Research proposal for Clinical Pharmacology Fellowship

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Pharmacogenomics of Drug Risk in Adult Oncology

For this position, the Clinical Pharmacology Fellow in Adult Oncology would be able to choose an adverse drug reaction (ADR) in oncology of specific interest and develop a clinical study with clinical and pharmacogenomic endpoints. The overarching goal is to discover and replicate a high-association biomarker of drug risk that could be used clinically to profile at-risk patients and prevent serious toxicity.

This team is ideally positioned to provide the required infrastructure to support the development and execution of such a study. In addition, the Clinical Pharmacology Fellow would be able to leverage the infrastructure of the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) as needed. The CPNDS was established in 2005 and is a pan-Canadian active ADR surveillance network that aims to reduce adverse reactions and improve drug safety and effectiveness. The CPNDS team, including 14 pediatric and 18 adult Academic Health Centers across Canada, has recruited 10,453 cases of ADRs and 95,192 drug-matched controls as of June 2020.

Ongoing CPNDS pharmacogenomic studies include cisplatin-induced ototoxicity, anthracycline-induced cardiotoxicity, methotrexate-induced mucositis, vincristine and cisplatin-induced peripheral neuropathy, l-asparaginase-induced hypersensitivity and pancreatitis, and corticosteroid-induced avascular necrosis. In addition, CPNDS has implemented pharmacogenomic testing for cisplatin-induced ototoxicity, anthracycline-induced cardiotoxicity and thiopurine-induced myelosuppression at 10 pediatric centres across Canada as part of a CIHR and Genome Canada funded research grant.

This position builds on four key areas of translation and innovation within the field of pharmacogenomics: 1. **Discovery/replication** of genomic variants highly predictive of drug outcomes; 2. **Validation** of mechanisms by which genomic variants significantly affect drug outcomes; 3. **Translational implementation science** of highly predictive and validated pharmacogenomic biomarkers into clinical practice; 4. **Commercialization research** to bring clinically meaningful findings to the rest of Canada and the world. The fellow will lead a research project of their choosing, with access to state-of-the-art genotyping and sequencing platforms to identify the genetic determinants of severe ADRs in oncology. In close collaboration with the CPNDS active surveillance network, genetic association and validation studies would be performed to define ADR causal genes and to develop clinical practice guidelines and diagnostic tests to offer personalized therapeutic recommendations and implementation into clinical practice.

Activities the Clinical Pharmacology Fellow will be responsible for:

- Development of study protocol and case definitions.
- Strategy for patient recruitment and collaboration with the CPNDS network
- Participate in knowledge translation activities
- Lead publication of research results
- Assist in the implementation of pharmacogenomic testing in clinical practice