Research proposal for Clinical Pharmacology Fellowship

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Implementation of Pharmacogenomics into the Clinical Practice- Developing a Rapid Pharmacogenetic Test Panel for Common HLA Risk Alleles Associated with Cutaneous Adverse Drug Reactions

Project Summary

Nearly all medications can cause adverse drug reactions (ADRs), dominantly affecting the skin. Growing evidence shows that the human leukocyte antigen (HLA) gene plays an important role in developing severe skin reactions by regulating the immune response. One of the most remarkable findings is that *HLA-B*15:02* is associated with a 2,500-fold risk increase in developing life-threatening skin reactions (i.e. SJS/TEN) induced by carbamazepine. Although high-resolution sequencing-based typing (SBT) has been the gold standard for HLA-based clinical applications, the high service cost (~$900 CAD), and complicated laboratory procedures (~3 days) remain huge barriers to widespread implementation. Screening a single HLA risk variant is becoming a promising strategy with certain drugs to prevent adverse events. **In this study, we aim to develop a handy, TaqMan assay-based HLA panel to rapid screen high suspected variants in cost-effective ($25 vs. $900) and time-saving (2 hours) manners, which can be appropriate for use in both basic research and clinical settings.** This would allow the return of genetic results more effectively to primary care providers to optimize patient and therapeutic outcomes. In addition, through this study, we will also collect necessary data to build another study population of those with no known strongly associated HLA alleles but who still developing cADRs.

The role of Clinical Pharmacology Fellow

- Case assessment and patient recruitment and enrollment
- Co-lead the development of the pharmacogenomics panel for HLA risk alleles
- Collaborate with a multi-disciplinary network
- Participate in knowledge translation activities to widely disseminate the concepts of pharmacogenomics
- Co-lead publication of research results
- Assist in the implementation of pharmacogenomic testing in clinical settings

What Clinical Pharmacology Fellow would learn

The Canadian Pharmacogenomics Network for Drug Safety (CPNDS) is a pan-Canadian active ADR surveillance network that aims to reduce adverse reactions and improve drug safety and effectiveness. The Network includes 14 pediatric and 18 adult academic health centers across Canada that has enrolled 10,453 cases of ADRs and 95,192 matched controls as of June 2020. With over 25 years of experience in drug safety and effectiveness, investigators and staff within the Network will assist the Fellow with patient recruitment and pharmacogenomic analyses. It can be expected that Clinical Pharmacology Fellow would develop extensive knowledge and practical skills underlying drug response heterogeneity, pharmacogenomics and bioinformatics that can be used within any medical subdiscipline in the future.