



Functional Characterization

Biologics and vaccine developers leverage our functional characterization expertise to translate the development of promising treatments in the lab to clinical trials. We also transfer our data and methods to Contract Research Organizations (CROs) and Contract Manufacturing Organizations (CMOs), enabling them to offer new services while strengthening the Canadian biopharma ecosystem.

Evaluating the behaviour of complex molecules

We excel at evaluating the behaviour of complex protein therapeutics and vaccines – including binding, signaling, internalization, mechanism of action, toxicity, biodistribution, immunogenicity, immunostimulation, efficacy, and safety – in living cells and organisms.

We can help you identify targets and biomarkers, and select hits through high-throughput screening. Our assays and documentation support you as you prepare your Clinical Trial Application (CTA) in Canada or Investigational New Drug (IND) application in the USA, ensuring that results generated in the lab are translated to the benefit of patients.

R&D expertise – *in vitro*

Genomics

- › Target and biomarker discovery through next generation sequencing and transcriptomics
- › Predictive cancer and brain biomarkers
- › Genotyping: Applied Biosystems 7500 Fast Real Time PCR System, ABI Prism 7000 Sequence Detection System, Raindance Digital PCR, and AB 3130x Genetic Analyzer
- › Systems biology: effects of changing conditions and interactions in the cellular environment

Primary assays

- › Target identification for complex protein therapeutics including bi-specific antibodies, antibody-drug conjugates (ADCs), antibody fragments, immunomodulators, and protein traps
- › High-throughput screening (HTS) in 96 and 384 well plates to identify hits: 4 robotic HTS platforms
- › Linker development and molecule conjugation in preparation for ADC cytotoxicity assays
- › Binding affinity and characteristics: flow cytometry, label-free protein-protein interaction reader for surface plasmon resonance (SPR), Octet system, Epic Corning system 384

- › Cellular function assays: signaling, internalization by automated high-content imaging, antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), cancer biology
- › Collaborative development and transfer of *in vitro* potency release assays to CROs and CMOs
- › Establishing the developmental target product profile (DTPP), designing assays in view of eventual clinical trial applications, and providing documentation in line with regulatory requirements
- › Design of non-standard assays to answer specific questions about therapeutic candidates

Electrophysiology

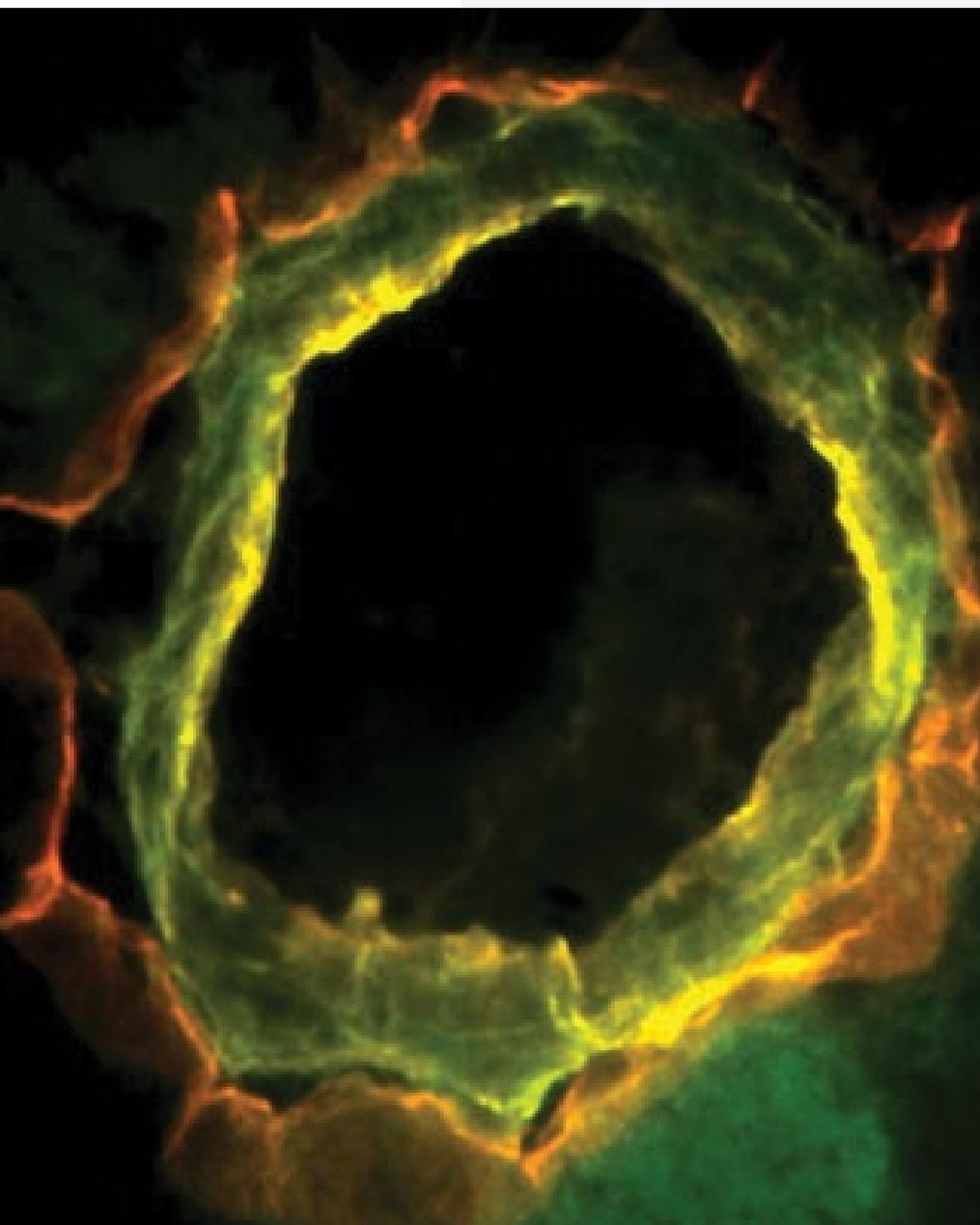
- › Ion channel and ion channel receptor physiology
- › Mechanism of action of therapeutic candidates on single cells and neuronal networks
- › Electrophysiology methods:
 - manual and automatic patch clamp systems
 - multi-electrode arrays (MEA)
- › Library screening for ion channel modulation: automatic patch clamp systems (Patch Xpress 7000A)
- › Primary neuronal cells and brain slice models

***in vitro* pharmacology**

- › Cellular and molecular assays to measure receptor binding, drug compound uptake, transcytosis, mechanism of action, drug target interaction, and toxicity
- › Protein assays such as live protein tracking, protein arrays, immunocytochemistry, Western blot, and ELISA
- › Assessment of receptor signaling pathways in cells for functional analysis of therapeutic candidates (phosphorylation, dephosphorylation, second messengers)
- › Rat and human stem cell-derived blood-brain barrier models
- › Evaluation of drug permeation across the blood-brain barrier in *in vitro* models
- › Drug evaluation in organoids: neuronal, glial, cardiac

Cancer immunology and immunomodulation

- › *in vitro* and *in vivo* models to evaluate immunotherapy and immunomodulation strategies
- › Development, optimization and qualification of assays to monitor innate, humoral and cell-mediated immunity, immunostimulation and immunotoxicity
- › Industry standard biochemical and immunological analysis of different body fluids including blood, urine and saliva samples
- › Mechanism of action studies to evaluate stimulation in various cell types
- › Systems biology to evaluate immune cell interactions for discovery of novel immunotherapy/immunomodulatory targets
- › Flow cytometry and cell sorting capabilities: up to 18 colours (Beckton Dickinson LRS Fortessa and FACSCanto), 6 way sorting (Beckman Coulter MoFlo Astrios)





R&D expertise – *in vivo*

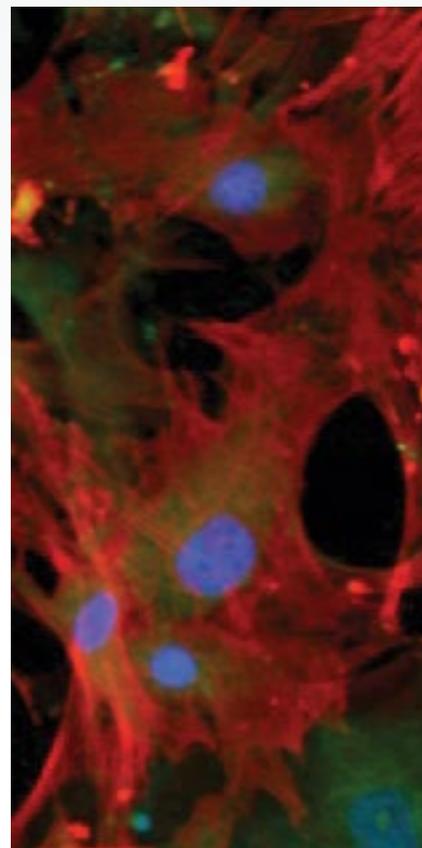
PK/PD modelling

- › Early pharmacodynamic read outs
- › Oncology efficacy models: xenograph, syngeneic, subcutaneous, orthotopic, bioluminescent
- › Pharmacokinetics and biodistribution
- › PK/PD modelling for experimental design and dose regimen (selection, scheduling, escalation)
- › Target engagement and therapy-monitoring biomarkers
- › Pathogen models and aerosol challenge
- › Immunomodulation models
- › Non-GLP immunotoxicology (ITOX) and safety
- › Data to support Clinical Trial Applications (CTA) , Module 4, Non-Clinical Study Reports:

- 4.2.1 Pharmacology
- 4.2.2 Pharmacokinetics
- 4.2.3 Toxicology
- › Preclinical to clinical biomarker translation and qualification

CNS pharmacology

- › CNS disease models: Alzheimer's, Parkinson's, stroke, epilepsy, traumatic brain injury (TBI)
- › Pharmacodynamic behavior and response models: anxiety, learning and memory, motor function, pain
- › Drug administration: intracerebral injection (IC and ICV), intravenous, subcutaneous, nasal, oral, mini-pump infusion
- › Ability of therapeutic molecules to cross the blood-brain barrier and pharmacological responses (efficacy and safety):



- Acute and serial collection of cerebrospinal fluid (CSF)
- *in situ* brain perfusion
- Collection of brain tissue for histochemical and biochemical analysis of various brain regions
- Analysis of drug concentration and biomarkers by mass spectroscopy MRM, ELISA and Western blot
- › Assessment of receptor signaling pathways in *ex vivo* brain tissue for functional analysis of target engagement (phosphorylation, de-phosphorylation, second messengers)

Preclinical imaging

- › *in vivo* imaging: molecular, anatomical, and functional:
 - eXplore Optix time domain optical imager for biodistribution
 - IVIS imaging system for bioluminescence and fluorescence
 - Micro computed tomography (microCT) for bone, tumour, and vascular analysis
- › Zeiss LSM multi-photon system for *in vivo* cranial window studies
- › Imaging, pharmacokinetics and biodistribution *in vivo*
- › Imaging probe development
- › Histology and immunostaining
- › Microscopy

- Epi-fluorescent microscopy: Widefield Olympus IX 81 Lifetime CellSens system
- Epi-fluorescent microscopy for calcium ion imaging: Widefield Olympus IX 81 Lifetime CellSens high-speed ratiometric imaging with infrared fluorescent capability
- Confocal microscopy: FV1000 Olympus confocal laser scanning microscope
- High-content screening: ImageXpress micro XLS widefield imaging system
- Stereology microscopy: Olympus BX 50
- › Image analysis: stereology, quantitation, specialized software packages

Interested?

We can help you determine how your molecule behaves *in vitro* and *in vivo*. Contact our experts today!



CONTACT

Jean Labrecque

Team Leader,
Primary Assays
Tel.: 514-240-3300
Jean.Labrecque@cnrc-nrc.gc.ca

Risini Weeratna

Team Leader,
Cancer Immunology
Tel.: 613-990-7934
Risini.Weeratna@nrc-cnrc.gc.ca

Simon Drouin

Team Leader,
Genomics
Tel.: 514-496-6370
Simon.Drouin@cnrc-nrc.gc.ca

Maria Moreno

Section Head,
In Vivo Pharmacology
Tel.: 613-990-0829
Maria.Moreno@nrc-cnrc.gc.ca

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