Rapid Whole Cell Biosensors for Sensitive Transplantation Diagnostics

Current Issues in Transplantation: Part of the transplantation procedure involves pre-transplantation screening of donors for healthy organs and post-transplantation monitoring of recipient patients. These typically involve blood testing or biopsies, which are time-consuming and technically demanding procedures, sometimes requiring specialized training in expensive machinery. Our project can address these issues through the development of a test tube culture-based whole cell biosensor tuned to the appropriate sensitivity required for diagnostic testing.

Proposed Project: A whole cell biosensor is a genetically modified organism, typically a bacterium, which has been reprogrammed to deliver a dosage-dependent signal in response to a stimulus. Many such biosensors have been constructed to sense a variety of molecules, including organic pollutants and inorganic toxins. However, none of these sensing systems have been engineered to respond to input stimuli with different sensitivities (Issue 1), and there have been no reports of cellular decision systems within these sensor constructs (Issue 2). We aim to address these two technical problems.

In our first project track, we will manipulate the sensitivity of a prototypical *E. coli* biosensor for arabinose by systematic site-directed mutagenesis of the regulatory regions of the *araBAD* promoter, fused to fluorescent protein reporters. This will enable us to tune the sensitivities of our biosensors appropriately for diagnostic blood testing, as well as implement rapid differential readouts of substrate concentration classes (e.g. non-toxic vs. toxic concentrations).

In our second track, we will implement a logic gate-based decision system by use of known protein regulatory networks that can be used to alter or integrate one or two distinct signals on a single output. This allows the biosensor to decide whether to produce a particular output or not, based solely on the chemical signals provided.

Relevance to Transplantation: Our project can simplify and speed up blood testing procedures. In the short term, a carefully designed whole cell biosensor would be a simple and inexpensive candidate replacement for current blood toxin detection systems. This could potentially shorten the time and cost required for donor screening in both developed and developing nations. Long-term goals include the simultaneous sensing of multiple blood-borne biomarkers of transplant rejection.

Relevance to the Graduate Training Program: As the iGEM team is primarily comprised of undergraduate students whose interests clearly lie in research, funding us would give your program significant exposure to our team. This would also be a way to positively encourage integrative, interdisciplinary and applied research within the transplantation field, as our project is not conventionally related to transplantation research. Finally, our presence at various conferences and events held at UBC and iGEM competition at MIT amongst an local and international audience can raise the world-wide profile of the BC Transplantation Research Foundation Graduate Training Program through advertising by the team.

In summary, this is the first year a team from BC is participating in this international competition, and despite over 100 teams from around the world participating, we believe we are developing a winning project with applications not only in basic biosensor research but also in applied areas such as transplantation. Our top sponsors will receive much international attention at the Competition Jamboree this November at MIT and we would like to count on the support of your organization to help our team accomplish our project goals and take home the grand prize, the BioBrick Trophy.