# Genomics

## MISSION AND OBJECTIVES

The mission of the Genomics Technology (GT) Program is to provide large-scale, next-generation sequencing (NGS) cancer genomics capabilities to researchers in Ontario and beyond.

GT accomplishes this mission through its ability to comprehensively characterize an assortment of sample types: tumours and matched normal tissues, xenografts, cell lines derived from tumours and circulating nucleic acids. In order to achieve translational results that could impact the health of cancer patients, GT enables the discovery of new pathways, targets and biomarkers across tumour types through rapid targeted sequencing of clinical samples for application in precision medicine activities.

GT has a synergistic and symbiotic working relationship with OICR's Informatics Technology Program to jointly deliver core, large-scale data sets needed for the discovery of genes and pathways that can be studied and targeted to improve cancer care. The two programs are linked through iterative cycles of data generation, analysis, hypothesis generation, verification of results, and validation of findings through follow-on studies.

The Program's objectives are to:

1. Provide state-of-the-art DNA/RNA sample preparation, library construction and sequencing capabilities to support translational research.
2. Evaluate and adopt/adapt new technologies and methodologies for research and clinical applications, and
3. Where no suitable technologies exist, develop and implement novel approaches and techniques.

## RESEARCH INTERESTS, EXPERTISE AND TRACK RECORD

GT focuses its capabilities in the area of human cancers, with proven success in generating reliable results from low input and/or low quality biospecimens and from formalin-fixed, paraffin-embedded (FFPE) samples. Generation of high quality data sets is achieved by incorporating multiple stages of quality checks into a systematic, project workflow involving:

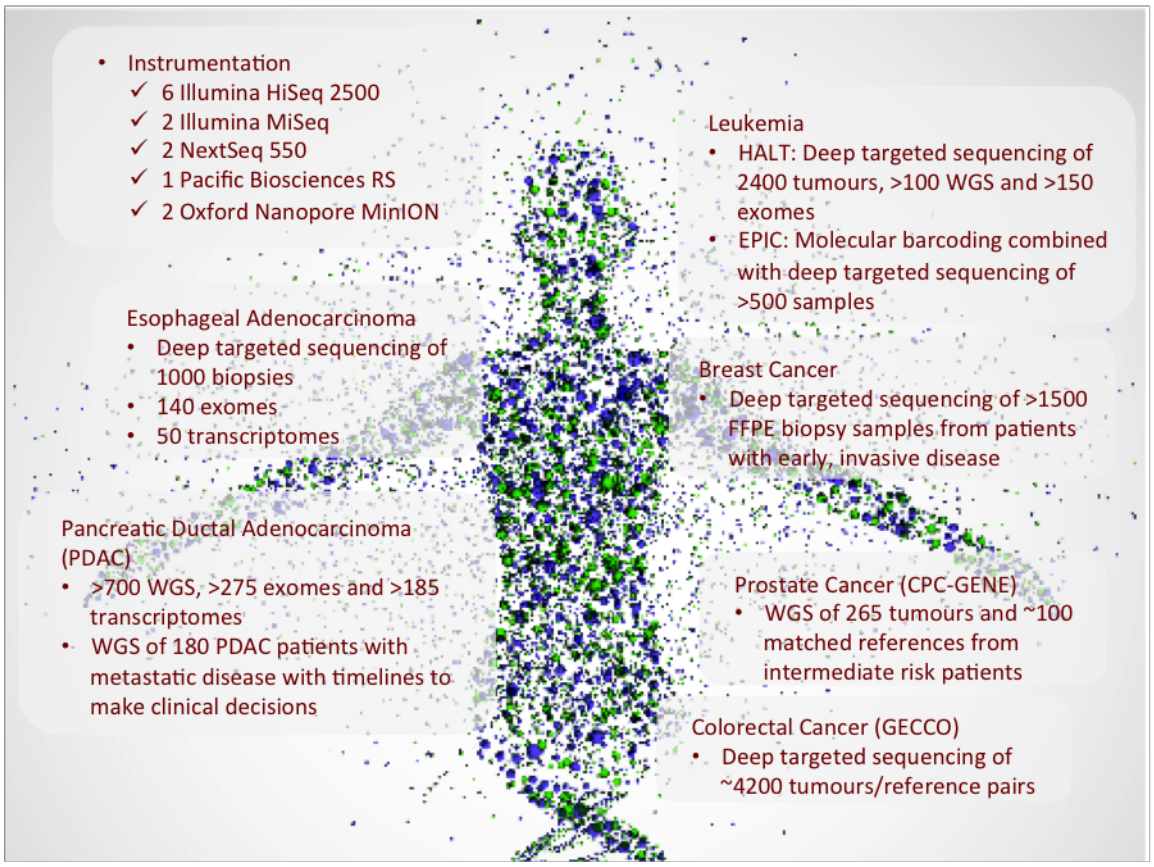
- Project design consultation
- Analyte extraction
- Library preparation
- Sequencing
- Analysis (optional)

} Open communications with collaborator/client

High-throughput processing of samples, accomplished by the use of leading-edge automation and robotics combined with a suite of Illumina sequencers, leads to the production of highly reproducible results across thousands of samples. In conjunction with OICR's Genome Sequence Informatics team, GT is able to provide collaborators with analyzed data ready to inform follow-on experiments.

In the last five years GT has contributed to a variety of human cancer projects including, but not limited to, the following:

1. **Pancreatic Adenocarcinoma (PDAC):** PanCuRx: Molecular classification and variant/pathway analyses, combined with well-annotated clinical data to identify prognostic and/or predictive markers, and facilitate the identification of drug targets for molecular therapy.
2. **Prostate cancer:** Canadian Prostate Cancer Genome Network (CPC-GENE): Develop biomarkers to stratify intermediate risk prostate cancer patients at high risk of recurrence versus those who can safely be placed under active surveillance protocols.
3. **Breast cancer:** Establish a diagnostic sequencing approach that provides biomarkers to develop personalized treatment of patients with early invasive breast cancer.
4. **Esophageal adenocarcinoma:** Discovery of key biomarkers that can be used to identify progression from Barrett's esophagus to invasive esophageal cancer.




5. **Leukemia:**
    a. Highly Active Anti-Leukemia Stem Cell Therapy (HALT): International collaboration to develop novel drugs that preferentially target leukemia stem cells in lymphoid and myeloid malignancies and to identify new therapeutic targets.
    b. European Prospective Investigation into Cancer and Nutrition Study (EPIC): Analyze genetic risk in preleukemic mutation (pLM) carriers who have developed acute myeloid leukemia using one of the largest cohort studies globally.
6. **Colorectal cancer:** Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO): Identify colorectal cancer-associated genetic variants as part of a large collaborative effort of researchers from North America, Australia, and Europe.

# CAPABILITIES

## Targeted sequencing

| Methods | Applications | Input type | Library input needs | Read lengths | Typical coverage |
|---|---|---|---|---|---|
| Agilent SureSelectXT2 Human All Exon | Somatic mutation characterization, germline polymorphisms | Intact DNA, FFPE DNA, ctDNA and cfDNA | 100 ng | 2x125 bp | 30X |
| Ampliseq (custom content or validated assays) | Cancer mutation characterization; biomarker signature development | | 10-40 ng | 2x125 bp | >1000X |
| IDT xGEN (custom content or validated assays) | | | 100 ng | 2x125 bp | >1000X |
| RainDance Thunderbolts Cancer Panel | | | 20 ng | 2x150 bp | >100X |

**Other targeted sequencing solutions** - Custom content products and other kit types can be accommodated as needed

## Whole genome sequencing

| Methods | Applications | Input type | Library input needs | Read lengths | Typical coverage |
|---|---|---|---|---|---|
| Standard coverage | Structural variant calling, copy number, INDEL, SNP/SNV (somatic and germline) | Intact and FFPE DNA | 50 ng | 2x125 bp | 30X |
| Deep coverage | Low frequency variant detection, structural variant calling, copy number, INDEL, SNP/SNV (somatic and germline) | Intact and FFPE DNA | 50-150 ng | 2x125 bp | 50-60X |

## Transcriptome sequencing

| Methods | Applications | Input type | Library input needs | Read lengths | Typical coverage |
|---|---|---|---|---|---|
| Stranded whole transcriptome | Gene expression; alternative splicing; gene fusion detection | Total RNA (RIN 7-8) | 1 ug | 2x125 bp | 80 M uniquely mapped reads |
| Stranded mRNA | | Total RNA (RIN 7-8) | 4 ug | 2x125 bp | 50 M uniquely mapped reads |
| Transcriptome capture, strand specific | | Total RNA, FFPE-compatible | 20-100 ng total RNA | 2x125 bp | 50 M uniquely mapped reads |
| miRNA | Expression of transcriptional/ translational repressors | Total RNA | 1.5 ug | 1x50 bp | 10 M uniquely mapped reads |

## Molecular barcoding approaches

| Methods | Applications | Input type | Library input needs | Read lengths | Typical coverage |
|---|---|---|---|---|---|
| Duplex sequencing | Rare variant Detection (~0.1%) | Intact and FFPE DNA | 100 ng | 2x125 bp | 200X |
| SiMSen-Seq | Rare variant Detection (~0.01%) | Intact and FFPE DNA | 10 ng | 1x250 bp | >10,000X |

## Long read sequencing

| Methods | Applications | Input type | Library input needs | Read lengths | Typical coverage |
|---|---|---|---|---|---|
| PacBio RSII (P6-C4) | Structural variations (somatic and germline); *de novo* assembly; hybrid assembly | Intact DNA | 15 ug | >10 kb | 5-10X |
| Oxford Nanopore | Structural variations (somatic and germline), methylation – *coming soon* | Intact DNA | 1-1.5 ug (direct sequencing)<br>20-100 ng (amplified) | >6 kb | TBD |

* DNA extraction from whole blood and tissue – including FFPE and LCM is supported by the Genomics Technology Program

## CONTACT INFORMATION

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Ontario
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