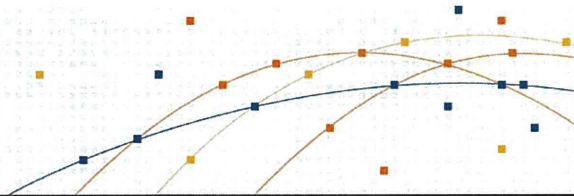


Agreement Process - NExT

- Applications – SEP members and Federal employees are subject to Confidentiality in relation to NExT Applications. Conflict of Interest (COI) conditions do apply.
- CDA's (Confidential Disclosure Agreements) – Necessary when bringing in non-NExT staff and outside experts for additional review.
- Collaborative Agreements – A variety of mechanisms necessary to memorialize interactions between the applicant and the NExT program, will vary based on stage/type of project. (CBC Participant's agreement, MTA, CTA, Collaborative Agreement, CRADA).

CDRD's Mission, Model and Milestones

March 2012



The Need for CDRD

- Governments continue to increase investment in health research but returns have not been maximized
- Venture capital investments continue to decline
- A gap between academic discovery and commercialization by industry persists
- Global pharma faces patent expirations and escalating drug development costs

Bridging the Gap Between Discovery and Commercialization



Discovery

Commercialization Gap
Infrastructure, expertise, funding

Commercialization

- Academic research doesn't take discoveries to an 'investable' point
- Traditional granting sources and angel funds are not sufficient to fuel the growth of the life sciences industry given the lack of venture funds
- Commercialization gap exists between discovery and commercial opportunity

The Centre for Drug Research and Development Mandate

CDRD was created to de-risk promising discoveries stemming from publicly-funded health research and transform them into commercially viable opportunities for the private sector....

The **Private Sector** is then responsible (and now much better positioned) to develop them into new treatments for patients....

And **Government** realizes the maximum economic and societal ROI on their research investment....and (hopefully) re-invests back into research.

Vision and Mission

Vision

To transform the culture of scientific innovation and commercialization impacting human health

Mission

- *To be a global leader in translating academic discoveries into new medicines*
- *To bridge the commercialization gap between drug discovery and private investment by creating partnerships between academia, industry, foundations and government*
- *To provide the next generation of uniquely-trained highly qualified personnel to drive the development of the medicines of tomorrow*

This Type of Translational Research Vehicle is Critical

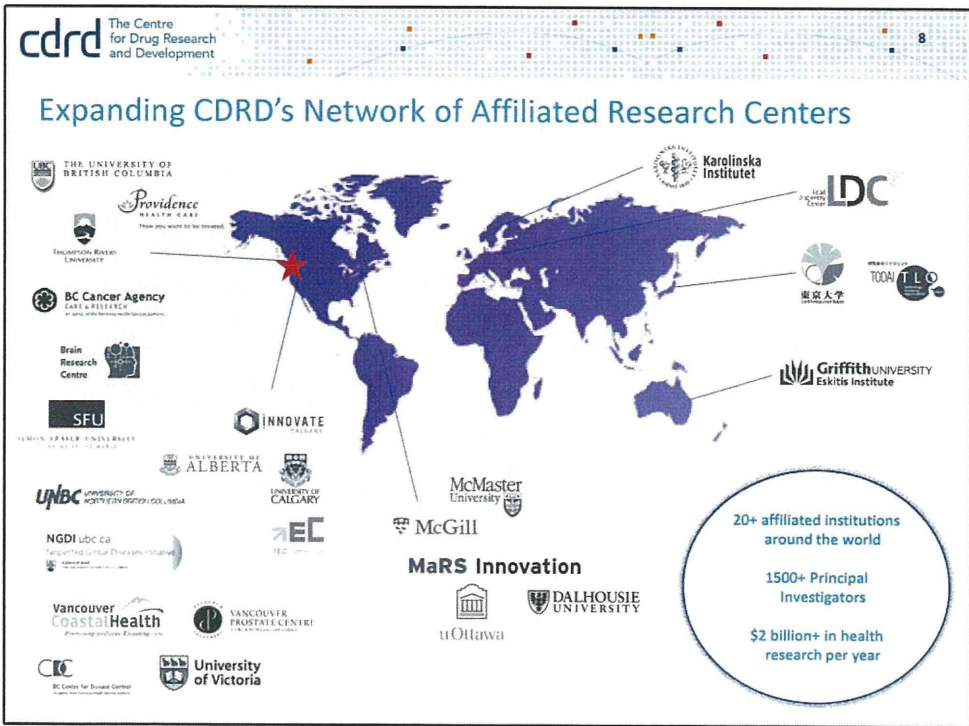
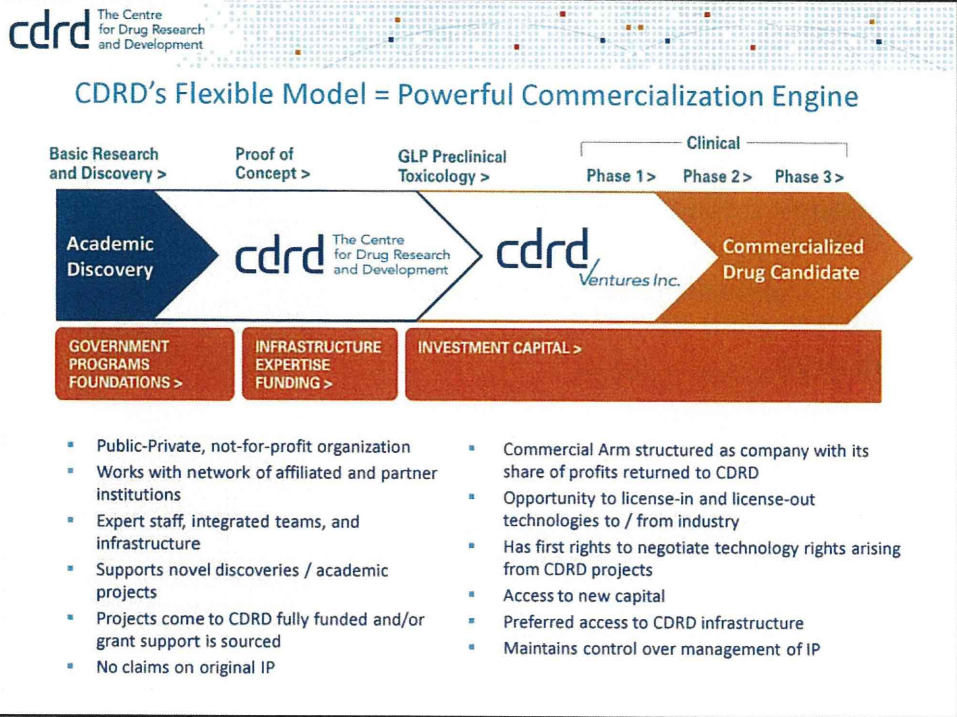
Academia Needs

- Funding for proof-of-concept studies to the level required for validation
- Drug development and commercialization expertise
- Specialized equipment and resources such as screening facilities and libraries

cdprd

Industry Needs

- Efficient access to innovative early-stage technologies
- An avenue to de-risk and validate those technologies
- Technology development to be managed by industry standards



These Affiliated Institutions Feed CDRD's Project Pipeline

- Collaborate with principal investigators to identify projects
- Screened against rigorous scientific and business criteria for commercial potential
- Full drug development platform
- *Outcomes-focused drug development under professional project management is then undertaken.*



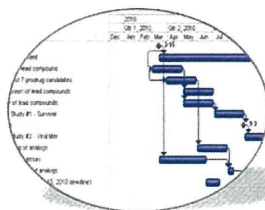
CDRD's Key Success Factors

Pipeline



- Extensive network of affiliate and partner institutions across Canada
- Dedicated search/evaluation team in targeted therapeutic areas
- Pipeline of novel targets / MOAs ("mechanisms of action")
- Expanding key strategic partnerships internationally

Process



- High industry standards of project management applied to all CDRD projects
 - Clearly articulated go/no-go decision points
 - GANTT chart review of progress and budgets
- Rigorous commercial and scientific evaluation
 - Clear understanding of unmet medical need
 - Clinical input from KOLs
 - Development of target product profile
 - Identification of critical experiments
 - Development of technology and commercialization dossiers

Partnerships



- Strategic Pharma Partners and Innovative Joint Development Funds
 -
 -
 -
 -
- Academic Institutions / Translational Centres / Centres of Excellence
 -
 -
 -
 -
- Local Biotech

Innovation and CVI Funds Raised with Partners



Pfizer-CDRD
Innovation Fund



Genome British Columbia

Genome BC-CDRD
Development Fund

Johnson & Johnson



Western Canada
Innovation Fund



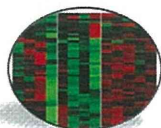
Roche Global CVI Fund

CDRD

CVI

CDRD Scientific Divisions

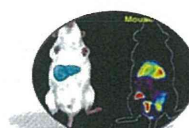
Target Validation



Drug Screening



Pharmacology/Toxicology



Drug Delivery



Medicinal Chemistry



Biologics



Each With Access to Drug Development Platforms at CDRD and Partner Sites

- **CDRD headquarters** - UBC Campus
 - **CDRD animal facilities** - BC Cancer Agency and Centre for Disease Modeling, UBC
 - **CDRD scale-up chemistry laboratory** - Simon Fraser University
-
- **Metabolomics Innovation Centre, Universities of Alberta and Victoria**
 - **Michael Smith Genome Sciences Centre, BC Cancer Agency**
 - **Eskitis Institute for Cell and Molecular Therapies, Griffith University (Natural Products Library)**
 - **Genome BC Proteomics Centre, University of Victoria**
 - **Centre for High-Throughput Biology, UBC**

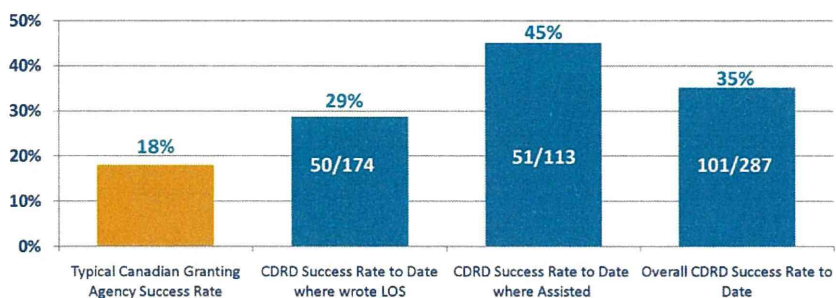
Project Selection

Key requirements:

- ✓ Willing and engaged Principal Investigator(s)
- ✓ Excellent, innovative science
- ✓ The potential to address an unmet medical need
- ✓ The potential for a solid IP position
- ✓ The potential to be commercialized
- ✓ Critical question(s) / experiment(s) can be identified
- ✓ Fit with CDRD's capabilities and capacity
- ✓ Fit within the strategic vision of CDRD

Grant Funding Success to Date

- Supported 287 grant applications that secured **a total of \$94M**
 - 35% overall success rate (101 successful applications)
 - Almost 2x the national average
 - 29% success rate where CDRD only supplied a letter of support
 - 45% success rate where CDRD played an active role in preparing the grant



Benefits of Working with CDRD (PI Perspective)

- Access to infrastructure and expertise that complements PI
- Project results can enhance PI's ability to secure research grants
- Ability to leverage additional grant support, including non-traditional
- Provide students with greater learning opportunities
- Ability to continue to stay with technology as it advances towards commercialization
- Potential for greater return

Benefits of Working with CDRD (Industry Perspective)

- One-stop, structured access to world class scientists and innovation pipeline in Canada and world-wide with access to:
 - NCEs
 - novel targets
 - novel mechanisms
 - validated data
 - discovery programs
- Transparency in use of funding and in progress of research
- Focused science with clear critical path to a product

Benefits of Working with CDRD (Industry Perspective) cont'd

- De-risking of earlier-stage opportunities
 - Cost-effective use of resources, experience, and infrastructure
 - Value creation and risk sharing with minimal dilution to investors
 - Advantage of tax benefits/government incentives
 - Sophisticated management of projects that are milestone-driven and outcomes-focused
 - Timely interim reporting
 - Assembly of a final dossier/package to facilitate efficient technology transfer

Highlights of Outcomes and Achievements to Date

Intermediates

Establishing Translational Research Infrastructure

- ✓ Built 20,000 sq. ft. of lab space with state-of-the-art equipment

Recruiting Talent

- ✓ Attracted ~85 highly skilled personnel with strong industry experience

Establishing and Expanding Provincial, National and International Affiliations

- ✓ Established partnerships with 20+ affiliated institutions (4 continents)

Building a Comprehensive Drug Development Platform for Small Molecules, and Building Competitive Advantage in Therapeutic Antibodies

- ✓ Established new biologics platform to develop therapeutic antibodies

Highlights of Outcomes and Achievements to Date

Endpoints

Advancing Project Development and Commercialization

- ✓ Supported 80 technologies, engaged some 490 researchers
- ✓ Advanced 4 technologies to be out-licensed to the private sector or optioned by CDRD Ventures

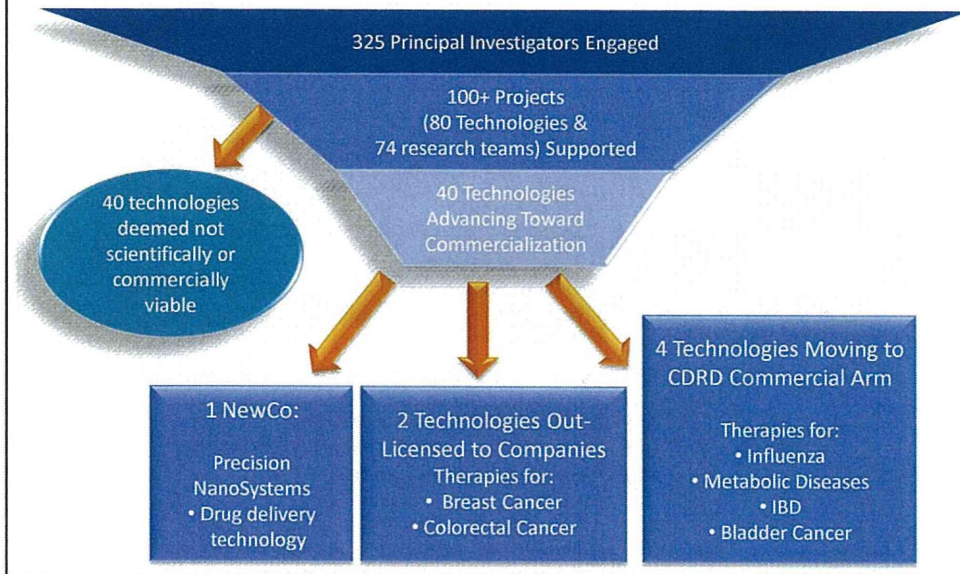
Attracting Private Sector Investment to Canada

- ✓ Attracted investment from top-tier global partners, Pfizer, Roche, J&J

Addressing Shortage of Highly Qualified Personnel

- ✓ Trained 83 Post-Doctoral Fellows, co-op students, and interns through our unique training program

Advancing Projects Toward Commercialization



CDRD's Unique Competitive Advantage

- Shared vision of government, industry and academia
- Commercialization as the single mandate – converting public investment in research into economic output and new therapies for patients
- National organization headquartered in BC, modernizing and innovating Canadian healthcare research
 - A Canadian Centre of Excellence for Commercialization and Research (CECR)
- Sole organization of its kind in Canada
 - The only fully-integrated centre with the expertise and infrastructure to source, evaluate, develop and commercialize new healthcare products
- Diverse number of global private and public sector partners
- Not-for-profit entity coupled with a commercial arm to support self-sustainability.

In Conclusion...Factors for Success

People



Place



Projects



Success requires an effective well-resourced interface between industry and academia with critical infrastructure, expertise and project pipeline.

Partnerships are Core to All of Our Success

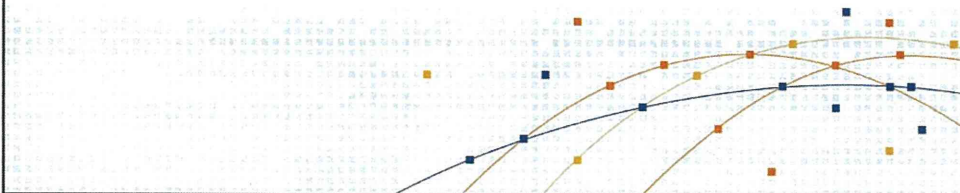
cdrrd The Centre for Drug Research and Development
Affiliates / Funders / Partners

Partners include:

- UNIVERSITY OF CALGARY
- THE UNIVERSITY OF BRITISH COLUMBIA
- SFU
- TEC Edmonton
- INNOVATE CALGARY
- Johnson-Johnson
- BC Cancer Agency CARE + RESEARCH
- University of Victoria
- Angiotech
- MERCK
- UOttawa
- DALHOUSIE UNIVERSITY
- XENON
- Pfizer
- McMaster University
- THOMPSON RIVERS UNIVERSITY
- Griffith UNIVERSITY Eskitis Institute
- BRITISH COLUMBIA
- Roche
- MaRS Innovation
- UNBC UNIVERSITY OF SOUTHERN BRITISH COLUMBIA
- Alberta
- NGDI ubc.ca
- 東京大学
- LDC
- VANCOUVER PROSTATE CENTRE
- CBC
- PANAMP
- Canada
- Western Economic Diversification Canada
- Brain Research Centre
- BC Centre for Disease Control
- Michael Smith Foundation for Health Research
- Provincial Health Services Authority
- Karolinska Institutet
- GenomeBritishColumbia
- Women's Health Research Centre
- Providence HEALTH CARE
- Vancouver Coastal Health
- CHILDREN'S HOSPITAL
- UNIVERSITY OF ALBERTA
- CIHR IRSC
- Canada Foundation for Innovation

cdrd The Centre
for Drug Research
and Development
Transforming Discovery into Opportunity

For further information on The Centre for Drug Research and Development,
please visit www.cdrd.ca





Creating an Unsurpassed Network of Animal Facilities & Expertise



Dr. Chris Harvey-Clark
Executive Director, BC Preclinical Research Consortium
Director, UBC Animal Care Centre
chclark@exchange.ubc.ca



BC Preclinical Research Consortium; Unique in Canada

A one-stop research toolbox

- ❑ Facilities, Equipment and Highly Qualified Personnel
- ❑ Creates a level playing field among BC academic institutions
- ❑ Industry access to specialised facilities and services
- ❑ Opportunities for collaboration and/or fee for service activities
- ❑ Operationally governed by 3 Executive Directors
- ❑ responsive to an advisory Managing Board representing all institutional members

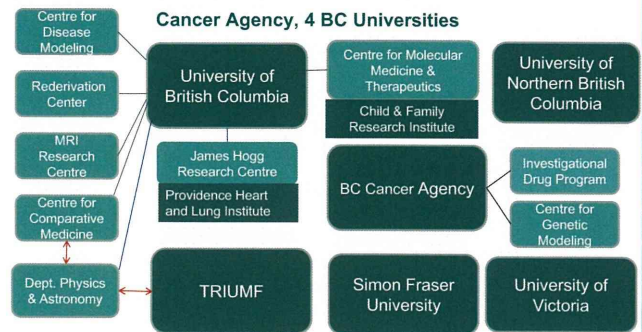


BC PRC MISSION

- Develop internationally competitive collaborative research network
- Provide cutting-edge technologies for the production of in vivo models of human disease that will revolutionize health care.
- Enable translational research critical for commercial opportunities in biotechnology



BCPRC MEMBERS: 7 UBC facilities, 4 Hospitals,



TransARC Service Core

Directed by:



Dr. Wilf Jefferies
Executive Director/
Director, TransARC Network

- Four research facilities offering a range of transgenic/*in vitro* reproductive technologies.



Embryonic Stem Cell Manipulation

Genetically Modified Animal Models

Cryopreservation

Rederivation



Pharmacology Service Core

Offering Solutions that Advance the Drug Discovery and Development Process including Research Models and Services

Directed by:

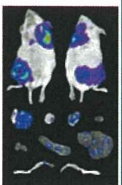


Dawn Waterhouse
Executive Director/
Director, Pharmacology



Marcel Bally
Founding Director

- In Vitro Screening
- In Vivo Pharmacology
- Rodent Surgical Models
- Rodent Tumor Models
- Rodent Cardiovascular Models
- Behavioural Testing
- Metabolic Caging
- Telemetry
- GLP Toxicology
- Validated Methods
- cGMP Parental Manufacturing
- Veterinary Pathology Services
- Drug Development Consulting



Pharmacology Core Services are offered through BC Cancer's Investigational Drug Program , UBC Centre for Disease Modeling, the James Hogg Research Centre and the UBC MRI Research Centre, which operate under a single management structure



Imaging

in vivo imaging of biological processes and structures at 4 locations; CCM, MRI Center, BC Cancer, St Pauls

Western Canada's first trimodal (all-in-one) SPECT/PET/CT preclinical imaging system, allowing three-dimensional tissue imaging of active biological processes using novel isotopes developed at TRIUMF.

- > IVIS 200 & Lumina Systems for Luminescent & Fluorescent tagged cells
- > CRI Maestro imaging system multiplexed fluorescence imaging
- > Siemens multi-modality Inveon® small animal PET-CT scanner
- > Intravital Microscopy for in vivo phenotyping
- > 7.0 Tesla Bruker Biospec MRI Scanner
- > Digital radiography, ultrasonography, fluoroscopy – large animals (CCM)
- > Kodak in-vivo Multispectral System FX
- > Custom 2-photon microscopes
- > Echocardiography & non invasive Blood Pressure Monitoring
- > Rodent Heart Perimed Doppler Imaging



Center for Comparative Medicine (CCM)

State-of-the-art 5000 gsm large animal translational research facility

Large animal and zoological species, CL II containment



CCM Capabilities:

- **Full Containment Level 2 (CL2)** area for housing and surgical/diagnostic procedures on non-human primates and sheep
- Conventional and spf barrier pigs, rabbits, gps, small animal species
- **Imaging** – digital radiography (X-rays), ultrasonography, fluoroscopy, SPECT
- **Training core** – 8 surgical stations, capability for real time projection of techniques and procedures
- **Surgical Theaters** – multistation CL I and II, transplant capable, full physiological monitoring, .
- **Research Procedure rooms**
- **Full diagnostic suite, Pathology services; board certified Veterinary Pathologist on staff, consulting pathology services including** necropsies/perfusion/tissue collection/ histopathological analysis
- **Highly Qualified Personnel:** veterinarians, managers, animal health technologists (AHTs), and technical staff experienced in a full suite of research procedures and support work



Summary: Services and Technology

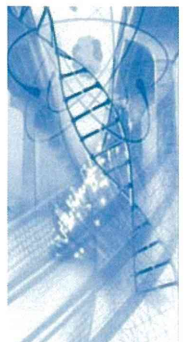


Organizations & Industry Utilizing Core Expertise: Pharmacology & Transgenics



Strategic Initiatives

- > **Grow toolbox of facilities, equipment, HQP and services**
 - > Phenogenomics core
 - > Imaging Core
 - > Modified Barrier Facility under construction-opens 2012
 - > CL III services in FINDER
 - > Ongoing in vivo techniques training workshops offered year round
- > **Building an Asset Map of preclinical resources and expertise**
- > **CALAS 2012 Vancouver June 2-5**



Thank you!



Internet: www.bcprc.ca
Dr. Samudra Dissanayake,
Samudra.dissanayake@ubc.ca

Pre-clinical Positron Emission Tomography

Vesna Sossi
 Professor
 Physics and Astronomy
 PET Director
 Univ. of British Columbia, Vancouver, Canada



PET program at UBC/TRIUMF (background)

Established in ~ 1985: collaboration between UBC (Dr. Brian Pate) and TRIUMF

First human scanner built at TRIUMF (Dr. J Rogers)



Next human (brain) PET (~commercial) scanners (ECAT 953B, *HRRT*, *GE Advance*)

Acquired a dedicated microPET ~ 2003



Program supported via research grants:

Pacific Parkinson's Research Centre providing main source of funding and medical scientific directions (D Calne, AJ Stoessel)

Mood disorders

Dementias (ADNI) + emerging research areas

Chemistry (and cyclotron supported by Triumf) located at Triumf (3 chemists supported by PPRC) – imaging (and **imaging physics** (NSERC+ others) V Sossi) at UBC

Tracers routinely used

Dopaminergic

- ¹⁸F-fluorodopa
- ¹¹C-dihydrotetabenazine
- ¹¹C-methylphenidate
- ¹¹C-raclopride
- ¹¹C-schering

Serotonergic

- ¹¹C-DASB
- ¹⁸F-setoperone

Noradrenergic

- ¹¹C-MRB
- ¹¹C-Yohimbine

Cholinergic

- ¹¹C-PMP

Plaque detection

- ¹¹C-PIB

Inflammation

- ¹¹C-PK11195

Energy metabolism

- ¹⁸F-FDG

We perform **quantitative analysis** for each tracer to obtain uptake rate constants, binding potentials, etc

Pre-clinical imaging resources

Imaging (V Sossi)

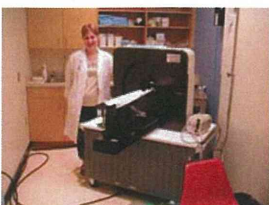
- Dedicated **microPET** (~ (1.5mm)³ resolution) located at **UBC**

Autoradiography
 Microdialysis
 Well counter/dose calibrator
 Surgery room
 Behavioral Room

- **microSPECT/PET + CT** (Milabs VECTor - CFI funds obtained (P.I. V Sossi, co-app U. Hafeli, P Schaffer) (<(1mm)³ resolution) – allows imaging of single gamma emitting radiotracers located at **CCM**

Novel radiotracer development(P. Schaffer)

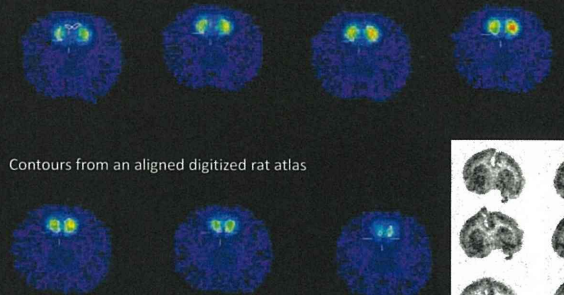
microPET Siemens Focus 120



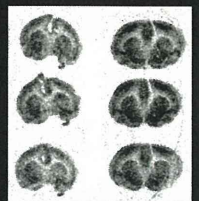
Typical imaging protocol:

- Animal anesthetized
- Positioned in the scanner
- Injected into tail vein (most often)
- Scans last ~ 1hr (depending on tracer and imaging protocol) – Animal being monitored for vital signs
- Data are acquired in list mode → we can 'frame' the data in an arbitrary way AFTER acquisition

RAT striatum 7 PET slices on the **Focus 120** 0.8 mm apart; resolution ~ (1.5mm)³

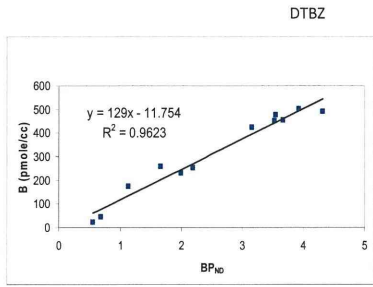


Contours from an aligned digitized rat atlas



autoradiography

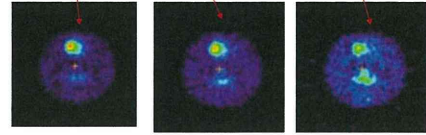
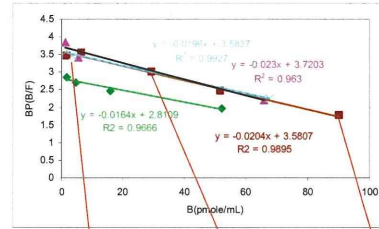
Relation between autoradiographic binding and PET (6-OHDA PD model)
Lesion severity up to ~90%



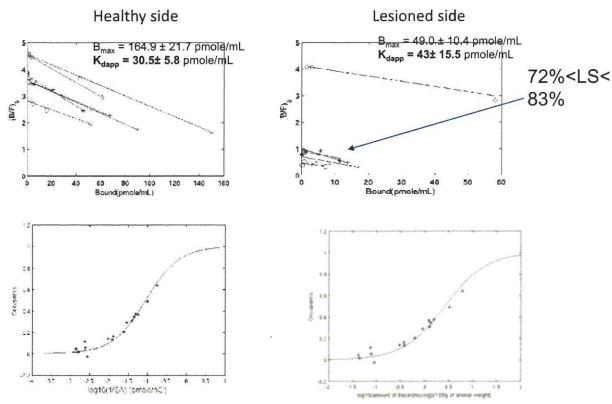
Topping et al Synapse 2010

Mass effect

Occupancy studies for VMAT2 DTBZ – Scatchard analysis



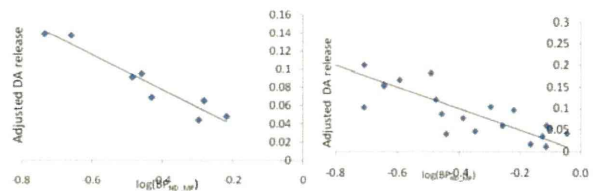
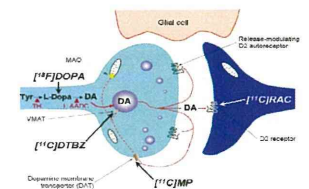
VMAT2 - DTBZ Scatchard analysis on unilaterally lesioned rats (V.Sossi, et al, JCBF 2007)



Useful range of SA for DTBZ

Question

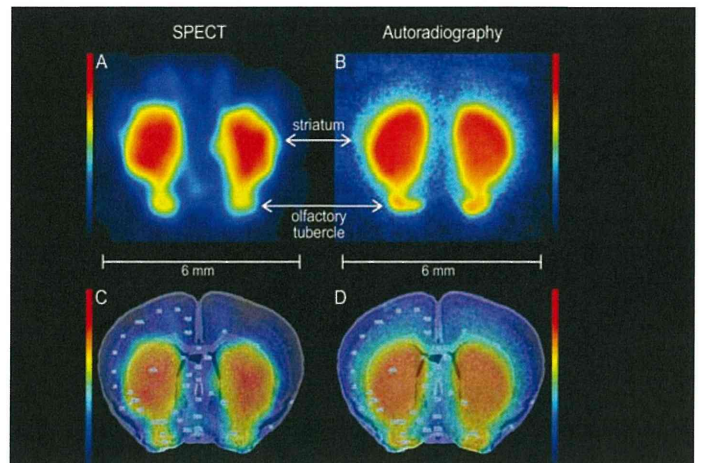
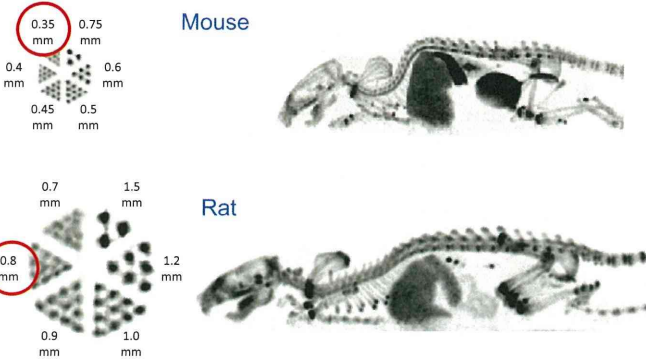
What is the role of DAT in Parkinson's Disease?



Humans (Sossi Annals of Neurology 2007)

Rats (Sossi J Neurochem 2009)

Milabs VECTOR
Sub-mm resolution total body imaging



nature publishing group

Courtesy of F. Beekman