirk/Dyrk1B, that

helps the cell resist chemotherapy. One way in which we could specifically target these cells and trigger apoptosis or some similar cell damaging response would be with digital circuit computation. Recently, Post Doctoral Fellows at the California Institute of Technology have designed digital cellular circuits that utilize DNA strand displacement and are capable of highly complex logic such as square roots, magnitudes, NOR gates etc as described in their paper, "Scaling Up Digital Circuit Computation with DNA Strand Displacement Cascades," (Lulu Qian *Science*). These circuits, however, are currently being tested *in vitro*. If we could transpose such circuits *in vivo* in mammalian cells using RNA, then we can create cell-classifying circuits capable of intricate responses. To affect PDAC, we can use RNA strand displacement to take as an input variable miRNA expression levels. Recent research has shown that PDAC miRNA expression levels change as the cancer progresses, characterizing different "microstates." If we can create digital circuits to recognize these microstates and destroy early forming cancer cells, then we can increase our probability of totally obliterating the cancer cells in the body.

This is an extremely ambitious project, but digital circuits as mentioned and applications such as cancer therapeutics are common themes of iGEM. I'm drawn to iGEM and synthetic biology because of the limitless range of practical applications that can help make a difference, for example, in treating diseases that have affected my family. I view iGEM as an amazing chance for me to gain experience in and explore the field of synthetic biology hands on by designing my own project, learning from experienced faculty mentors, collaborating with brilliant peers and presenting our project to the world. To put it simply, I wish to make an impact on the field of synthetic biology by making cancer therapeutics easier to engineer.