

Biomarkers – A new way to predict and diagnose organ rejection?

Transplantation is currently the most common and best therapy for patients with organ failure. This involves putting a donated organ into a “foreign” environment of the patient receiving the new organ. While the transplantation procedure itself may go smoothly, the recipient’s immune system (white blood cells) may react to the new organ.

White blood cells are the primary players involved in the recognition, attack and destruction of foreign tissues leading to organ rejection and dysfunction. A major problem facing clinical caregivers in the management of organ rejection is determining whether a transplanted organ is undergoing rejection. Most of the current rejection detection methods require the use of highly invasive and risky procedures, such as tissue biopsies. **These expensive procedures cause both emotional and physical discomfort to the patient and may result in findings that are inconclusive.**

Organ Rejection

In order to prevent organ rejection, powerful therapy is used to suppress a patient’s immune system. While this approach reduces the probability that the patient’s own body will attack the transplanted organ, it does so at a high cost. Impairment of a patient’s immune system leaves them susceptible to infections, malignancies and may cause functional complications in their newly transplanted organs.

Individuals vary in their response to immunosuppressive therapy and understanding this variation would help physicians and nurses to balance the necessity of the therapy with its possible side-effects. The capacity to *personalize* immunosuppression for each individual patient would not only alleviate patient discomfort and undesirable side effects, but would also reduce the enormous costs associated with over-prescription of immunosuppressive drugs and other diagnostic procedures.

The Research

The Biomarkers in Transplantation initiative involves working with many of Canada’s foremost experts in clinical transplantation, immunology, pathology, biochemistry, statistics and computer science. The Biomarkers in Transplantation Team is using the most advanced genomic (study of genes), proteomic (study of proteins) and bioinformatics (information science) tools to develop an inexpensive, non-invasive and accurate diagnostic and prognostic test for organ rejection and immunosuppressive therapy response.

Team members are focusing on patients who have undergone the transplantation of one of three organs: the liver, heart or kidney. **The ability to predict and diagnose rejection of transplanted organs using a simple blood test would significantly reduce the use of invasive testing procedures and allow physicians to react to organ rejection in a timely, painless and cost-effective manner.**

Using carefully collected blood samples from 600 patients, **the team has identified several new blood biomarker panels for the diagnosis of acute rejection in the first few weeks after transplantation and for chronic rejection one year or later after transplantation.** These panels include genes and proteins that are available in a test using a simple blood draw.

The next step involves analyzing these blood genes and proteins with specific clinical data (e.g., blood pressure) to maximize the ability of the biomarkers to fully identify those patients with rejection from those without rejection. **The team is now ready to test these biomarker panels in a more diverse group of patients with heart transplants across Canada. Funding is being secured from multiple partners to run a nation-wide biomarker trial that will begin in the spring of 2009 and will run for two years.**

The Collaboration

The Biomarkers in Transplantation initiative is currently supported by the Prevention of Organ Failure Centre of Excellence (**PROOF**), a federally launched Centre of excellence for Commercialization and Research. The initiative has also been supported for the last four years by many partners including Genome Canada, *Novartis Pharma*, *IBM*, St. Paul's Hospital Foundation, Vancouver Hospital Foundation, University of British Columbia, Genome BC, The James Hogg iCAPTURE Centre, BC Transplant Research Institute, *Affymetrix* and *Eksigent*. Numerous other partners have now joined in support including Provincial Health Services Authority and *Pfizer Canada*.

The PROOF Centre is a translation and commercialization nucleus that fuses biomarker expertise, technology, and market transfer capabilities to reduce organ failure and improve its treatment. It is based at St. Paul's Hospital. By vetting the best ideas, validating biomarkers, and proactively crafting partnerships between scientists and commercialization interests, the PROOF Centre will lead the way in implementing individual biomarkers of disease. This "personalized medicine" approach to heart, lung and kidney failure will reduce the burden of disease and improve health in Canada and worldwide. www.proofcentre.ca