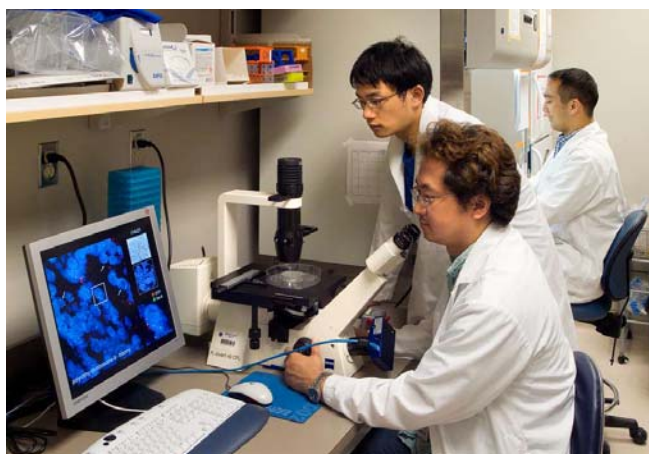


CANCER ENDOCRINOLOGY

BCCA CANCER RESEARCH CENTRE

675 West 10th Avenue, Vancouver, BC

Telephone: 604-675-8010



Our Research Focus:

Our research is focused on the prevention, early diagnosis and treatment of solid tumors, including prostate cancer. Our main objective is to delineate biochemical, immunological, genetic and molecular characteristics underlying the development of prostate cancer through the use of novel animal models, with a view to generating new diagnostic and therapeutic agents. Our Prostate Cancer Research Program is

part of the Vancouver Centre of Excellence for Prostate Cancer Research. Another important area of investigation is gene expression profiling during embryonic development and stem cell commitment. The major focus of this work is to define the transcriptional regulatory networks that guide pancreas development, as well as adult pancreas function and regeneration. Such studies are likely to provide important insights into the molecular mechanisms that go awry during the development of pancreas cancer and may also assist in the development of effective strategies for generating a replenishable supply of glucose-responsive, insulin secreting cells from embryonic stem or pancreas progenitor cells.

Progress Highlights during 2005-2006

- First to successfully grow low-grade human prostate cancer tissue as well as PIN lesions in SCID mouse hosts using subrenal capsule grafting techniques (Wang et al., Prostate, 2005). The new xenograft models allow researchers to study low-grade human prostate cancer in vivo, which was hitherto not possible. The methodology has also been used for other types of human cancers, such as lung, bladder, renal, ovarian, pancreatic cancers with > 95% survival and tumor take rate (Lee et al., Gyn Oncol, 2005; Cutz Clinical Cancer Res 2006). Based on these achievements, a Living Tumor Centre for Therapeutic Efficacy Assessment is under development.



- First to prove that human prostate cancer heterogeneity can be dissected and subpopulations of cancer cells can be isolated and enriched using subrenal capsule xenografting, and that human prostate cancer grafts can metastasize to mouse bone (Wang, Lab Invest. 2005). The study was highlighted by the Journal of Laboratory Investigation and a picture was selected as cover art for the Journal.
- Using in vivo models, evidence has been obtained that sulfasalazine, an FDA-approved drug for inflammatory bowel disease and rheumatoid arthritis, can sensitize tumors and is potentially useful for combination chemotherapy of prostatic and pancreatic cancers.

Key Research Staff

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Yuzhuo Wang	PhD Anatomy	Senior Scientist Adjunct Professor, Division of Urology, Surgery, UBC
Cheryl D Helgason	PhD Biochemistry	Senior Scientist Assistant Professor, Surgery, UBC Associate Member, Microbiology and Immunology, UBC
Peter W Gout	PhD Biochemistry	Senior Scientist Emeritus Emeritus Scientist, Cancer Endocrinology, BCCRC
Juergen Vielkind	PhD Genetics	Senior Scientist Emeritus Associate Professor Emeritus, Pathology & Lab Medicine, UBC

Training

A.) Course Instruction

CD Helgason	UBC Micro 430
CD Helgason	UBC MEDI 502
CD Helgason	UBC Biology 448 (Directed Studies)

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>
15	4	5	6	-

C.) Current Students – Degrees Completed

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>
MSc		
Ida Zhang	CD Helgason	2005
Lien Hsu	CD Helgason	2006

D.) Trainee Awards

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Amy Tien	CD Helgason	CIHR/MSFHR Transplantation Training Scholarship (2004 – 2006)
Dong Lin	YZ Wang	Cancer Research Society Graduate Stipend (2006-2009)
Hisae Nakamura	YZ Wang	Zonta International Research Scholarship Award: from Japan district (2005)

Selected Personal Awards and Honours

<i>Name</i>	<i>Distinguished Award/Honour</i>
CD Helgason	MSFHR Scholarship (2003-2008)
	CIHR New Investigator Award (2001-2006)
YZ Wang	Prostate Cancer Foundation Research Award (2006)

Selected Current Contributions

<i>Name</i>	<i>Membership/Committee Involvement</i>
CD Helgason	Member, Experimental Medicine, Genetics, and Interdisciplinary Oncology Graduate Studies Programs, UBC
	Member, MSFHR Biomedical Trainee Evaluation Committee
	Member, CIHR New Investigator "A" (Biomedical) Awards Committee
YZ Wang	Member, CIHR Training Program in Molecular Pathology of Cancer

Current Research Projects³

1. A novel mouse model for large scale siRNA screening in islets	
<i>PI: CD Helgason Juvenile Diabetes Research Foundation International US \$110,000 (2006–2007)</i>	The goal is to develop and test the tools needed to carry out large scale screens to identify factors that play critical roles in regulating islet cell survival, proliferation and insulin gene expression.
2. Application of pharmacogenomics for rational chemotherapy of lung cancer	
<i>PI: S Lam, V Ling Co-I: YZ Wang et al</i>	For a summary of this project see Cancer Imaging.
3. Dendritic cells in autoimmunity and cancer	
<i>PI: CD Helgason MSFHR Establishment Grant \$125,000 (2003-2005)</i>	The goal is to study dendritic cell development and function in mouse models of prostate cancer.
4. Development of pre-neoplastic and early-stage human lung cancer xenograft models	
<i>PI: YZ Wang Co-I: S Lam, J English (VHHSC) BC Lung Assoc. \$50,000 (2003-2005)</i>	The objective is to develop in-vivo preclinical models of early stage human lung cancer and pre-neoplastic lesions.

³ 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 list of acronyms)

5. Development of a function-blocking peptide for treatment of cancer	
<i>PI: PW Gout</i> <i>Co-PI: YZ Wang</i> <i>CIHR POP</i> <i>\$150,000 (2005)</i>	The goal is to develop a blocking peptide specifically directed against a transporter protein important in cell survival and drug resistance. Such a peptide would have potential for use in therapy of cancers, as well as for their diagnosis and prognosis.
6. Dissecting gene regulatory networks in mammalian organogenesis	
<i>PI: P Hoodless, M Marra</i> <i>Co-I: CD Helgason et al</i>	For a summary of this project see Genome Sciences Centre.
7. Frequency and clinical significance of functional loss of protein involved in DNA double strand break repair in ovarian cancer	
<i>PI: CB Gilks</i> <i>Co-PI: YZ Wang</i> <i>CIHR</i> <i>\$105,298 (2006–2008)</i>	The goals are: 1) to ascertain the proportion of ovarian cancers associated with loss of BRCA1 and/or BRCA2 function; 2) to identify surrogate markers for BRCA1 or BRCA2 loss of function, through the use of pathological and immunohistochemical markers, and the mechanism of BRCA1 or BRCA2 loss on patient outcome cases of ovarian cancer (N=540) with long term follow-up data; and 3) to test the ability of inhibitors of nucleotide excision repair pathway to cause tumor cell death in a xenograft model of ovarian cancer.
8. Mechanisms of prostate cancer tumor cell-mediated immunosuppression: Examination of dendritic cell survival, maturation and function in response to prostate cancer	
<i>PI: CD Helgason</i> <i>US Dept of Defense</i> <i>US\$375,000 (2002-2005)</i>	The goal is to study the mechanisms by which prostate tumor cells alter immunity with a particular emphasis on dendritic cells and regulatory T cells.
9. Molecular signatures for predicting metastatic potential of primary human prostate cancers: Applications of a new cancer modeling system	
<i>PI: YZ Wang</i> <i>Cancer Research Society Inc</i> <i>\$450,000 (2006 – 2009)</i>	The goal is to identify gene expression profiles for predicting metastatic potential of prostate cancer. Such “molecular signatures” should contribute to improve patient outcomes.
10. New in vivo model of low-grade human prostate cancer (PCa): Potential applications for molecular analysis and diagnostic screening	
<i>PI: YZ Wang</i> <i>NCIC</i> <i>\$483,951 (2003 – 2006)</i>	The novel mouse xenograft model will be used to study prostate cancer progression and the stages it involves. The group will study how the cancer cells grow and change, what genetic changes occur as they do so, and what triggers the death of these cells at early stages of progression.
11. Novel approach for prostate cancer therapy: Application of a unique xenograft model	
<i>PI: YZ Wang</i> <i>Co-PI: PW Gout</i> <i>US DOD</i> <i>US\$448,800 (2004 – 2007)</i>	The goal of this study is to see if use of sulfasalazine can lead to the arrest of growth of human PCa tissue grafts in a xenograft model and, in particular, of advanced cancers resistant to current therapies.
12. Quantitative and comprehensive atlas of gene expression in mouse development	
<i>PI: P Hoodless, M Marra</i> <i>Co-I: C Helgason et al</i>	For a summary of this project see Genome Sciences Centre.