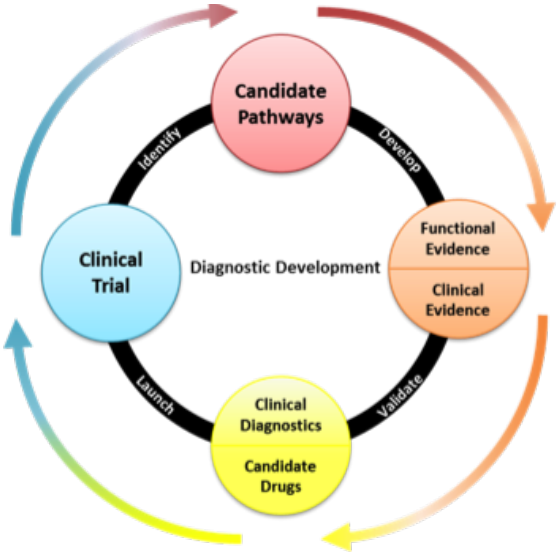
Diagnostic Development

MISSION AND GOALS

The Diagnostic Development Technology Program's mission is to initiate, disseminate and nurture expertise in the development of diagnostic assays and support its rapid implementation of precision medicine through personalized diagnosis and treatment. A key component of our mission is to extend support and expertise to the cancer research community through an active collaborative approach across Ontario and beyond.



The Biomarker Pipeline

Our program goals are:

- To accelerate the development of discoveries into diagnostic assays;
- To increase access to technologies and expertise for tissue-based cancer research and for diagnostic development;
- To actively engage with a network of clinical, academic and commercial partners;
- To train the next generation of molecular pathologists and clinician scientists.

The past five years in our program have been a period of intense activity that has accelerated discoveries of diagnostic value and resulted in the submission of four provisional patents. Our close ties with the Fight Against Cancer Innovation Trust (FACIT), OICR's commercialization partner, can bring specialized biomarker commercialization expertise to projects early in the discovery process.

RESEARCH INTERESTS, EXPERTISE AND COLLABORATIONS

The Diagnostic Development Program is focused on the development and validation of objective clinical assays to improve therapeutic selection for early cancers. Alongside the program's core research deliverables, we support or have supported research in bladder, breast, ovarian, pancreatic and prostate cancers, amongst others. Some of our collaborations across Ontario and beyond include:

- Evaluation of novel diagnostic approaches for early prostate cancer in partnership with Prostate Cancer Canada and Movember, funded by the PRONTO program and with researchers across Ontario including Queen's University (Queen's), Sunnybrook Health Sciences Center (SHSC), University Health Network, London Health Sciences Centre, OICR and the Institute for Clinical Evaluative Sciences;
- Development and validation of novel diagnostic assays for personalized medicine in early breast cancer in partnership with Canadian Clinical Trials Group, Ontario Clinical Oncology Group and SHSC;

- Development of both manual "macro-dissection" and focused laser capture micro-dissection techniques to support genomics analysis for the PanCuRX Translational Research Initiative;
- Pilot of novel technologies both in the research and diagnostic space at six diagnostic sites to evaluate focused copy number variation (CNV)/mutational analysis by targeted sequencing in partnership with researchers at OICR and Queen's/SHSC;
- Development of strong collaborative links with OICR's programs (Genomics, Informatics and Bio-computing, Drug Discovery, Health Services Research and Imaging Translation) and across Canada to provide access to a comprehensive pipeline of services for tissue based cancer research; and
- Over 100 publications with more than 150 collaborators and four oral presentations at the San Antonio Breast Cancer Symposia (2012-2014).

UNIQUE CAPABILITIES AND TECHNOLOGY PLATFORMS

Diagnostic Development supports capabilities across the spectrum of tissue-based research, from sample curation and evaluation, extraction of high quality miRNA, RNA, DNA, to analysis (*in situ*, mRNA/DNA panel based). All procedures performed within the Diagnostic Development Laboratory suite are supported by good laboratory practice (GLP) and good clinical practice (GCP) compliant standard operating procedures (SOPs), which are fully available to partner researchers. Some of the unique technology platforms are:

Multiplex CNV profiling using MLPA: Multiplex Ligation dependent Probe Amplification (MLPA) is currently used to analyze 20-50 CNVs simultaneously with DNA extracted from cell lines, frozen or formalin-fixed, paraffin-embedded (FFPE) tissues. MLPA provides a comprehensive analysis of specific CNVs within tumour subtypes, pathways or regions of complex rearrangement. Combined with validation by fluorescence *in situ* hybridization (FISH) or targeted sequencing panels, this provides a robust approach to CNV detection across tissue samples.

Targeted sequencing and library construction from FFPE DNA/RNA: Wider targeted profiling covering both mutations and CNVs is currently being developed using the ONCOMINE™ targeted sequencing panel with evaluation across Ontario. This provides a focused, locked targeted sequencing approach to rapidly survey key known mutations across multiple cancer types. Additionally, in collaboration with scientists from Genome Technologies and Informatics and Bio-computing, we developed "bespoke" panels for targeted sequencing.

Quantitative FISH including automated image analysis: FISH represents a "gold standard" for the determination of copy number alterations in tumours/cells. Combining extensive expertise in development, execution and quantitative image analysis, using the BioView image analysis platform, we support all aspects of FISH analysis and experimental design.

NanoString™ mRNA/miRNA and proteomics profiling: The N-counter system developed by NanoString technologies represents a highly flexible platform for quantitative assessment of multiple RNA/miRNA and potentially protein species isolated from FFPE tissues. We have applied this technology for panels of between 50-800 genes simultaneously using input mRNA amounts as low as 25 ng. Integrated panels for miRNA/mRNA and proteins are available. For smaller experiments we have expertise in qPCR.

Quantitative IHC including quantitative image analysis: We have validated quantitative image analysis algorithms designed to accelerate sub-cellular (nuclear, cytoplasmic, membrane) expression of multiple proteins. We support validation and development of novel immunohistochemistry approaches, rapidly progressing research from concept to completion.

Laser Capture Microdissection: To support focused analysis of specific tumour types, especially those with low cellularity, we have developed both manual "macro-dissection" and focused laser capture micro-dissection techniques to support genomics analysis of pancreatic cancer.

Tissue handling/extraction: We have developed GLP/GCP-compliant processes for all aspects of tissue extraction and management. We perform DNA, RNA and combined DNA/RNA extraction from frozen and FFPE tissues, with or without macro/micro dissection.

Tissue Microarray (TMA) construction: We construct TMAs for multiple tissue types, performing all aspects of tumour marking/area selection. We have capabilities for curation and sectioning staining (hematoxylin and eosin (H&E)) of frozen and FFPE samples, with a fully equipped pathology suite available to support researchers.

INFRASTRUCTURE

The Diagnostic Development Program provides access to a dedicated laboratory suite for molecular biology and histopathology equipped with state-of-the-art instruments that includes but is not limited to:

- Nanostring nCounter
- Roche Benchmark XT
- Zeiss Laser Capture Microscope
- BioView Imaging and Analysis automation
- NanoDrop One UV-Vis Spectrophotometer
- Beecher Tissue Micro-arrayer for TMA Construction
- Ariol FISH Image Analysis
- Tissue Studio (Definiens)
- Leica Bond, microtome, embedding machine
- Leica CM1850 Cryostat
- Leica DM6000
- LifeTech Veriti Thermocycler

CONTACT INFORMATION

TECHNOLOGY PROGRAM: Diagnostic Development

INSTITUTION: Ontario Institute for Cancer Research (OICR)
MaRS Centre, 661 University Avenue, Suite 510, Toronto, Ontario, Canada, M5G 0A3

PROGRAM DIRECTOR: **John Bartlett**
John.Bartlett@oicr.on.ca | 416-259-4251

PROGRAM MANAGER: **William To**
William.To@oicr.on.ca | 647-260-6481

Ontario

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