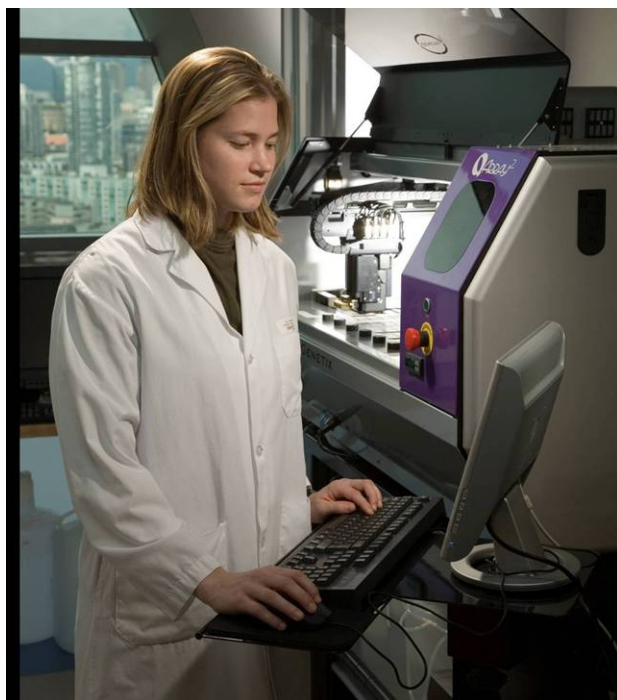


CANCER GENETICS & DEVELOPMENTAL BIOLOGY

BCCA CANCER RESEARCH CENTRE

675 West 10th Avenue, Vancouver, BC, V5Z 1L3

Telephone: 604-675-8111



Our Research Focus:

We are interested in the discovery of genetic changes and signaling and metabolic pathways associated with cancer and tumor progression. In partnership with others, we seek to exploit these discoveries in the development of new diagnostic and therapeutic strategies. Current activities include:

1. Identification and characterization of cancer stem cells using transgenic mouse models;
2. Elucidating the mechanism of signal transduction mediated by the extracellular matrix (ECM) particularly the family of integral plasma membrane receptors called integrins and integrin-linked kinases;
3. Establishing novel models of cancer metastasis, and identifying genes involved in the establishment of organ-specific metastasis;
4. Investigating the family of energy dependent ATP-binding membrane transport proteins associated with chemotherapy resistance, hormone secretion and programmed cell death;
5. Developing novel cell-based screens to discover new targets and therapeutics against cancer cell invasion and survival, and tumour angiogenesis; and
6. Identifying genetic and epigenetic changes that parallel cancer progression and developing molecular systems approaches to decipher the biological consequences causal genetic events.

Progress Highlights during 2005/2006:

- Identification of cancer cell dependent signaling pathways and their inhibition, with novel small molecule therapeutics resulting in tumor growth arrest;
- Identification of a gene involved in sudden heart failure;
- Development of whole genome methylation profile analysis;
- Showed the prognostic value of genetic markers in oral cancer progression.

- Novel technology for identifying genetic changes in premalignant lesions. We developed a PCR based technology called SMAL (Scanning of Microdissected Archival Lesions) that simultaneously evaluate hundreds of loci for alterations;
- Discovery of genes involved in lung, breast, oral and lymphoma cancer progression through whole genome analysis and gene expression profiling of pre-cancerous and cancerous stages. This effort has generated the world's largest collection of whole genome array CGH profiles as well as serial analysis of gene expression library data in lung and oral cancer;
- Identification of cancer cell dependent signaling pathways and their inhibition, with novel small molecule therapeutics resulting in tumor growth arrest.

Key Research Staff

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Victor Ling	PhD Biochemistry	Head of Department & Vice President of Research, BCCA
		Professor, Biochemistry and Molecular Biology, UBC
		Professor, Pathology and Medicine, UBC
		Assistant Dean Research, Faculty of Medicine, UBC
Shoukat Dedhar	PhD Pathology	Senior Scientist
		Professor, Department of Biochemistry and Molecular Biology, UBC
Sharon Gorski	PhD Developmental Biology	Senior Scientist
		Senior Scientist, Genome Sciences Centre
Wan Lam	PhD Biochemistry	Senior Scientist
		Associate Professor, Pathology & Laboratory Medicine, UBC
Marco Marra	PhD Genetics	Director, Senior Scientist, Genome Sciences Centre
		Associate Professor, Medical Genetics, UBC
		Adjunct Professor, Biochemistry and Molecular Biology, SFU
Raymond Ng	PhD Computer Science	Associate Scientist
		Professor, Computer Science, UBC

Training

A) Course Instruction

S Dedhar	UBC Med Gen521	W Lam	UBC Path 548F Histopathology
S Dedhar	UBC Path 531 Mol & Cell Biology of Cancer	W Lam	UBC Path 548F Microdissection
S Dedhar	UBC Biochem 511	W Lam	UBC Path 548C Bioinformatics
S Dedhar	UBC Biochem 509	W Lam	UBC Biol 448 Directed Studies
S Dedhar	UBC Biochem 514	W Lam	UBC Pharmacology 448 Dir Study
		W Lam	Path 548 Genome Analysis

B) Summary of Trainees

	<i>Total No. of Current Students</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
2005	29	9	13	7	--
2006	39	14	15	10	--

C) Current Trainees – Degrees Completed

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>
MSc		
Corisande Baldwin	W Lam	2005
Eric Lee	W Lam	2006
Isabella Mak	V Ling	2005
PhD		
Iveta Dobreva	S Dedhar	2005
Andrew Fielding	S Dedhar	2005
Arusha Olooumi	S Dedhar	2005
Cathie Garnis	W Lam	2005
Theresa Mastracci	W Lam	2005
Dennis Leveson-Gower	V Ling	2006

D) Trainee Awards

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Sarah Atwell	S Dedhar	NSERC Scholarship (2000)
Clara Tan	S Dedhar	CIHR Scholarship, MD/PhD Program Studentship (2001-2006)
Timon Buys	W Lam	CIHR Canada Graduate Scholarship (2006-2010)
		BCCRC Travel Award (2006)
		MSFHR - Graduate Scholarship (Junior) (2005-2007)
		Keystone Symposium ("Emerging Genomic Biomarkers: Impact on Drug Discovery and Clinical Practice") Travel Scholarship (2006)
		BC Cancer Agency Betty Rice Award (2005)
Raj Chari	W Lam	Betty Rice Award (2006)
		APIII Conference, Best Scientific Presentation – Bioinformatics (2006)
Bradley Coe	W Lam	MSFHR Senior Graduate Scholarship (2005-2008)
		NSERC Post Graduate Scholarships (2003-2007)
Jonathan Davies	W Lam	MSFHR - Graduate Scholarship (Junior) 2005
		NSERC Post Graduate Scholarship Masters (2004-2006)
		AACR-AFLAC Scholar-in-Training Award (2006)
		NSERC Canada Graduate Scholarships (2006 – 2008)
		World Microarray Congress - Best Student Abstract Award (2006)
NSERC Post Graduate Scholarships (2005-2006)		
Ron deLeeuw	W Lam	NSERC Canada Graduate Scholarship (2005-2008)
		MSFHR - Graduate Scholarship (2006 -2008)
Cathie Garnis	W Lam	Life Sciences Research Foundation Postdoctoral Fellowship, 2006
		NSERC Post Graduate Scholarships (2003-2005)
		MSFHR Graduate Studentship (2005)
Alice Kuo	W Lam	NSERC Canada Graduate Scholarships (2006-2010)
William Lockwood	W Lam	MSFHR Trainee Award (2006-2008)
		CIHR Canada Graduate Scholarship – Doctoral Award (2006-2009)
Ashleen Shadeo	W Lam	NSERC Post Graduate Scholarship Masters (2004–2005)
		MSFHR Junior Graduate Scholarship (2004 -2006)
Ivy Tsui	W Lam	UBC Roman M. Babicki Scholarship (2006)
		AACR Scholar-In-Training Award (2006)
		CIHR/ Bio-Contact Next Generation Award (2006)
		University of Pittsburg, Best Scientific Poster (2006)

Ian Wilson	W Lam	UBC Hardwick Scholarship (2005-2006) UBC University Graduate Fellowship (2006)
Maria Ho	V Ling	UBC University Graduate Fellowship (2004-2005)
Maisie Lo	V Ling	CIHR Doctoral Res Award (2005-2007)
Scott Zuyderduyn	V Ling	MSFHR Senior Graduate Trainee Award (2006-2009) CIHR Doctoral Research Award (2006-2009)

Current Awards and Honours

<i>Name</i>	<i>Distinguished Award/Honour</i>
Shoukat Dedhar	MSFHR Distinguished Scholar (2001-2005)
Wan Lam	NCIC/ CCS William E. Rawls Prize, Young Investigator Award (2006) Certificate of Recognition, Faculty of Medicine, UBC (2005)
Victor Ling	MSFHR Scholar (2001-2005) Doctor of Science, honoris causa, Trinity Western University (2006) Terry Fox Medal BC Medical Association (2006)

Select Current Contributions

<i>Name</i>	<i>Membership/Committee Involvement</i>
Shoukat Dedhar	Chair, NCIC Grants Panel B Panel Member, CIHR, Cell Physiology Panel Member, CIHR, Cancer Biology and Therapeutics Member, Ontario Cancer Research Network Translational Research Grants Panel Chair, MSFHR, Biomedical Research Evaluation Committee Member, Faculty of Medicine & Graduate Studies MD/PhD Evaluation Committee Chair, Scientific Professional Staff Association, BCCA Member, Canadian Breast Cancer Research Alliance Research Advisory Committee Member, NCI/NIH Grants Review Panel for RFA-CA-06-014 Tumor Microenvironment Network
Wan Lam	Member, CIHR, Genomics panel Member, NCIC, Pathology and Biomarkers Panel Member, MSFHR, Postdoctoral Trainees Panel Member, MSFHR, Biomedical Research Evaluation Committee Member, Ontario Cancer Research Network, Biomedical Panel Member, CIHR, IGT/NGH Panel
Victor Ling	Member, Scientific Advisory Council, Alberta Heritage Fdn for Medical Research Member, Scientific Advisory Committee, Goldhirsch Foundation Member, Scientific Advisory Board, Active Pass Pharmaceuticals Member, Canadian Strategy for Cancer Control Committee Member, Governing Council, CIHR Member, Premier's Technology Council Member, Medical Advisory Committee, Gairdner International Foundation

Current Research Projects¹

1. ABC transporters and clinical response to therapy	
PI: V Ling NCIC \$150,000 (2005) \$150,000 (2006) \$750,000 (2005-2010)	The goal is to study cancer cells from patients whose cancers are resistant to all anticancer drugs from the beginning. This is called "intrinsic resistance" and the team hopes to identify the molecules that cause it. They will also continue their work on the TAPL transporter to determine its role in cancer prevention.
2. Application of pharmacogenomics for rational chemotherapy of lung cancer	
PI: V Ling, S Lam Co-I: W Lam, C MacAulay, N Murray, R Ng, et al. Genome Canada, Amgen, Merck	For project description see Cancer Imaging.
3. Biology of cancer: Follicular lymphoma as a model of cancer progression	
PI: J Connors Co-I: W Lam, et al NCIC	For project description see Pathology and Laboratory Medicine.
4. BC Cancer Agency Institutional Infrastructure Award	
PI: V Ling MSFHR \$799,407 (2005) \$799,407 (2005) \$3,197,508 (2003-2006)	<i>The BC Cancer Agency Institutional Infrastructure Award includes the following sub-projects:</i>
	Tumour Tissue Repository \$69,540 (2005) \$69,540 (2006) The goal is to support generation and adoption of high level of QA/QC procedures for recruitment, procurement, processing, storage and information collection for translational cancer research.
	Joint Animal Facility \$100,000 (2005) \$100,000 (2006) The goal is to support cryopreservation of animal models for the move to the Animal Resource Centre in the new Research Centre.
	Health Outcomes and Economics \$97,295 (2005) \$97,295 (2006) The goal is to recruit an health economist to establish a research program in the health economics of cancer control.
	Targeting & Tumour Specific Research Group \$191,297 (2005) \$191,297 (2006) The goal is to support pre-grant development for translational and interdisciplinary research groups.
	Imaging \$99,812 (2005) \$99,812 (2006) The goal is to establish a partnership with TRIUMF to generate radiopharmaceuticals for research, and to support the growth in research activity associated with the new PET/CT clinical facility at the Vancouver Cancer Clinic.
	Technology Transfer Office \$45,000 (2005) \$45,000 (2006) The goal is to support value-added management of technology development.

¹ Key to abbreviations: PI = Principal Investigator, Co-I = Co-investigator; CIHR* = Funding Institution; \$150,000 (2005-2007) = Total Project Funding for Given Years (*see pages 16-17 for a list of acronyms)

	<p>Capacity Building – Information Technology \$98,464 (2005) \$98,464 (2006) The goal is to provide state-of-the-art IT infrastructure in the new Research Centre to support scientific collaborations</p> <p>Capacity Building – Training and Recruitment \$98,000 (2005) \$98,000 (2006) The goal is to provide targeted support to increase the recruitment of students training at the new Research Centre and to increase opportunities for interdisciplinary exposure in their training.</p>
5. Cancer genomics – Genome Canada Competition I Award	
<p><i>PI: V Ling, M Marra, C Eaves</i> <i>Co-I: K Humphries, S Jones, S Lam, W Lam, P Lansdorp, C MacAulay, M Rosin, M Sadar, J Vielkind</i> <i>Genome Canada/ Genome BC/ Province of BC</i> \$16,778,433 (2001-2006)</p>	<p>The objective of this program is to identify genetic and proteomic changes using high throughput technologies (SAGE, cDNA, array CGH and SELDI) and methods for isolating cell populations from fresh, frozen and fixed tissues representing the earliest stages of cancer and stem cell development. The cancers studied include breast, cervix, colorectal, gastric, liver, lung, lymphoma, myeloid, oral and prostate; as well as immortalized and human and mouse stem cells.)</p>
6. Cell-extracellular matrix interactions in differentiation and oncogenesis	
<p><i>PI: S Dedhar</i> NCIC \$150,000 (2005) \$150,000 (2006) \$750,000 (2003-2008)</p>	<p>The goal is to further study ILK with the aim of learning how it controls the attachment of cells to the ECM, how it stops cells from attaching to one another, and how it encourages cells to become cancerous. We will also investigate the possibility that ILK overactivity contributes to the growth of new blood vessels within cancers and see whether this can be reversed. Finally, we will create genetically altered mice in which ILK is overactive in certain organs and determine whether this causes cancer growth.</p>
7. Clonal changes in oral lesions of high-risk patients	
<p><i>PI: M Rosin</i> <i>Co-I: W Lam</i> NIH</p>	<p>For project description see Cancer Control Research.</p>
8. Collaborative research on ILK as a cancer therapeutic target	
<p><i>PI: S Dedhar</i> <i>QLT Inc., Kinetek, and Boehringer Ingelheim</i> \$47,000 (2005-2006)</p>	<p>The objective of this work is to show that ILK is a promising target for the treatment of breast cancer.</p>
9. Development and validation of comparative genomic hybridization arrays for clinical use in cancer	
<p><i>PI: W Lam, D Horsman</i> <i>Co-I: P Eydoux (C&W), R Ng, A Karsan, C MacAulay</i> <i>Genome Canada</i> \$4,611,538 (2005-2007)</p>	<p>This grant focuses on technical development of BAC array CGH, and its validation in the diagnosis of clinical cancer cases.</p>
10. Early detection research network	
<p><i>PI: W Lam</i> NIH US \$70,000 (2004-2007)</p>	<p>To identify potential biomarkers for early detection/risk assessment and to generate test/antibodies for clinical applications. To establish unique immortalized cultures from non-malignant bronchial epithelium.</p>

11. Epigenetics and human reproductive health	
<i>PI: W Robinson (UBC)</i> <i>Co-I: W Lam</i> <i>CIHR</i> <i>\$1,457,250 (2005-2010)</i>	This work focuses on the role of DNA methylation in normal development and cancer.
12. Epigenomic profiling: The role of DNA methylation in normal development and cancer	
<i>PI: W Lam</i> <i>CHIR</i> <i>\$672,670 (2005-2010)</i>	This work focuses on developing techniques to identify the genes in cancers that may be frequently turned off by DNA methylation. If successful, these techniques could be used in the clinic to improve prognosis and to tailor treatments to individual patients.
13. Genomic profiles of lung cancer that predict prognosis and response to adjuvant chemotherapy	
<i>PI: MS Tsao (OCI)</i> <i>Co-I: W Lam</i> <i>OCRN</i> <i>\$450,000 (2004-2008)</i>	The focus of this project is whole genome profiling by BAC Array CGH analysis.
14. Identification of novel genes involved in breast cancer using the breast cancer family registry	
<i>PI: I Andrulis (U Toronto)</i> <i>Co-I: W Lam</i> <i>CIHR</i> <i>\$359,994 (2005-2008)</i>	The overall objective is to understand the genetic basis of breast cancer and to translate the research findings into improvements in prevention, detection, diagnosis and treatment of breast cancer.
15. Modules for the identification of novel molecular targets and therapeutics for organ specific metastasis of breast cancer	
<i>PI: S Dedhar</i> <i>Co-I: C Overall, C Roskelley (UBC), A Karsan et al</i> <i>CBCRA</i> <i>\$765,973 (2005)</i> <i>\$649,685 (2006)</i> <i>\$3,364,713 (2005-2010)</i>	The goal of this program is to create new experimental models and imaging, gene and protein analysis technologies to identify and characterize genes and proteins which are crucial for the growth of breast cancer metastasis in different organs.
16. Molecular signatures to improve diagnosis and outcome prediction in NHL	
<i>SPEC Project Leader: J Chan</i> <i>PIs: W Lam et al.</i> <i>NIH</i> <i>\$7,500,000 (2005-2010)</i>	To develop & validate a DNA micro-array that can accurately classify lymphomas into important diagnostic subgroups.
17. New molecular targets in mantle cell lymphoma (MCL)	
<i>PI: R Gascoyne</i> <i>Co-I: D Horsman,</i> <i>R Klasa, W Lam</i> <i>LRF (USA)</i>	For project description see Pathology and Laboratory Medicine.
18. New technologies for surveillance of biowarfare agents and identification of engineered virulence genes	
<i>PIs: W Lam, R Fernandez</i> <i>Health Canada, CRTI</i> <i>\$822,657 (2006-2007)</i> <i>\$3,727,433 (2003-2007)</i>	The objective is to develop a two-dimensional DNA display technology for mutation detection in pathogens.

19. Novel molecular prognostic markers and potential therapeutic targets in non small cell lung cancer	
<i>PL: MS Tsao</i> <i>Co-I: W Lam</i> NCIC \$150,000 (2005) \$150,000 (2006) \$750,000 (2005–2010)	The goal is to develop new molecular diagnostic tests for routine pathological diagnosis of lung cancer patients.
20. Optical systems for in vivo molecular imaging of cancer	
<i>PL: R Richard-Kortum</i> <i>Co-I: W Lam, C MacAulay</i> NIH	For a project description see Cancer Imaging
21. Role of Integrin-Linked Kinase (ILK) in regulation of e-cadherin expression and wnt signaling	
<i>PI: S Dedhar</i> CIHR \$79,161 (2005) \$34,580 (2006) \$207,483 (2003-2006)	The goal is to investigate how ILK suppresses E-Cadherin, and investigate whether blocking the function of ILK in cancer cells can restore E-Cadherin and eliminate the malignant property of cancer cells. This work has the potential of identifying novel therapeutics for cancer control.
22. Role of Integrin-Linked Kinase (ILK) in Prostate Cancer Progression	
<i>PL: P Rennie (UBC)</i> <i>Co-PI: M. Gleave, S Dedhar, et al</i> <i>Terry Fox / NCIC program</i> \$780,250 (2006-2007) \$6,770,728 (2006-2011)	The Terry/Fox NCIC program of which this project is a part is studying how prostate cancers change from being dependent on male sex hormones to not needing them.
23. The role of sister of P-glycoprotein in liver function and enterohepatic circulation of bile acids	
<i>PL: V Ling</i> <i>Co-I: R Wang</i> CIHR POP \$100,000 (2006)	This research will lead us to discover drugs and develop new molecular strategies to treat PFIC2. Currently the only available effective therapy is liver transplantation.
24. Translational acceleration program: ILK as a potential therapeutic target for breast cancer	
<i>PI: M Bally, K Gelmon</i> <i>Co-I: S Dedhar</i> CBCRA TAG grant	For a description of this project see Advanced Therapeutics
25. Whole genome array CGH of progressing oral dysplasia: Discovering genetic markers predictive of oral cancer progression	
<i>PI: W Lam, M Rosin</i> NIH \$1,080,000 (2004-2008)	The goal of this proposal is to integrate development of optical imaging systems and contrast agents with advances in functional genomics.