TPMI Presents: Translational Genomics Research Update, Opportunities and Challenges

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Outline

• What is the translational genomics laboratory (TGL)
  • Goal and equipment

• Update on current projects

• Highlight future projects

• A great opportunity exists

• Challenges to overcome
Translational Genomics Lab

• TGL is a modern, high throughput, high capacity genomics facility that translates research findings for a number of human disorders including autoimmune diseases, hCRC, hBOC, cardiomyopathies, and a variety of other complex human diseases.

• The goal of translational genomics is to employ genetic discoveries to improve disease outcomes by developing smarter diagnostics and targeted therapeutics.
Equipment

NanoDrop  
Cubit  
Agilent TapeStation  
ABI 7500  
Sequenom MassArray 4  

Luminex 100/200  
ABI 3500XL Genetic Analyzer  
Agilent Microarray  

Ion Chef  
Ion Torrent PGM  
Ion Torrent Proton
Projects for 2016

- Stargardt disease recurrent mutation panel
- Hereditary hearing loss recurrent mutation panel
- \( HLA-B^*27 \) tagSNP screening assay
- Cardiomyopathy recurrent mutation panel
- Sanger sequencing for common CRC genes (\( MLH1, MSH2, MSH6, PMS2 \) and \( APC \))

- **Comprehensive CRC Project**
  - Hereditary CRC/BOC recurrent mutation panel
  - Hereditary cancer NGS panel (21 genes)
  - Exon deletion/duplication assay for all 21 cancer genes
  - MSI assay for CRC (5 markers)

- Genome-wide CNV microarray test for developmental delay
- Oncomine Focus Oncology NGS panel
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**HLA-B*27 tagSNP Screen Assay**

- *HLA-B*27 is a first-line test for patients with ?axSpA.
- ~500 tests ordered annually in NL (positivity rate=17.0%).

- *HLA-B*27 tagSNP validation:
  - Analytical sensitivity=97.6%
  - Analytical specificity=99.9%
  - Analytical accuracy=99.6%
  - Analytical precision=100%

- The total sample cost of the current clinical test is $64.91, whereas the total sample cost the tagSNP assay is $3.28, which represents ~20-fold cost reduction (>$30,000/year).

- Expected policy change: ordering of the more expensive *HLA-B* locus test will be restricted to specialists with GPs permitted to only order tag-SNP screen assay.
Cardiomyopathy Mutation Panel

- A diagnostic panel of >20 mutations previously identified in the NL population known to cause cardiomyopathy has been designed.

- Assay optimization and validation to be completed by September, 2016.

- Expected policy change: cardiomyopathy recurrent mutation panel will be utilized as a first-line test. Only those patients who test negative will reflex to gene sequencing panel.
Genetic Testing for Colorectal (CRC) & Breast/Ovarian Cancer (BOC)

- Recurrent mutation panel for CRC and BOC
- Sanger sequencing assay for CRC (MLH1, MSH2, MSH6, PMS2 and APC) and BOC (BRCA1 & BRCA2)
- Multi-gene sequencing panel
- Exon deletion/duplication assay
- MSI assay for stage II CRC (5 markers)

- **Expected policy change:** recurrent mutation panel for CRC/BOC will be utilized as a first-line test for individuals at moderate- or high-risk of CRC/BOC. Only those patients who test negative will reflex to gene sequencing and multi-exon array panels. The mutation panel will replace targeted Sanger sequencing for families with known mutation.

Estimated savings: $250,000/year
Projects – 2017 to 2018

• Cardiomyopathy targeted multi-gene NGS panel
• Hematological oncology multi-gene NGS panel
• Clinical whole-exome NGS panel
A great opportunity exists

- A single provincial medical genetics program (PMGP)
- A single medical genetics laboratory (MGL)
  - Shares footprint with the TGL
  - Vast array of genomic technologies in a single laboratory.
- Capitalize on IBM infrastructure through CHIA
  - Genetic variant database development; filtering and annotation pipeline; optimize testing algorithms.
- Funding exists through researchers at MUN & TPMI to investigate the genetics of specific diseases in the NL population & translate findings to the clinic.
Challenges to overcome

• Lack of available funding directed specifically towards translational genomics.

• Reach agreements between EH and MUN for equipment maintenance, replacement, test validation of genomic discoveries and human resource allocation.

• Genomic service provision agreement with MUN-MRP.

• Funding for lab technologist to perform genomic services.

• Infrastructure and operational funding for the BioBank.
Funding

Faculty of Medicine