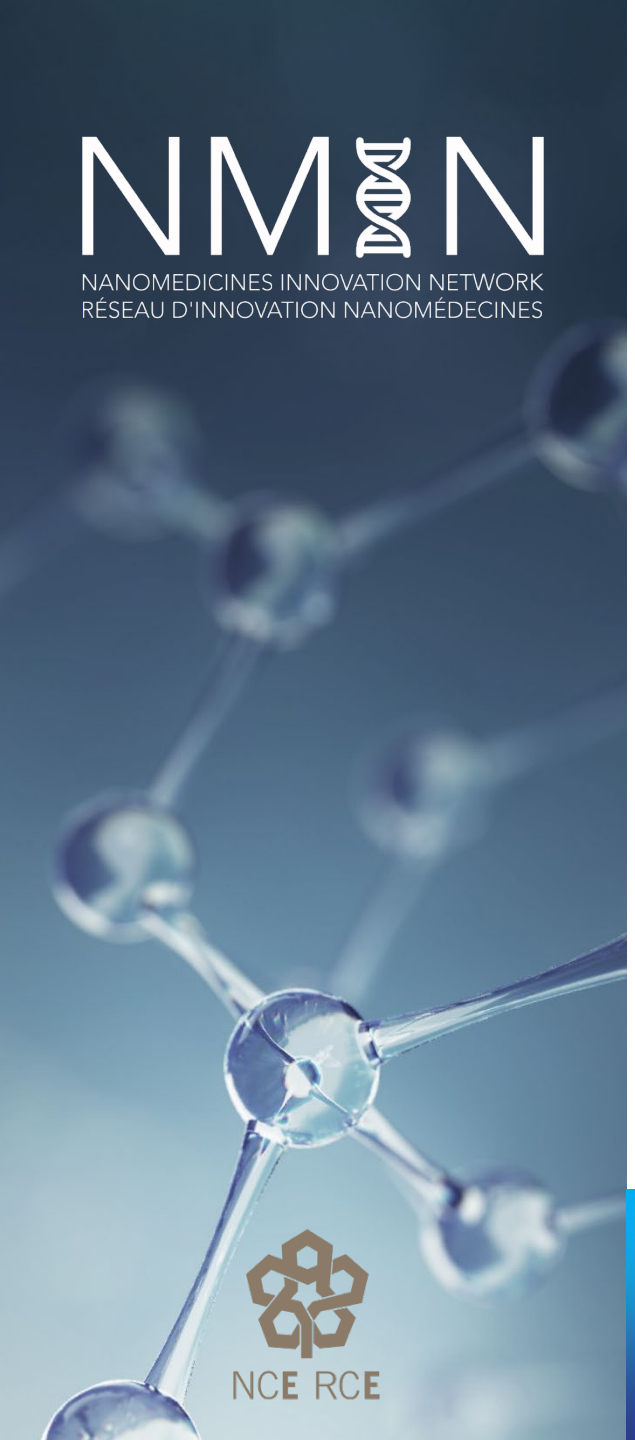

Nanomedicines Innovation Network (NMIN)

PharmaCore

Preclinical, Scale-Up Manufacturing and Project Management Core Facility

Principal Investigators: Dr. Marcel Bally & Dr. Shyh-Dar Li
PharmaCore Operational Lead: Dr. Nancy Dos Santos
(Email: ndossantos@bccrc.ca)

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Mission

To provide support to **NMIN investigators and research partners** to facilitate the preclinical and clinical development of novel nanomedicines through **formulation development, characterization, biological activity in cell models and animals models** as well as **manufacturing** designed to meet regulatory requirements to advance new therapeutics from bench to clinic

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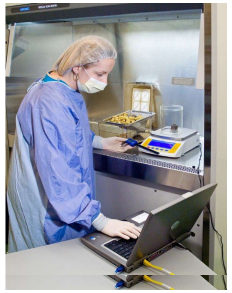
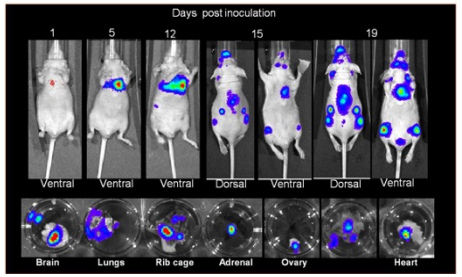
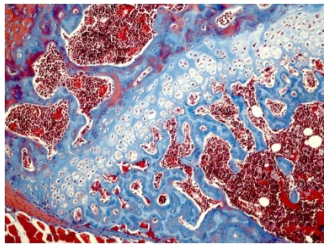
Moving from Bench to Clinic

In Vitro





In Vivo



Safety Pharmacology / *GLP

Accredited by Standards Council of Canada

Discovery → Preclinical Studies → Clinical Studies- Phase I-III → Regulatory Approval

Formulation / Analytical

Scale up/GMP Manufacturing

Quality Management

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Drug Development Process Flow

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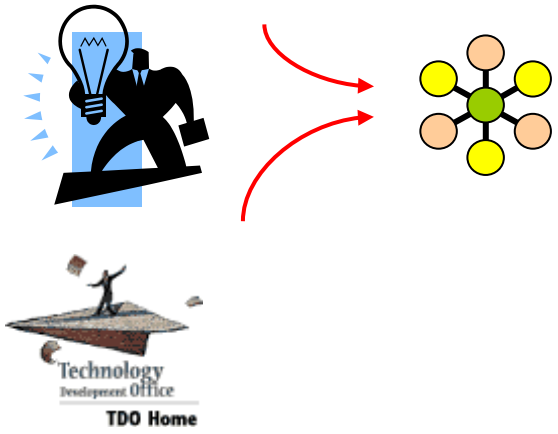

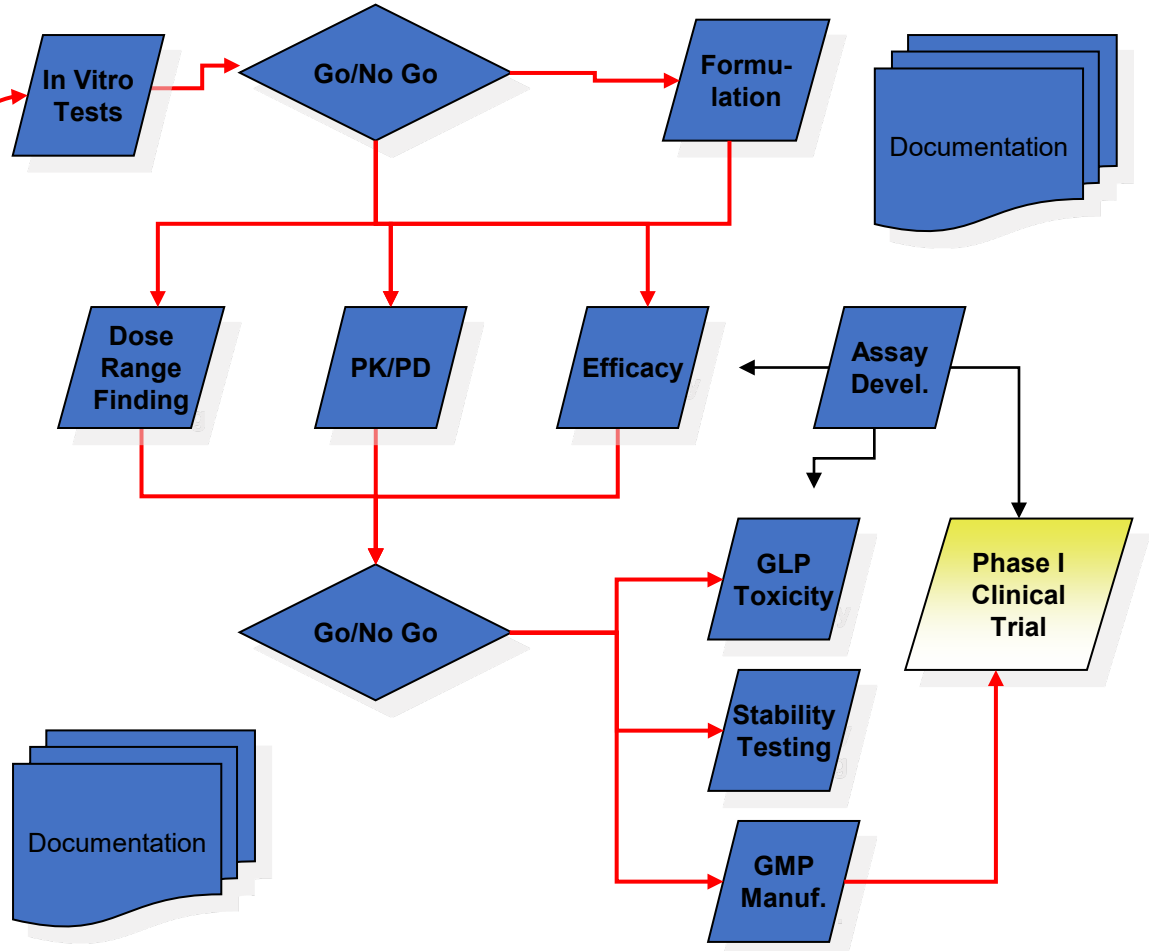

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Drug Discovery – In Vitro

- **Cytotoxicity**
  - MTT
  - Alamar Blue/Cell Titre Glo
  - IN CELL Analyzer (Live/Dead)
  - Incucyte
- **Drug Combination Screens**
- **IN CELL® High Content Screening**
- **Tissue Culture Assays (FACs)**
- **Western Blotting**
- **Other**

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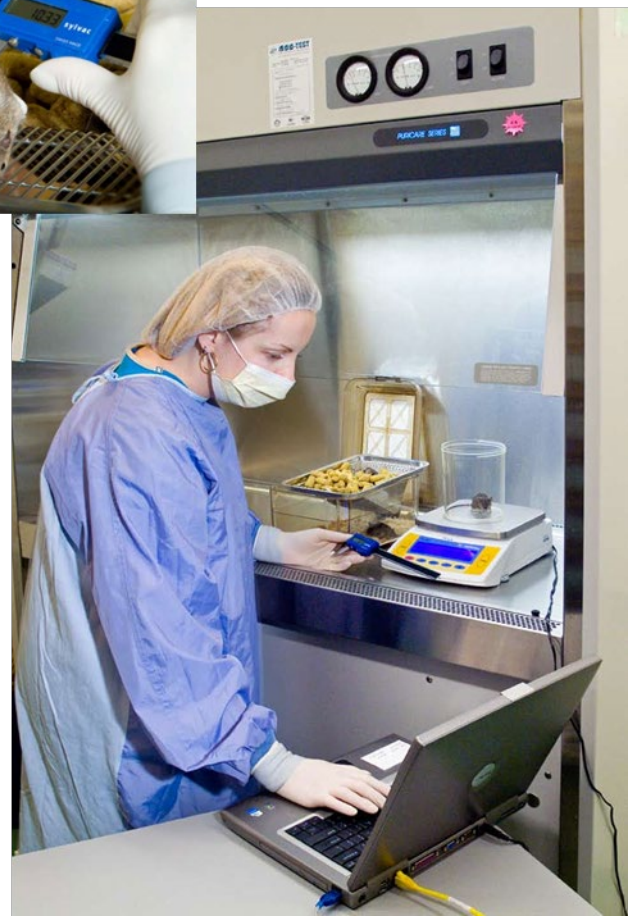
Pre-Clinical Studies - In Vivo

- **Tolerability (DRF, MTD)**
- **Pharmacokinetic**
- **Biodistribution**
- **Pharmacokinetics / Pharmacodynamics**
- **Model Development**
- **Efficacy**
  - Syngeneic tumour models
  - Xenograft models
  - Orthotopic
  - Patient Derived Xenografts (pancreatic)
  - Other



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Pre-Clinical In Vivo Imaging

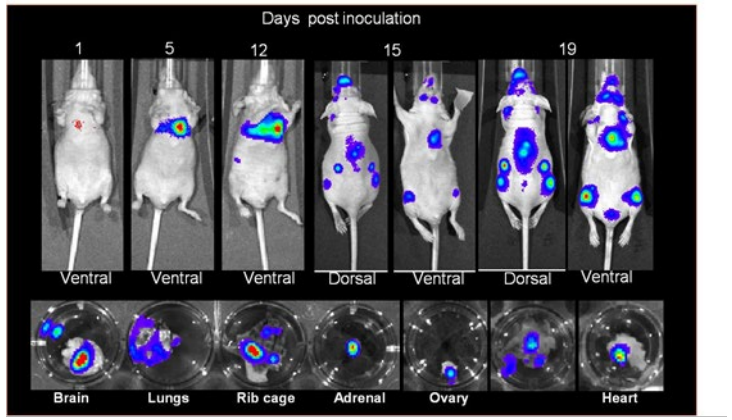
- ***in vitro* or *in vivo* Imaging**

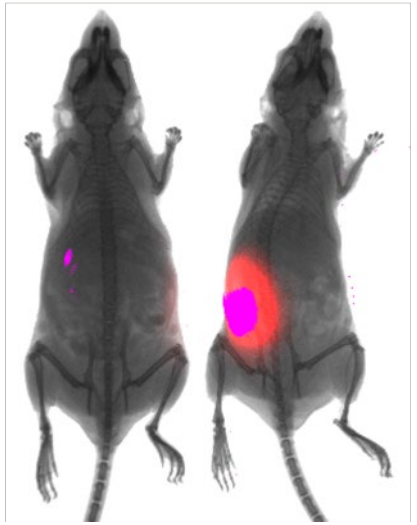
- **IVIS**
  - Non-invasive live imaging
  - Bioluminescence and fluorescence

- **Multispectral System**
  - Additional x-ray overlay possible
  -

- **MicroPET/CT**

- **MRI**





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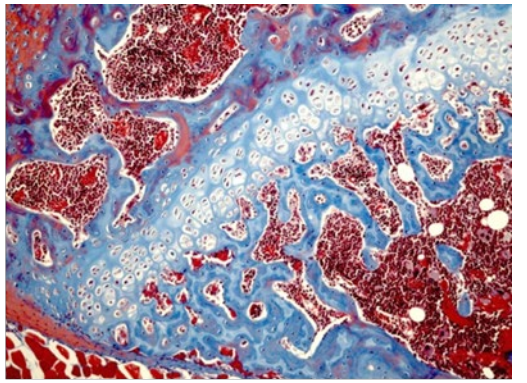
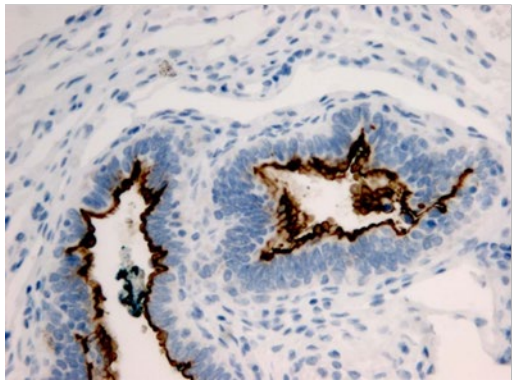
GLP Toxicology / Safety Pharmacology

- SOP driven (QMU)
- Fulfills requirements for IND or CTA for rodent studies (manufacturing)
- Single or repeat DRF
- Acute, chronic or subchronic toxicity
- Includes comprehensive CBC/Diff and blood chemistry analysis
- Histopathology
- Accredited by Standards Council of Canada





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GMP Manufacturing - A Brief History

- The Investigational Drug Program was established in 1995 with initial funding and loans by the BC Ministry of Special Programs and Western Economic Diversification. The cost of building the infrastructure was minimal, approximately $350K

- Maximum capacity reached by 1997

- To date over 125 successful parenteral batches to date

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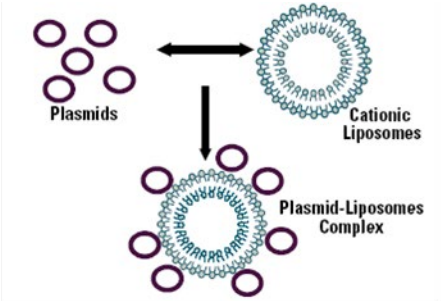
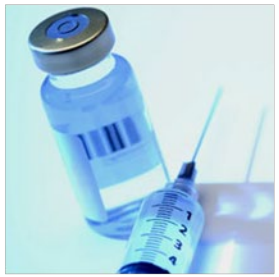
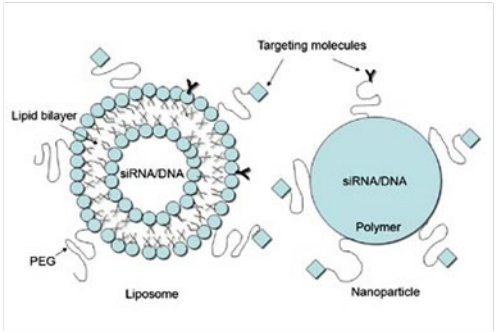
Manufacturing of Nanomedicines

- Liposomes
- Liposomal cytotoxics
  - Topotecan
  - Vinorelbine
  - Vincristine
  - Vinblastine
  - Doxorubicin
  - Cephalotaxine
- Liposomal therapeutics (Non-cytotoxic)
- Visudyne
- Oligonucleotides, ASO, RNAi
- Liposomal siRNA, mRNA
- Liposomal plasmids
- Small molecules







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Prep Room

Batching Room

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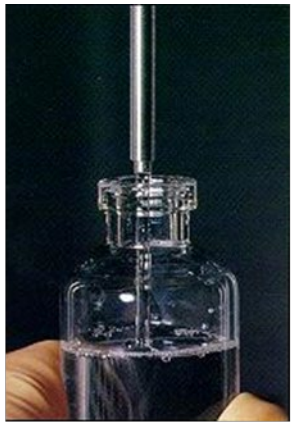
GMP Manufacturing

- GMP and bench batches of formulated pharmaceutical agents, both conventional aqueous-based and emulsions



- Product inspection & labelling

- Stability protocols
- Documentation, Documentation

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Storage / Archiving Facilities

- Storage of Raw Materials, supplies and final drug products in controlled access area
- Emergency power and 24 hr temperature monitoring
- Equipment rooms are monitored for temperature and humidity
- Storage of Final Product
- Stability storage and sampling
- Quarantine and released raw materials & GLP tox materials

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Quality Control

- Approves or rejects manufactured drug products
- Oversees adequate laboratory facilities
- Qualification and maintenance of equipment & validation of testing methods
- Documentation control system
- Oversees stability testing and reporting
- Responsible for training related to GxP
- Development and implementation of SOPs, validation/study/qualification protocols and reports

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Quality Assurance

- Assess the conformance of activities in the quality management systems in place, including:
- Conducts audits and inspections (both internal and external)
- Monitors for compliance with SOPs GMP and GLP Documentation review for compliance with OECD, Health Canada and FDA regulations
- Archive Management
- Document control
- Change control

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Thank you

Team Members

Marcel Bally
Nicole Wretham
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Norman Chow
Brent Sutherland
Tetyana Denyssevych
Sharon Smith
Susie Yoo
Beata Kosciolek

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