THE IMMUNOLOGY LABORATORY: LEADING THE PRECISION MEDICINE REVOLUTION IN TRANSPLANTATION AND IMMUNE DISEASES

Sherwood,K., Lan, J., Allan, L. Lan J, and Keown, P
for the Genome Canada Transplant Consortium

Introduction:

- Pathology and laboratory medicine is in a period of dramatic change from simple serology to cutting-edge diagnostic methods
- Sponsored by Genome Canada, the BC Immunology Laboratory is driving this change in the field of renal transplantation
- We have pioneered new sequencing technologies for HLA gene typing that are now being adopted across Canada and around the world
- And we are introducing new methods of immune investigation that promise to transform our understanding of transplantation and the causes and mechanisms of other complex immune diseases

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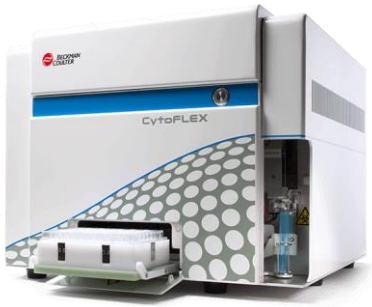
Methods: Deep immunophenotyping, Nanopore sequencing, microfluidic proteomics, single-cell biology

1

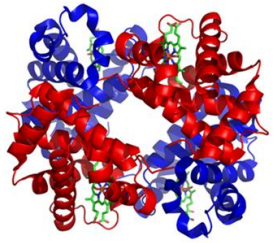


Deep immunophenotyping allows us to quantitate dozens of immune cell types in blood and tissue, including T-cells, B-cells, NK cells, dendritic cells and monocytes and to measure changes in numbers and functions according to the immune status of the patient

2

Nanopore sequencing uses real-time single molecule detection of immune genes allowing us to perform HLA genotyping in just **45 minutes** instead of the 3 days now routinely required and enabling us to type organ donors with this powerful technique.

3



Microfluidic proteomic analysis characterises protein interaction of serum antibody to detect the presence and binding of donor-specific alloantibodies in transplant patients with great precision

4

Single-cell biology combines gene expression of immune cells, with simultaneous detection of cell surface makers to identify cell subtypes and gene utilization to allow for **biomarker** discovery and **disease progression** monitoring

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Conclusions

- The Genome Canada Transplant Consortium is developing these novel assays to transform patient testing before and after transplant.
- We have made great strides in a very short time. New approaches include:
  - the introduction of HLA sequencing to enable BC to become the first place in the world to introduce epitope-based typing and reduce the risk of rejection;
  - the novel use of revolutionary Nanopore sequencing to obtain rapid and precise HLA typing of donors and recipients;
  - the investigation of T-cell receptor sequencing to detect the earliest signs of the rejection response;
  - and a variety of immune monitoring assays and non-invasive cell-free donor-derived DNA testing to monitor graft health and predict rejection.
- Genomic, transcriptomic and proteomic data are now being integrated to build a deep understanding of individual patients rejection responses
- We are linking these complex datasets using machine learning and artificial intelligence to transform the fields of transplantation.

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