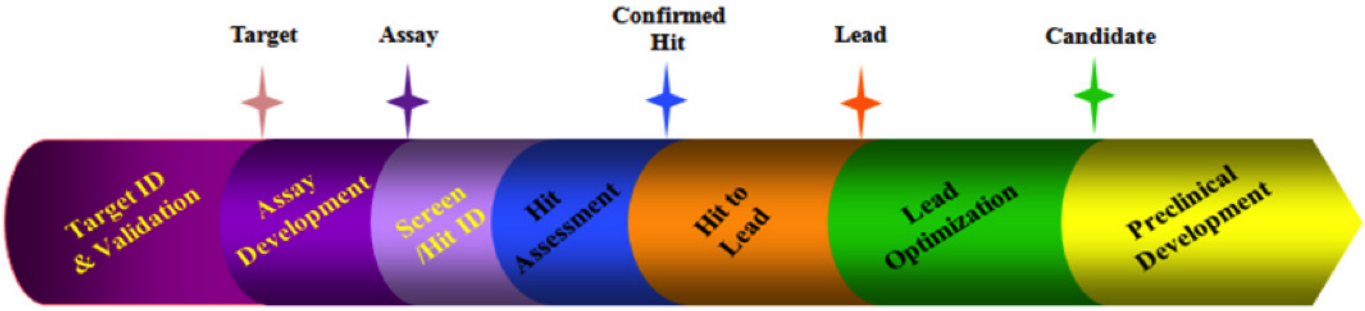
Medicinal Chemistry

ABOUT OICR'S MEDICINAL CHEMISTRY

OICR's Medicinal Chemistry team is comprised of approximately 30 researchers with extensive experience in pharma, biotech and academia. The group's collective expertise spans the entire drug discovery process from target identification and validation to clinical candidate identification and its mission is to help efficiently translate Ontario's academic discoveries into novel therapies.



Through the establishment of mutually beneficial collaborations the Medicinal Chemistry team can aid in the advancement of early stage projects requiring target validation and assay development/ optimization. Once appropriate assays have been identified, several unique and well annotated screening libraries that OICR has assembled can provide excellent starting points for successful drug discovery projects. As an alternative approach, hits can be identified computationally through a virtual screen. OICR's scientists have significant experience in hit assessment and in selecting the most promising hits for follow up and subsequent optimization through a focused hit to lead Structure-Activity Relationship (SAR) campaign.

The study of the absorption, distribution, metabolism, excretion and pharmacokinetic (ADME/PK) properties are required for the optimization and *in vivo* evaluation of small molecules. OICR's Medicinal Chemistry team has the required state-of-the-art instrumentation and expertise to evaluate and iteratively improve the ADME/PK profile of small molecule hits, leads and candidates. A range of *in vitro* and *in vivo* experiments are available such as:

i. Metabolic stability or metabolite ID using liver microsomes or primary hepatocytes
ii. Cellular permeability and efflux in Caco-2 cells
iii. Inhibition of cytochrome P450 (CYP450) enzymes as a predictor of potential DDI issues
iv. Plasma protein binding
v. Solubility and stability profiling
vi. *In vivo* pharmacokinetic profiling including plasma, organ and/or tumour exposure after iv, ip or oral routes of administration
vii. Formulation optimization
viii. Blood-brain barrier (BBB) permeability
ix. Maximum tolerated dose (MTD) studies
x. *In vivo* tumour model development
xi. PK/PD experiments
xii. *In vivo* efficacy experiments

INFRASTRUCTURE

Dedicated lab space for chemistry and biology with state-of-the-art equipment including:

- NMR
- Synapse G2S MS with ion mobility
- LC/MS/MS QTRAP 5500
- Preparative HPLCs
- Biacore
- FACS
- HP dispenser
- Operetta plate reader
- A variety of well annotated small molecule screening libraries (e.g., 140K, 20K, 600 compound kinase inhibitor library, 250 membered tool compound library and others)

CAPABILITIES

- Synthetic chemistry
- Medicinal chemistry
  - Hit to lead
  - Lead optimization
- Analytical chemistry
  - Method development
- Computational chemistry
  - Molecular modeling
  - Virtual screening and chemoinformatic assessment
- ADME
  - *In vitro* metabolism and metabolite ID, CYP450 profiling, permeability, plasma protein binding and stability etc.
  - *In vivo* pharmacokinetics, blood-brain barrier, MTD and efficacy studies
  - Formulation
- Biochemistry and cell biology
  - Target assessment and validation (shRNA, CRISPR)
  - Assay development and optimization
  - Low throughput screening

CONTACT INFORMATION

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Ontario

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