

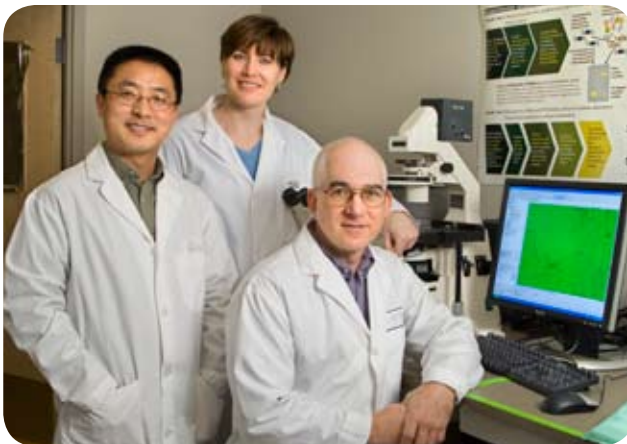


BC Cancer Agency

CARE & RESEARCH

An agency of the Provincial Health Services Authority

Annual Research Report – 2004



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From the President

BC Cancer Agency – Annual Research Report – 2004

Canada is fortunate among Nations to benefit from investments in cancer control directed towards reduced incidence, reduced mortality and enhanced quality of life. Notwithstanding, even within Canada we see disparities in cancer outcomes – east to west; north to south; rural to urban – disparities that reflect the fact we have yet to fully mitigate the impact of geography on outcomes.

Geography is, of course, a surrogate for a number of other relevant attributes – gender, access, ethnicity, education, socio-economic status, etc. A good cancer control strategy will address these issues through ensuring, to the degree possible, that we apply what we know to be effective to the population – equitably, on the principle that cancer control is a 'right', not a 'privilege'.

Much of the BC Cancer Agency's activities are directed to ensuring that what we know to be effective (evidence-based) is put into practice, through population-based programs deploying evidence-based standards of practice, management according to established clinical practice guidelines and analysis of outcome data as a basis for continuing improvement. However, even if we were universally effective in our deployment of evidence-based care, we would not control cancer. Perhaps 40% of patients would still die because we simply do not know enough to remove the life threat of cancer.

Effective, well planned cancer control strategies recognize that controlling cancer requires investment in not only applying what one knows to be effective, but also defining what one does not know, so that relevant new knowledge can be discovered, and effective novel approaches brought into application.

This report outlines the Cancer Agency's commitment to cancer research. Of importance are the concepts of discovery, clinical validation and population application, interdisciplinary 'team' science, and bringing science and medicine to a closer, more timely and effective, relationship. The report acknowledges a broad range of partners who share our commitment, and who work with us – either as funders and donors, co-investigators or collaborators, or as friends, recipients and users of this knowledge.

A commitment to enhance cancer control outcomes is a commitment to discover, transfer and apply knowledge on the foundation of good cancer control practice. Cancer research, whether in the laboratory, the clinic or in the community is a 'cornerstone' of the Agency's cancer control mandate and a defining element of the provincial cancer control program.



Simon Sutcliffe, MD, FRCPC

President

From the Vice President, Research

BC Cancer Agency – Annual Research Report – 2004

Our most pressing goal is to move more rapidly towards our vision of a world free from cancer within the next 50 years. Recent advances in identifying the multiplicity of genes and signaling pathways that make human cells cancerous and the responsiveness of different individuals to specific interventions has focused renewed attention on the concept of “personalized medicine” in the setting of cancer control. The translation of this concept into a new approach to cancer control is likely to have a huge impact on our society. A few examples of the basis for starting to realize this change in approach to cancer control include:

- Identification of the genetic basis of heritable risks for particular types of cancer.
- Development of new test systems to predict the role of environmental, nutritional and occupational carcinogens with greater accuracy.
- Early detection of cancer through “high risk” population screening.
- Development of new molecules for *in vivo* functional imaging of abnormal cells and tissues.
- Development of molecular-based criteria for tumour classification.
- Generation of novel therapeutics that target specific gene functions (e.g., oncogene inhibitors, antisense molecules, tumour vaccines), or key physiological processes of malignant and normal cells (e.g., cell oxygenation, cycle status, apoptosis, invasion, angiogenesis).

This research report recognizes the exceptional efforts of a talented group of researchers, clinicians, nurses, healthcare professionals and their staff and students. These individuals seek to integrate their research efforts in laboratory research, in clinical research and in population-based research across the cancer domain.

2004 has been marked by a number of firsts. We celebrate discoveries that provide new insight into disease, for example – the discovery of a new gene called RTel which is involved in the way in which cells die¹, a new role for inhibition of a protein called ILK and the effect it has upon formation of blood vessels that are necessary to supply cancer cells with nutrients², and the development of a new DNA microarray with complete coverage of the human genome³, - to name a few. Our researchers were also busy contributing to international genomics efforts – publishing the full sequence of the rat⁴, and the physical map of the chicken⁵.

Overall, the research endeavour of the BC Cancer Agency has grown at 18% per year in-value for the past two to three years. This is a testament to the productivity of all our researchers who have added 237 unique items of new knowledge and understanding of cancer through peer-reviewed publications. A further 33 inventions

¹ Ding H *et al.* Regulation of murine telomere length by RTel: An essential gene encoding a helicase-like protein. *Cell* 117: 873-886, 2004.

² Tan C *et al.* Regulation of tumor angiogenesis by Integrin-linked Kinase. *Cancer Cell* 5: 71-90, 2004

³ Ishkanian *et al.* A tiling resolution DNA microarray with complete coverage of the human genome. *Nature Genetics* 36 299-303, 2004.

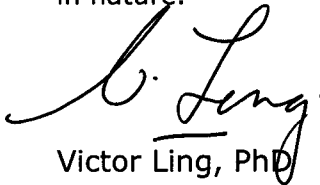
⁴ Rat Genome Sequencing Project. Genome sequence of the brown norway rat yields insight into mammalian evolution. *Nature* 428(6982): 493-521, 2004.

⁵ Wallis W *et al.* A physical map of the chicken genome. *Nature* 432(7018), 761-4, 2004

have arisen during the course of their research, which are being protected by patent applications, and prepared for commercialization.

During 2004, construction work on the new BC Cancer Research Centre neared completion. The entire research staff is excited by the prospect of coming together in one building, for the first time, all eight research departments of the BC Cancer Research Centre. This \$95 million project is funded by the Canadian Foundation for Innovation, the Province of British Columbia, and donors of the BC Cancer Foundation.

This report has been organized by department for ease of reference[§]. First by clinical departments whose have the key responsibility to care for patients affected by cancer, second by research departments whose primary responsibility is research, , and finally by regional centre, which provide exceptional care for patients in their region at the same time as conducting mission directed research. Much of the research described here crossed these artificial barriers and is truly interdisciplinary in nature.

A handwritten signature in black ink, appearing to read 'V. Ling', with a stylized flourish at the end.

Victor Ling, PhD

Vice President, Research

[§] Since many research projects span multiple departments there is duplication in listing projects. However, we have cross-referenced these projects, and provide a project description only once.

DEPARTMENT OF MEDICAL ONCOLOGY

BC CANCER AGENCY

Telephone: 604-877-6000 ext. 2738

<i>Researcher name</i>		<i>Position & Cross-Appointments*</i>
Susan O'Reilly	MD	Head, Medical Oncology, Provincial Leader, Systemic Therapy Program, BCCA (on Sabbatical) Clinical Professor, Medicine & Head, Medical Oncology, UBC
Joseph Connors	MD	Acting Head, Medical Oncology; Chair, Lymphoma Tumour Group Clinical Professor, Medical Oncology, UBC
Kim Chi	MD	Medical Oncologist, BCCA/VCC Clinical Associate Professor, Medicine, UBC
Karen Gelmon	MD	Medical Oncologist; Chair, Breast Cancer Tumour Group, BCCA/VCC; Head, Investigational Drug Program Clinical Professor, Medical Oncology, UBC
Stephen Chia	MD	Medical Oncologist, BCCA/VCC Assistant Professor, Medical Oncology, UBC
Christopher Lee	MD	Medical Oncologist, BCCA/VCC Clinical Instructor, Medical Oncology, UBC
Sharlene Gill	MD	Medical Oncologist, BCCA/VCC Assistant Professor, medical Oncology, UBC
Richard Klasa	MD	Medical Oncologist, BCCA/VCC Clinical Assistant Professor, Medical Oncology, UBC
Kerry Savage	MD	Medical Oncologist, BCCA/VCC Assistant Professor, Medical Oncology, UBC
Hagen Kennecke	MD	Medical Oncologist, BCCA/VCC
Nicol MacPherson	MD	Medical Oncologist, BCCA/VCC Clinical Assistant Professor, Medical Oncology, UBC
Caroline Lohrisch	MD	Medical Oncologist, BCCA/VCC
Janessa Laskin	MD	Medical Oncologist, BCCA/VCC Clinical Assistant Professor, Medical Oncologist, UBC
Nevin Murray	MD	Medical Oncologist, BCCA/VCC Clinical Professor, Medical Oncology, UBC
Barbara Melosky	MD	Medical Oncologist, BCCA/VCC Clinical Assistant Professor, Medical Oncology, UBC
Christian Kollmansberger	MD	Medical Oncologist, BCCA/VCC

* KEY: CCSI = Cancer Centre of the Southern Interior, Kelowna; FVCC = Fraser Valley Cancer Centre; VCC = Vancouver Cancer Centre; & VICC = Vancouver Island Cancer Centre, Victoria.

Paul Hoskins	MD	Medical Oncologist, BCCA/VCC Clinical Professor, Medical Oncology, UBC
Brian Thiessen	MD	Medical Oncologist, BCCA/VCC Clinical Assistant Professor, Neurology, UBC
Tom Ehlen	MD	Medical Oncology, Gyne Oncology, BCCA/VCC Assistant Prof, Obstetrics & Gynaecology, UBC
Pippa Hawley	MD	Medical Oncologist, BCCA/VCC Clinical Instructor, General Internal Medicine, UBC
Margaret (Meg) Knowling	MD	Medical Oncologist; Chair, Sarcoma Tumour Group, BCCA/VCC Clinical Assistant Professor, Medical Oncology, UBC
Laurie Sehn	MD	Medical Oncologist, BCCA/VCC Clinical Instructor, Medical Oncology, UBC
Martin Gleave	MD	Chair, Prostate Tumour Group, BCCA Professor, Surgery, UBC; Director, Clinical Research, Prostate Centre, VGH
Grant MacLean	MD	Medical Oncologist, BCCA/VCC Clinical Professor, Medical Oncology, UBC

Clinicians of the Department of Medical Oncology, BCCA are cross-appointed to academic appointments in the Division of Medical Oncology, UBC. The Department of Medical Oncology comprises medical oncologists organized as the BCCA Provincial Systemic Therapy Program located at four regional centres (Cancer Centre for the Southern Interior, Kelowna; Fraser Valley Cancer Centre, Surrey; Vancouver Cancer Centre and Vancouver Island Cancer Centre, Victoria).

OUR RESEARCH FOCUS: Our objective is to address the rising incidence of cancer, related to the aging population and, even more importantly, the increasingly complex treatment programs incorporating new targeted small molecules and immunotherapeutic agents. Clinical research includes a wide variety of Phase I, II, III and IV clinical trials. These include the development of new anti-cancer drugs, the evaluation of new doses schedules and combinations of drugs in the phase II setting and participation in multi-institutional phase III studies and post-marketing phase IV trials evaluating effective new cancer treatments. These clinical studies are supported directly by three important programs:

1. The **Clinical Trials Unit** undertakes carefully designed investigation of new treatments or combinations of old and new treatments in human patients. Drugs studied include chemotherapy drugs, hormone treatments, immune treatments, or new drugs designed to attack or block the function or growth of cancer cells in new ways. The Clinical Trials Unit provides expertise protocol development, and clinical trials nurses for the conduct of different phases of clinical trials research. Recently all current clinical trials have been put on the BC Cancer Agency's website, where additional information about clinical trials can be accessed at www.bccancer.bc.ca under 'Clinical Trials Research'.

2. The **Phase I Investigational New Drug Program** is growing rapidly due to the commitment and expertise of the translational research clinical and scientific teams and the increasing availability of new agents for testing in North America. The Department of Advanced Therapeutics is able to evaluate new biological response modifiers, gene therapy and pharmaceutical agents through all stages of testing, from in-vitro testing in the laboratory to evaluation in human volunteers. The VCC has the only Clean Room in an academic centre in Canada that is equipped and licensed for the packaging and formulation of pharmaceutical agents in small quantities for clinical testing (see Department of Advanced Therapeutics for further detail).

3. **Pharmacy Drug Mart & Pharmacoeconomics programs.** The Systemic Program has a Pharmacy Drug Mart that comprises a single longitudinal table of prescription data going back to 1995. The prescription data includes the patient identifier (BC Cancer Agency number), prescription number; dispensing date; drug; dose; quantity dispensed; prescribing physician and for drugs dispensed from BC Cancer Agency centre, the protocol code.

The BC Cancer Agency is the sole payer for cancer drugs in the province of BC. Thus information captured in the Pharmacy Data Mart covers all chemotherapy and most hormonal agents dispensed to cancer patients in BC going back to 1995. This makes this data mart unique in Canada. The data mart gives the Systemic Program the ability to carry out population based analyses on drugs utilization to specific groups of cancer patients and/or drugs and drug therapies.

The Systemic Therapy pharmacoeconomics service has recently grown into a Pharmaco-Oncology Forecasting and Feedback unit. Pharmacoeconomic principles and data from the drug datamart are used for evidence-based, population-based, financial planning for the treatment of cancer in the province. Outcomes research (cost-effectiveness analyses), is also performed to justify and maintain appropriate funded programs. The expertise and extensive data available also permit quality assurance and other research projects. Work performed via our pharmacoeconomics and drug datamart capabilities has been presented and published in local, national, and international conferences and journals.

RESEARCH KEYWORDS:

Clinical Trials, systemic chemotherapy, tumour biology, tumour immunology, investigational new drugs, pharmacoeconomics

TRAINING

A.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Trainees</i>	<i>Med Onc. Residents</i>	<i>Other program Residents</i>	<i>Fellows</i>	<i>Under- graduates</i>
16	7	7	2	

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Total Value</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value</i>
84	n/a	n/a	n/a

During 2004, a total of 241 patients were entered into 73 clinical trials and revenue of \$1.6 million.

Current Clinical Trials – Vancouver Cancer Centre (VCC)
1. An open-label, phase II trial of ZD1839 (Iressa®) in patients with malignant mesothelioma BCCA PI: C Lee; AstraZeneca Canada Inc.; 2002-2006
2. A phase I pharmacokinetic and pharmacodynamic study of weekly and twice weekly OSI-77S4 BCCA PI: S Chia; BCCA CODE: P1ERLOT opened in October 2004
3. A phase I, multi-centre, open-label, dose-escalation study to evaluate the safety, tolerability and pharmacokinetics of HGS-TR2J (fully human monoclonal antibody to the trail-R2) in subjects with advanced solid malignancies BCCA PI: K Gelmon; BCCA CODE: P1THTR2J opened in August 2004
4. A phase I study of MGCD0103 given as a three-times weekly oral dose in patients with advanced solid tumours or Non-Hodgkin's lymphoma BCCA PI: K Gelmon; BCCA CODE: P1TMGDC

VCC - Breast Cancer Clinical Trials
5. A double blind re-randomization to Letrozole or placebo for women completing five years of adjuvant Letrozole in the MA. 17 study BCCA PI: Shenkier; BCCA CODE: BRMA17R opened in December 2004
6. A randomized active-controlled study of AMG 162 in breast cancer subjects with bone metastasis who have not previously been treated with bisphosphonate therapy BCCA PI: H Kenencke; BCCA CODE: BRTAM162
7. Protocol A: Proposal for neoadjuvant chemotherapy with 5-fluorouracil, epirubicin and cyclophosphamide (FEC 100) followed by docetaxel, cisplatin and herceptin (TCH) for ER-2 overexpressing locally advanced breast cancer BCCA PI: S Chia; BCCA CODE: BRTDCECF opened in November 2004
8. Protocol B: Proposal for neoadjuvant chemotherapy with 5-fluorouracil, epirubicin and cyclophosphamide (FEC 100) followed by docetaxel and capecitabine (XT) for HER-2 non-overexpressing locally advanced breast cancer BCCA PI: S Chia; BCCA CODE: BRTDCECF opened in November 2004
9. A randomized, double blind, multicentre study to compare the efficacy and tolerability of fulvestrant (FASLODEX™) vs exemestane (AROMASIN™) in postmenopausal women with hormone receptor positive advance breast cancer with disease progression BCCA PI: S Chia; BCCA CODE: BRTEFECT opened in May 2004

<p>10.A randomized phase III trial of exemestane vs anastrozole with or without celecoxib in postmenopausal women with receptor positive breast primary cancer BCCA PI: N MacPherson; BCCA CODE: BRMA27 opened in June 2004; NCIC CTG MA. 27</p>
<p>11.A phase III adjuvant trial of sequenced EC+ neopogen followed by taxol versus sequenced AC followed by Taxol versus CEF as therapy for premenopausal and early postmenopausal women who have had potentially curative surgery for node positive BCCA PI: K Gelmon; BCCA CODE: BRMA21 ; NCIC MA21</p>
<p>12.A randomized three-arm multi-centre comparison of 1 year and 2 years of Herceptin® versus no Herceptin in women with Her2-positive primary breast cancer who have completed adjuvant chemotherapy BCCA PI: C Lohrisch; BCCA CODE: BRMA24</p>
<p>13.A4031001-Phase I safety and pharmacokinetic/pharmacodynamic study of CP-724, 714 in patients with advanced malignant solid tumours that express HER2 BCCA PI: K Gelmon; BCCA CODE: P1TCP724</p>
<p>14.Phase II multi-centre study to assess the positive predicative value of Positron Emission Tomography (PET) in the preoperative evaluation of internal mammary lymph nodes in breast cancer patients BCCA PI: V Bernstein; BCCA CODE: B RTPET2 opened in April 2003</p>
<p>VCC - Head and Neck Cancer Clinical Trials</p>
<p>15.A phase III randomized, stratified, parallel-group, multi-centre, comparative study of ZD1839 (Iressa®) 250mg and 500mg versus Methotrexate for previously treated patients with squamous cell carcinoma of the head and neck BCCA PI: S Chia; BCCA CODE: HNTIRMTX opened in November 2004</p>
<p>16.Phase I/II trial of weekly Docetaxel and Cisplatin for Locoregionally recurrent and/or metastatic squamous cell carcinoma of the head and neck BCCA PI: S Chia; BCCA CODE: P1THNDC opened in July 2003</p>
<p>17.A phase III, randomized, open-label study of IV Edotecarin or Camustine (BCNU) or Lomustine (CCNU) in patients with Glioblastoma Multiforme that has progressed/reccurred after Alkylator (neo)adjuvant chemotherapy BCCA PI: B Thiessen; BCCA CODE: CNTEDTCL</p>
<p>VCC - Non-Small Cell Lung; Small Cell Lung Cancer Clinical Trials</p>
<p>18. A phase 1-2 study of weekly OGX-011 plus Gemocitabine and Cisplatin in patients with stage IIIB or IV non small cell lung cancer: phase I component BCCA PI: J Laskin; BCCA CODE: LUTOGX11 opened in September 2005</p>
<p>19.A phase III randomized, double blind, placebo controlled trial of the epidermal growth factor receptor antagonist, ZD1839 (Iressa®) in completely resected primary non-small cell lung cancer BCCA PI: J Laskin; BCCA CODE: LUBR19</p>
<p>20.A phase II study of ZD6474 or placebo in small cell lung cancer patients who have complete or partial response to induction chemotherapy ±</p>

radiation therapy BCCA PI: N Murray; BCCA CODE: LUBR20 opened in May 2004; NCIC BR20
21.A phase III trial of Cisplatin/Etoposide/Radiotherapy with consolidation Docetaxel followed by maintenance therapy with ZD1839 or placebo in patients with Inoperable locally advanced stage III non-small cell lung cancer BCCA PI: N Murray; BCCA CODE: LUBR15
22.An open-label, randomized, multicenter, phase II study to determine hemoglobin dose response, safety and pharmacokinetic profile of RO 50-3821 given subcutaneously once weekly or once every 3 weeks to anemic patients with stage IIIB or IV non-small cell lung cancer BCCA PI: B Melosky; BCCA CODE: LUTROQ13
VCC - Genitourinary – Renal Cell; Prostate; Bladder Cancer Clinical Trials
23.Three-arm randomized phase II clinical study of Iroflufen/Prednisolone, Iroflufen/Capecitabine/Prednisolone or Mitozantrone/Prednisolone in Docetaxel-pretreated hormone refractory prostate cancer patients(protocol IROF-018) BCCA PI: K Chi; MGI Pharma; BCCA CODE: GUTIROF opened in December 2004
24.A phase 2 study of GTI-2040 in combination with docetaxel and prednisone in hormone-refractory prostate cancer BCCA PI: K Chi; MPH Phase II Consortium/US NIH; 2004-2005; BCCA CODE: GUGTIDP opened in December 2004
25.A phase III, randomized study of SU011248 versus Inteferon alpha as first-line systemic therapy for subjects with metastatic renal cell carcinoma BCCA PI: C Kollmannsberger; BCCA CODE: GUTSUIFN
26.A phase II study of Triapine (NSC 663249) in previously untreated patients with recurrent renal cell carcinoma BCCA PI: C Kollmannsberger; BCCA CODE: GUIND161
27.A phase II study of BAY 43-9006 (NSC 724772) in patients with hormone refractory prostate cancer (IND167) BCCA PI: K Chi; NCIC CTG; BCCA CODE: GUIND167 opened in Aug 2004 – on hold
28.A randomized phase II trial of Strontium-89 with or without Cisplatin for the palliation of bone pain secondary to hormone refractory prostate cancer BCCA PI: K Chi; Prostate Cancer Research Foundation of Canada; 2003-2004; \$50,000 per year; Σ \$100,000; BCCA CODE: GUTPPS2 opened in July 2003
29.A phase I/II (Clusterin Antisense Oligonucleotide) prior to radical prostatectomy in patients with prostate cancer BCCA PI: K Chi; US Army in collaboration with OncoGenex; 2004-2005; Σ \$377,720
30.EPO-CAN-29 randomized trial of Epoetin Alfa in men with hormone refractory prostate cancer and anemia BCCA PI: K Chi; Ontario Clinical Oncology Group; 2004-2005; \$32,000
31.Phase I/II study of combination neoadjuvant hormone therapy and weekly OGX-011 prior to radical prostatectomy in patients with localized prostate cancer BCCA PI: K Chi; US Dept of Defense Medical Program; 2002-2005; \$283,000USD per year; Σ \$1,132,000USD; BCCA CODE: P1IND154

32. phase I study of a second generation clusterin antisense oligonucleotide targeted to clusterin (OGX-011) in combination with docetaxel BCCA PI: K Chi; NCIC; 2002-2005; \$244,333 per year; Σ \$897,332; BCCA CODE: P1IND154 opened in April 2003
33. Molecular predictive and prognostic factors in hormone refractory prostate cancer BCCA PI: K Chi; Abbott Canada; 2004-2007; \$100,000 per year; Σ \$400,000
34. A phase I study of AEG35156/GEM640 and docetaxel give once every 3 weeks in pts with solid tumours BCCA PI: K Chi; NCIC CTG; BCCA CODE: P1IND166 opened in June 2005
35. A phase I study evaluating the efficacy and safety of ABT-751 in patients with hormone refractory prostate cancer BCCA PI: K Chi; Abbott Laboratories; 2004
36. Ascent study: A phase II/III multicenter, randomized, double blind study of Docetaxel plus Dn-101 or placebo in prostate cancer BCCA: K Chi; Novartis, Inc; 2003-2004
37. Phase III trial comparing Paclitaxel/Cisplatin/Gemcitabine and Cisplatin/Gemcitabine in pts with urothelial ca without prior systemic therapy BCCA PI: K Chi; NCIC CTG/EORTC; 2003-2004
38. A phase II study of neoadjuvant docetaxel and neoadjuvant/adjuvant hormone therapy and locoregional radiation therapy for high risk localized adenocarcinoma of the prostate BCCA PI: K Chi. M McKenzie; Aventis Pharma; 2002-2005
39. Multicentre, single-arm open label study combination neoadjuvant hormone therapy and weekly taxotere prior to radical prostatectomy in localized prostate cancer BCCA Co-PI: K Chi, M Gleave; (Prostate Cancer, VGH); Aventis Canadian Oncology Group; 2001-2004
40. Randomized phase III trial comparing immediate versus deferred chemotherapy after radical cystectomy in patients with pT3-pT4, and/or N+M0 transitional cell carcinoma (TCC) of the bladder BCCA PI: K Chi; NCIC CTG/EORTC; 2003-2004; BCCA CODE: GUBL8 opened October 2002; NCIC BL8
41. A Phase II study evaluating the efficacy and safety of ABT-751 in patients with renal cell carcinoma BCCA PI: K Chi; Abbott Laboratories; 2003-2004

VCC - Ovarian Cancer Clinical Trials

42. An international multi-centre randomized phase III study comparing upfront debulking surgery versus neo-adjuvant chemotherapy in patients with stage IIIC or IV epithelial ovarian carcinoma BCCA PI: T Ehlen; BCCA CODE: GOOV13
43. A phase III study of Cisplatin plus topotecan followed by paclitaxel plus carboplatin versus paclitaxel plus carboplatin as first line chemotherapy in women with newly diagnosed advanced epithelial ovarian cancer BCCA PI: P Hoskins; BCCA CODE: GOOV16

44. An open-label, multicenter, non-comparative phase II study of the combination of intravenous topotecan and gemcitabine administered once weekly for three weeks every 28 weeks every 28 days as second-line treatment in patients with recurrent platinum-sensitive ovarian cancer

BCCA PI: P Hoskins; BCCA CODE: GOTOVTG

VCC - Symptom Management Clinical Trials

45. A multicentre, randomized, double-blind, placebo-controlled parallel-design trial of the efficacy and safety of subcutaneous tetrodotoxin (Tectin) for moderate to severe inadequately controlled cancer related pain (WEX014)

BCCA PI: P Hawley; BCCA CODE: SCTTETRO opened in August 2004

46. A multicentre, randomized double blind placebo controlled study of Dabepoetin Alfa for the treatment of anemia of cancer (Amgen232)

BCCA PI: P Hoskins; BCCA CODE: SCTDA232 opened June 2004

47. A multicentre, open-label, long-term efficacy and safety continuation study of subcutaneous tetrodotoxin (Tectin™) for moderate to severe cancer-related pain (WX-0140L)

BCCA PI: P. Hawley; BCCA CODE: SCTTETOL opened in August 2004

VCC - Colorectal; Esophagus; Gastric; Pancreatic Cancer Clinical Trials

48. A phase III randomized study of Cetuximab (Erbix, C225) and best supportive care versus best supportive care in patients with pretreated metastatic epidermal growth factor receptor (EGFR) – positive colorectal carcinoma

BCCA PI: H Kennecke; BCCA CODE: GICO17; NCIC CTG trial CO.17

49. A phase II study of G3139 in combination with Doxorubicin in advanced Hepatocellular carcinoma

BCCA PI: S Gill; BCCA CODE: GITG3139 opened in Sept 2004 – temporarily on hold

50. A 2x2 factorial randomized phase III study of intermittent oral capecitabine in combination with intravenous Oxaliplatin (Q3W) (XELOX) with/without intravenous Bevacizumab (Q3W) vs Bolus and continuous infusion Fluorouracil/Intravenous Leucovorin with Int

BCCA PI: B Melosky; BCCA CODE: GITOXELF

51. Phase I study of safety and immunogenicity of ALVAC-CEA/B7.1 vaccine administered concurrently with chemotherapy or following chemotherapy in patients with stage III colorectal adenocarcinoma

BCCA PI: C Lohrisch ; BCCA CODE: GITAJVAC

52. A phase III randomized double-blind study of adjuvant STI571 (Gleevec) vs placebo in patients following the resection of primary gastrointestinal stromal tumour (GIST) protocol Z9001

BCCA PI: M Knowling; BCCA CODE: SAZ9001

VCC - Lymphoma Clinical Trials

53. An open-label, multicenter, randomized, comparative, phase III study to evaluate the efficacy and safety of rituximab plus fludarabine and cyclophosphamide (FCR) versus fludarabine and cyclophosphamide alone (FC) in previously treated patients with CD20 positive B-cell chronic

lymphocytic leukemia BCCA PI: P Hoskins; BCCA CODE: LYTCRFC opened in September 2004
54.A phase I study of G3139 antisense oligonucleotide (Obimersen) in combination with CHOP and Rituximab in untreated advanced stage diffuse large B-cell lymphoma BCCA PI: R Klasa; BCCA CODE: LYTG3139; NCI protocol #5818
55.A phase II study of PS-341 (NSC 681239) in patients with untreated or relapsed mantle cell lymphoma BCCA PI: L Sehn; BCCA CODE: LYIND150; NCIC IND150

VCC - Gyne – Ovarian Cancer Clinical Trials
56.A phase II study of CCI-779 in patients with metastatic and/or locally advanced recurrent endometrial cancer BCCA PI: P Hoskins; BCCA CODE: GOIND160 opened in October 2004; NCIC IND.160
57.An international multi-centre randomized phase III study comparing upfront debulking surgery versus neo-adjuvant chemotherapy in patients with stage IIIC or IV epithelial ovarian carcinoma BCCA PI: T Ehlen; BCCA CODE: GOOV13 opened in April 2000; NCIC OV13

VCC - Sarcoma Clinical Trial
58.A phase III randomized double blind study of adjuvant STI571 (Gleevec) vs placebo in patients following the resection of primary Gastrointestinal Stromal Tumour (GST) Protocol Z9001 BCCA PI: M. Knowling; BCCA CODE: SAZ9001 opened in December 2004

VCC - Skin – Melanoma Clinical Trial
59.Phase III randomized study of four weeks high dose Interferon -α2b in stage T3 – T4 or N1 (microscopic) melanoma BCCA PI:K Savage; BCCA CODE: SMME10 opened in September 2004; NCIC ME10

CURRENT RESEARCH PROJECTS – MEDICAL ONCOLOGY

Research Projects – VCC
60.Expression of EGFR and VEGF in malignant pleural mesothelioma: defining potential therapeutic targets PI: C Lee; WCB, 2002-2005; Σ \$34,802 This study will confirm early positive results of staining for mesothelioma for two proteins, one involved in cell signaling, epidermal growth factor receptor (EGFR), and the other in blood vessel formation, vascular endothelial growth factor (VEGF). The possible relationship between these proteins and survival will also be looked at. In particular, if staining for EGFR can predict the effect of an EGFR inhibitor in a clinical trial in patients with malignant mesothelioma.
Interdisciplinary Research Projects
61.Organochlorines, ultraviolet radiation and gene environment PI: J Connors; Co-PI: J Spinelli; NCIC; 2003-2006; Σ \$563,333 For a summary of this project see Cancer Control Research.
62.G3: a multidisciplinary approach to healthy aging Co-PIs: M Marra, J Connors; NCIC; 2003-2008; Σ \$250,000 For a summary of this project see Genome Sciences Centre.

63. Mantle cell lymphoma project

PI: R Gascoyne; Co-applicants: J Connors, R Klasa, W Lam, M Dyer, R Siebert, C Brown and D. Horsman; Lymphoma Research Foundation USA; 2003-2006; Σ \$3,200,000USD

For a summary of this project see Department of Pathology and Laboratory Medicine.

64. Multi-target combination therapy to delay progression to androgen independence

PI: M Gleave; Co-PI: K Chi; NCIC; 2001-2006; \$175,760 per year; Σ \$1,054,560

Current Clinical Trials – Cancer Centre of the Southern Interior (CCSI)**65. A randomized Phase III trial of exemestane vs. anastrozole in postmenopausal women with receptor positive primary breast cancer**

BCCA PI: M Taylor; BCCA CODE: NCIC CTG MA.27 opened January 2004

66. A randomized Phase III trial comparing immediate vs. deferred chemotherapy after radical cystectomy in patients with pT3-pT4, and/or transitional cell carcinoma of the bladder

BCCA PI: S Ellard; BCCA CODE NCIC CTG Bl.8 opened July 2002

67. A randomized Phase III study comparing androgen suppression and elective pelvic nodal irradiation followed by a high dose of 3-D conformal boost vs. androgen suppression and elective nodal irradiation followed by a 125Iodine brachytherapy implant boost for patients with intermediate and high risk localized prostate cancer

BCCA PI: R Halperin; BCCA CODE: ASCENDE-RT opened August 2004

68. A randomized Phase II trial of Strontium-89 with or without cisplatin for the palliation of bone pain secondary to hormone refractory prostate cancer

BCCA PI: S Ellard; BCCA CODE: GUPPS2 opened June 2004

69. A Phase II study of ZD6474 or placebo in small cell lung cancer patients who have complete or partial response to induction chemotherapy +/- radiation therapy

BCCA PI: S Rao; BCCA CODE: NCIC CTG BR.20 opened July 2003

70. An open-label, Phase II trial of ZD1839 (Iressa) in patients with malignant mesothelioma

BCCA PI: S Rao; BCCA CODE: AZ1839IL-0094 opened December 2003

71. A Phase II multicentre randomized, parallel group, double blind placebo controlled study of ZD1839 plus best supportive care (BSC) vs. placebo plus BSC in chemotherapy-naïve patients with advanced (Stage IIIB or IV) non small cell lung cancer and poor performance status

BCCA PI: S Rao; BCCA CODE: AZ1939IL-0711 opened December 2004

72. A Phase III randomized study of four weeks of high dose IFN-2b in Stage T3-T4 or N1 (microscopic) melanoma

BCCA PI: S Rao; BCCA CODE: NCIC CTG ME.10 opened August 2004

Current Clinical Trials – Fraser Valley Cancer Centre (FVCC)**73. A randomized Phase III trial of exemestane vs. anastrozole with or without celecoxib in postmenopausal women with receptor positive primary breast cancer**

BCCA PI: LA Martin; BCCA CODE: NCIC CTG MA.27 opened March 2004

74. Expression of EGFR and VEGF in malignant pleural mesothelioma: defining potential therapeutic targets

BCCA PI: C Lee; opened September 2003

75.A Phase 2 multicentre randomized, parallel group, double blind placebo controlled study of ZD1839 (iressa) (250mg tablet) plus best supportive care (BSC) vs. placebo plus BSC in chemotherapy-naïve patients with advanced (Stage IIIB or IV) non small cell lung cancer and poor performance status

BCCA PI: C Lee; BCCA CODE: AZ0711 opened December 2004

Current Clinical Trials – Vancouver Island Cancer Centre (VICC)

76.A double-blind re-randomization to letrozole or placebo for women completing five years of adjuvant letrozole

BCCA PI: S Allan; BCCA CODE: NCIC CTG MA.17R opened December 2004

77.Gene expression changes during the development of hormone resistance in metastatic breast cancer

BCCA PI: N Macpherson; Opened 2003

78.A multi-centre study to assess the positive predictive value of Positron Emission Tomography (PET) in the preoperative evaluation of internal mammary nodes in breast cancer patients

BCCA PI: V Bernstein; NCI opened October 2000

For a summary see Vancouver Island Cancer Centre

79.A Phase II adjuvant trial in pancreatic ductal adenocarcinoma comparing 5FU and leucovorin vs. gemcitabine

BCCA PI: B Weinerman; BCCA CODE: NCIC PA.2 opened May 2004

80.A Phase III evaluation of gabapentin for the treatment of hot flashes in prostate cancer patients undergoing androgen deprivation therapy

BCCA PI: H Pai; ACURA opened November 2003

81.An open-label, Phase II trial of ZD1839 (Iressa) in patients with malignant mesothelioma

BCCA PI: H Anderson; BCCA CODE: AZ1839IL-0094 opened December 2003

82.Expression of EGFR and VEGF in malignant pleural mesothelioma: defining potential therapeutic targets

BCCA PI: H Anderson; opened December 2003

83.A Phase III randomized study of four weeks of high dose IFN-2b in Stage T3-T4 or N1 (microscopic) melanoma

BCCA PI: K Wilson; BCCA CODE: NCIC CTG ME.10 opened July 2003

84.A Phase III randomized double-blind study of adjuvant ST1571 (Gleevec) vs. placebo in patients following the resection of primary gastrointestinal stromal tumour (GIST)

BCCA PI: A Attwell; BCCA CODE CTSU Z9001 opened December 2004

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

No of peer-reviewed papers	No of books and book chapters	No of presentations	No. of poster abstracts	Patent Applications
24	0	0	0	0

DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE
BC CANCER AGENCY
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<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Diponkar Banerjee	MBChB, PhD	Program Leader, Cancer Pathology Director, Pathology & Lab Medicine Clinical Professor and Medical Director, Pathology and Laboratory Medicine, UBC
Aly Karsan	MD	Hematopathologist & Senior Scientist, Medical Biophysics Associate Professor, Pathology and Laboratory Medicine, UBC
David Huntsman	MD, PhD Genetics	Genetic Pathologist Assistant Professor, Pathology and Laboratory Medicine, UBC
Doug Horsman	MD	Pathologist Director Hereditary Cancer Program Clinical Professor, Pathology and Laboratory Medicine, UBC
Randy Gascoyne	MD	Hematopathologist Clinical Professor, Pathology and Laboratory Medicine, UBC
Mukesh Chhanabhai	MD	Hematopathologist Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC
Terry Bainbridge	MD	Pathologist Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC
Malcolm Hayes	MD	Pathologist Clinical Professor, Pathology and Laboratory Medicine, UBC
Bryan Knight	MD	Pathologist
Robert O'Connor	MD	Cytopathologist Clinical Professor, Pathology and Laboratory Medicine, UBC
Wes Schreiber	MD	Medical Director, Tumour Marker Laboratory Professor, Pathology and Laboratory Medicine, UBC
Brian Skinnider	MD	Pathologist Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC
Thomas Thomson	MD	Cytopathologist Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC
Dirk van Niekerk	MD	Pathologist Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC

Torsten Nielsen	MD/PhD	Pathologist Assistant Professor Pathology and Laboratory Medicine, UBC
Andrew Weng	MD, PhD Molecular Genetics and Cell Biology	Hematopathologist / Senior Scientist Assistant Professor, Pathology and Laboratory Medicine, UBC

OUR RESEARCH FOCUS: The major research efforts of the department are in translational and applied genomics and proteomics of lymphoma, breast cancer, lung cancer, prostate cancer, and tumor immunology, working closely with clinical tumour groups and basic scientists at the BC Cancer Agency and with other research laboratories worldwide.

In lymphoma, the research focuses on basic biology of various lymphomas including Hodgkin lymphoma and non Hodgkin lymphoma, the establishment of genomic and transcriptomic signatures that predict classification and response to therapy or treatment failure. The department has systematically studied the cytogenetics of lymphomas and has banked thousands of frozen samples which allow rapid assessment of new biomarkers and correlation with clinical outcome, as all the samples are from patients who have been uniformly treated with optimized protocols based on published evidence, and followed up for one or more decades. Through the sustained efforts of individuals such as Drs. Randy Gascoyne, Doug Horsman and Joseph Connors, the Lymphoma Tumour Group Chair, BCCA has now become recognized as a world leader in lymphoma research. Dr. Andrew Weng, a recent recruit, is working on Notch signaling in T-cell acute lymphoblastic leukemia, in normal lymphoid development, and on the molecular genetics of follicular lymphoma. Dr. Aly Karsan, a Haematopathologist and Senior Scientist, is an expert in angiogenesis, endothelial cell biology, and proteomics as applied to human cancer. Dr. Diponkar Banerjee is characterising novel proteins expressed by Hodgkin lymphoma and aggressive non-Hodgkin lymphomas.

In breast cancer, Drs. David Huntsman, Torsten Nielsen, and colleagues from the Breast Tumour Group and Vancouver Hospital have spearheaded a major effort in the molecular taxonomy of breast cancer and the validation of novel biomarkers of breast cancer, having established the Genetic Pathology Evaluation Centre (GPEC) at the Prostate Research Centre, and GPEC II at the BCCA Vancouver Centre. The recent arrival of Dr. Sam Aparicio as Chair, Molecular Oncology and Breast Cancer Research creates a significant momentum in breast cancer research and we expect to see major new programs in molecular oncology of breast cancer. Dr. Torsten Nielsen is also pioneering efforts in the molecular taxonomy of soft tissue sarcomas.

In collaboration with Dr. Wan Lam, Dr. Doug Horsman is validating the clinical utility of submegabase resolution tiling (SMRT) array CGH in studying gene copy number alterations in human cancers.

PROGRESS HIGHLIGHTS IN 2004

- We were successful in obtaining 12 new grants totaling \$6.9 million and published 29 peer-reviewed papers, and 39 abstracts.

RESEARCH KEYWORDS

Cancer biology, molecular classification of human cancers, tumor-associated antigens, immunohistochemistry, flow cytometry, tumour recurrence, molecular cytogenetics, molecular pathology, tumour immunology, monoclonal antibodies, multi-colour karyotyping, chromosome microdissection, fiber FISH, translocation breakpoint cloning using LDI-PCR, tissue microarrays, genetic pathology, expression profiling, array CGH

TRAINING**Summary of Trainees and Degrees Completed**

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
8				8

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Jean-Claude Cutz, MD, FRCP	W Lam	Research Fellowship (CIHR Training Program in Molecular Pathology)
Pedro Farinha, MD	R Gascoyne	Research Fellowship (CIHR Training Program in Molecular Pathology)
Ashish Rajput, MD	D Huntsman	Research Fellowship (CIHR Training Program in Molecular Pathology)
Blaise Clarke, MD	D Huntsman	Research Fellowship (CIHR Training Program in Molecular Pathology)
Nathalie Johnson, MD	R Gascoyne	Research Fellowship (CIHR Training Program in Molecular Pathology)
Jefferson Terry, MD MSc	T Nielsen	Roman M. Babicki Fellowship in Medical Research (UBC)

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
David Huntsman	Scholar – MSFHR (2002 – 2007)
Torsten Nielsen	Scholar – MSFHR (2003 – 2008)

RESEARCH PROJECT & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Total Value</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value</i>
38	\$45,228,296	12	\$6,887,772

CURRENT RESEARCH PROJECTS⁶

Pathology
<p>1. Angiogenesis in ischemia <i>PI: A Karsan; Heart & Stroke Fdn.; 2001-2004; \$95,000 per year; Σ \$380,000</i> The goal is to study molecular mechanisms of neovascularization in ischemia</p>
<p>2. Automated digital imaging system for tissue microarrays <i>PI: T Nielsen; CFI New Opportunities; 2003-2008; Σ \$309,000</i> This funding enabled installation of a system to captures digital images from microscopic slides. Installed at the Genetic Pathology Evaluation Centre, this equipment allows permanent secure archiving of digital images, enhanced visual and automated quantitation of biomarker expression on tumor specimens, and on-line international collaboration and publication of primary data.</p>
<p>3. *Clinical implications of EMSY gene amplification events † <i>PI: D Huntsman; Co-PI: C Bajdik and K Gelmon; CIHR; 2004-2007; Σ \$113,812</i> The goal is to determine whether EMSY amplification is an independent marker for poor prognosis through the study of 6,500 cancer cases. The project will assess the frequency of EMSY amplification events in in-situ breast cancers to determine whether EMSY amplification events occur early in or late in breast cancer oncogenesis. These studies are key to determine whether the detection of EMSY amplification should be further developed as a clinical biomarker.</p>
<p>4. Clinical implications of EMSY gene amplification events[†] <i>PI: D Hunstman; CBCRA; 2003-2006; Σ \$219,899 [part of Translating target discovery into better health outcomes for women with breast cancer program; PI: K Gelmon; Σ1,941,731]</i> This study will assemble and examine 6,500 breast cancer cases to determine whether the presence of extra copies of the EMSY gene is a marker of poor prognosis for breast cancer patients. This study will also examine whether amplifications of the EMSY gene happens early or late in the formation of breast tumours and whether they play a different role in male breast cancer than in female breast cancer.</p>
<p>5. Development of a national strategy to enhance integrated and collaborative research to improve evidence-based clinical service delivery for hereditary cancer syndromes <i>PI: D Horsman; CIHR; 2004; Σ \$75,000</i> The objectives of this project are to 1.) build a pan-Canadian interdisciplinary Hereditary Cancer Task Force to address issues relating to development, quality and delivery of hereditary cancer genetic services in Canada, in partnership with existing clinical and research programs, and provincial and federal government agencies; 2.) to pursue the collaborative development of consensus policy</p>

⁶ Key to Abbreviations: PL = Project Leader; PI = Principal Investigator, Co-I = Co-investigator; CBCRA = Canadian Breast Cancer Research Alliance, CIHR = Canadian Institutes of Health Research, MSFHR = Michael Smith Foundation for Health Research, NCIC = National Cancer Institute of Canada; Σ = total amount of project funding committed, * = New Projects in 2004, † = Inter-departmental project.

guidelines, standards of practice and quality assured genetic testing, and 3.) to foster the development of common database structures/content across provincial clinical and research programs that will facilitate the collection and analysis of national data, while respecting confidentiality and data ownership.	
6. *Double stranded break surveillance genes and susceptibility to non-Hodgkin's lymphoma[†]	<p>PI: A Brooks-Wilson; Co-PI: J Spinelli, J Connors and R Gascoyne; NCIC; 2004-2007; \$149,531; Σ \$444,593</p> <p>For a summary of this project see Genome Sciences Centre.</p>
7. EMSY amplification: clinical relevance in ovarian cancer	<p>PI: D Huntsman; Marsha Rivkin Center for Ovarian Cancer Research 2004 – 2005: \$42,000;</p> <p>The goal of this pilot study is to determine the role that a newly identified gene has in ovarian cancer. EMSY amplification has been implicated in breast cancer progression.</p>
8. Endothelial to mesenchymal transformation[†]	<p>PI: A Karsan; Co-PI: P Hoodless; CIHR; 2003-2008; Σ \$290,188</p> <p>For a description of this project see Medical Biophysics.</p>
9. *Familial gastric cancer frequency and molecular genetics	<p>PI: D. Huntsman; NCIC 2004 – 2007; \$96,728 in 2004; Σ \$297,000</p> <p>The goal is to look for genetic alterations not previously detected in families at high risk of stomach cancer, and to develop new tests to determine whether other genetic alterations indicate a high risk of cancer.</p>
10. *Genetic Pathology Evaluation Centre	<p>PI: D Huntsman; Co-I: T Nielson, B Gilks; MSFHR; 2004 – 2008; \$147,000; Σ\$441,000</p> <p>Researchers at the centre are using tissue microarray technology to systematically validate whether certain biomarkers – cellular or molecular substances found in cancers – can be used to improve cancer diagnostics or predict the course of disease. With the ability to test hundreds of tumour samples at a time, researchers can assess the value of potential biomarkers with an efficiency that would have been unimaginable just a few years ago</p>
11. *Hereditary diffuse gastric cancer – genetics, frequency, clinical features	<p>PI: D Huntsman; Co-PI: S Gallinger, B McGillivray and C Roskelley; 2004-2007; Σ \$269,210</p> <p>This project will find ways to identify persons who are most likely to develop stomach cancer so that members of families at risk can make more informed choices about their health. The project hopes to do this by using a new technique that will look for genetic alterations that could not be previously detected and developing new tests to determine whether other genetic alterations indicate a high risk of cancer.</p>
12. Lipopolysaccharide signaling in endothelial cells[†]	<p>PI: A Karsan; CIHR; 2003-2008; Σ \$557,395</p> <p>For a description of this project see Medical Biophysics.</p>
13. *Mechanisms of ischemic neovascularization	<p>PI: A Karsan;</p> <p>Heart & Stroke Foundation; 2004-2009; \$108,470 per year; Σ \$542,350</p> <p>This project will try to determine whether Notch activation in endothelial cells plays a role in arteriogenesis by promoting endothelial transformation to smooth muscle cells.</p>
14. Mechanisms of tumour angiogenesis[†]	<p>PI: A Karsan; NCIC; 2003-2006; \$144,110 per year; Σ \$432,330</p> <p>For a description of this project see Medical Biophysics.</p>

<p>15. Molecular classification of B-cell non-Hodgkin's disease <i>PI: R Gascoyne; NIH; 1999-2005; Σ \$3,200,000</i> The goal of this research is directed towards a molecular classification of B-Cell Non-Hodgkin's Disease</p>
<p>16. Molecular mechanisms of endothelial survival/apoptosis <i>PI A Karsan; Heart & Stroke Foundation; 2003-2006; Σ \$273,258</i> This project is to determine whether Notch4 can protect endothelial cells from death triggered by glucose, homocysteine and oxidized lipids.</p>
<p>17. New Molecular Targets in Mantle Cell Lymphoma <i>PI R Gascoyne; Lymphoma Research Foundation (USA) 2003-2006; Σ US\$3,200,000</i> The goal is to investigate various aspects of new molecular targets in mantle cell lymphoma.</p>
<p>18. Notch Signaling in Lymphoid Development and Neoplasia <i>PI: A Weng; NCI; 2003 – 2006 Σ USD\$387,000</i> Notch signaling in T-cell acute lymphoblastic leukemia and normal lymphoid development</p>
<p>19. Structure-function studies of cell surface molecules R24.1 and R26.8 expressed by Hodgkin lymphoma and anaplastic large cell lymphoma <i>PI: D Banerjee; CIHR; 2003-2006; Σ \$291,540</i> This proposal will study the function of anaplastic large cell lymphoma, a unique antibody that reacts with cancer cells of Hodgkin's disease and a form of malignant lymphoma. The mechanisms by which these antibodies influence the multiplication of cancer cells will be studied. The molecules recognized by these antibodies and the gene encoding such molecules will be identified.</p>
<p>20. *Synovial sarcoma: translating gene expression into clinical care <i>PI: T Nielsen; Terry Fox Foundation; 2004; Σ \$336,756</i> This research seeks to develop new treatments for synovial sarcoma using retinoic acid-related drugs, and others agents interfering with the genes expressed in this malignancy. In doing so, it would demonstrate how the clues revealed by gene microarray profiling can quickly be turned into practical approaches for treating cancer.</p>

Interdisciplinary
<p>21. The assessment and validation of new and novel prognostic and predictive markers in breast cancer with tissue microarrays† <i>PI: Chia, S; Co-I Huntsman; NCIC; 2002-2004; Σ \$116,000</i> The goal is to use a newly developed breast cancer tissue microarray system to provide validation of molecular markers / reagents for predictive and prognostic use in breast cancer.</p>
<p>22. *Cardiovascular and respiratory stem cell plasticity <i>PI: J Galipeau; Co-I: A Karsan, P Lansdorp, P Liu, L Megeney, J Stewart; CARE/NET-CIHR, Stem Cell Network, Heart & Stroke Foundation; 2004-2009; Σ \$1.5 million</i> For a description of this project see Medical Biophysics.</p>
<p>23. Cancer genomics: A multidisciplinary approach to the large-scale high-throughput identification of genes involved in early stage cancers† <i>PI: V Ling, C Eaves, M Marra; Co-I: T. Bainbridge & others</i> Genome Canada; 2001-2005; Σ, \$16,778,000 For a description of this project please see Cancer Genetics & Dev. Biology.</p>
<p>24. Clinician scientists in molecular oncologic pathology† <i>PI: MS Tsao; Co-PI: S Asa, D Banerjee, A Brooks-Wilson, DW Hedley, D Horsman, D Huntsman, S Jones, S Kamel-Reid, A Karsan, W Lam, V Ling, M</i></p>

<p><i>Marra, J Squire, J Vielkind; CIHR; 2002-2008; Σ \$1,097,333</i> To train next generation clinician-scientists and research pathologists with transdisciplinary competence in histopathology, genomics, proteomics, molecular cytogenetics and advanced molecular micro-imaging techniques.</p>
<p>25.*Development and validation of comparative genomic hybridization arrays for clinical use in cancer[†] <i>Co-PIs: D Horsman & W Lam; Genome BC/Canada; 2004-2007; Σ \$2,305,769</i> For a summary of this project see Cancer Genetics and Developmental Biology.</p>
<p>26.Evaluation of sotrasterol sulphate for use in therapeutic angiogenesis <i>PIs: A Karsan, R Anderson, UBC; CIHR; 2003-2004; Σ \$98,682</i> For a description of this project see Medical Biophysics.</p>
<p>27.Genomic and expression profiling of malignant peripheral nerve sheath tumors in neurofibromatosis patients <i>PI: M van de Rijn; co-I: T Nielsen, BP Rubin. US Dept of Defense 2002-2007 Σ USD\$1,472,013</i> cDNA microarray profiling of benign and malignant nerve sheath tumors, and related sarcomas, is being used to understand the biology of tumor progression, and to develop new diagnostic markers and targeted therapies.</p>
<p>28.Organochlorines, ultraviolet radiation and gene-environment interactions in non-Hodgkin's lymphoma[†] <i>Co-PIs: A Brooks-Wilson, J Connors, R Gascoyne and J Spinelli; NCIC; 2003-2006; For 2004 - \$563,333; Σ \$2,253,332</i> For a description of this project please see Cancer Control Research.</p>
<p>29.Proteomic assessment of women being diagnosed with breast cancer <i>Co-PI: K Gelmon, A. Karsan; Co-I: M Hayes, J Spinelli, D Harrison, P Switzer, P Hassell, M Stilwell; CBCF; 2003-2004; \$55,516 per year; Σ \$111,1032</i> The purpose of this project is to identify serum biomarkers for breast cancer..</p>
<p>30.*Simulation of a population-based genetic testing program for genetic susceptibility[†] <i>PI: C Bajdik; Co-I: D Huntsman, R Gallagher, D Horsman, and J Spinelli; CIHR 2004 – 2007; Σ \$145,282</i> For a summary of this project see Cancer Control Research.</p>
<p>31.Solid tumour progression research unit <i>PL: C. Roskelley, UBC; Co-I: S Dedhar, R Anderson, A Karsan, A Minchinton, M Roberge; MSFHR; 2003-2007 \$149,914 per year; Σ \$599,656</i> For a description of this research unit see Medical Biophysics.</p>

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

Pathology				
<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
29	0	0	39	0

DEPARTMENT OF RADIATION ONCOLOGY

BC CANCER AGENCY

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<i>Researcher name</i>	<i>Position & Cross-Appointments</i>
Thomas J. Keane	Head, Radiation Oncology; Provincial Leader, Radiation Therapy Program, BCCA & Professor, UBC[†]
Alex Agranovich	Radiation Oncologist, FVCC & Clinical Assoc Prof, UBC
Susan Balkwill	Radiation Oncologist, FVCC & Clinical Instructor, UBC
Eric Berthelet	Radiation Oncologist, VICC & Clinical Assoc Prof, UBC
Paul Blood	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Graeme Duncan	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Randall Fairey	Radiation Oncologist, CCSI & Clinical Assoc Prof, UBC
Karen Goddard	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Clive Grafton	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Ross Halperin	Radiation Oncologist, CCSI & Clinical Asst Prof, UBC
John Hay	Radiation Oncologist, VCC & Clinical Professor, UBC
David Hoegler	Radiation Oncologist, CCSI & Clinical Asst Prof, UBC
Howard Joe	Radiation Oncologist, VICC & Clinical Instructor, UBC
Sam Kader	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Anand Karvat	Radiation Oncologist, FVCC & Clinical Instructor, UBC
Mira Keyes	Radiation Oncologist, VCC & Clinical Asst Prof, UBC
David Kim	Radiation Oncologist, CCSI & Clinical Instructor, UBC
Charmaine Kim-Sing	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Ed Kostashuk	Radiation Oncologist, FVCC & Clinical Professor, UBC
Winkle Kwan	Radiation Oncologist, FVCC & Clinical Asst Prof, UBC
Stephan Larsson	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Pamela Leco	Radiation Oncologist, CCSI & Clinical Instructor, UBC
Carson Leong	Radiation Oncologist, FVCC & Clinical Asst Prof, UBC
Wing Yee Leung	Clinical Associate, VCC & Clinical Instructor, UBC
Lim, Jan	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Peter Lim	Radiation Oncologist, VCC & Clinical Asst Prof, UBC
Mitchell Liu	Radiation Oncologist, FVCC & Clinical Asst Prof, UBC
Charles Ludgate	Radiation Oncologist, VICC & Clinical Assoc Prof, UBC
Roy Ma	Radiation Oncologist, VCC & Clinical Asst Prof, UBC
Michael McKenzie	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Islam Mohamed	Radiation Oncologist, CCSI & Clinical Instructor, UBC
James Morris	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC

[†] All academic appointments are in the Division of Radiation Oncology & Developmental Radiotherapeutics, Division of Radiation Oncology, University of British Columbia

Ivo Olivotto	Radiation Oncologist, VICC & Clinical Professor, UBC
Howard Pai	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Christina Parsons	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Tom Pickles	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Milton Po	Radiation Oncologist, FVCC & Clinical Asst Prof, UBC
Melanie Reed	Radiation Oncologist, CCSI & Clinical Asst Prof, UBC
Barry Sheehan	Radiation Oncologist, VCC & Clinical Asst Prof, UBC
Simon Sutcliffe	Radiation Oncologist, VCC; President, BCCA
Paul Truong	Radiation Oncologist, VICC & Clinical Assoc Prof, UBC
Scott Tyldesley	Radiation Oncologist, VCC & Clinical Asst Prof, UBC
Nicholas J. Voss	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Elaine Wai	Radiation Oncologist, VICC & Clinical Asst Prof, UBC
Lorna Weir	Radiation Oncologist, VCC & Clinical Assoc Prof, UBC
Don Wilson	Radiation Oncologist, FVCC & Clinical Asst Prof, UBC
Jane Wilson	Radiation Oncologist, CCSI & Clinical Asst Prof, UBC
Frances Wong	Radiation Oncologist, FVCC & Clinical Professor, UBC
Jonn Wu	Radiation Oncologist, VCC & Clinical Asst Prof, UBC

Clinicians of the Provincial Radiation Therapy Program hold academic appointments in the Division of Radiation Oncology and Developmental Radiotherapeutics, Department of Surgery, UBC. The Department of Radiation Oncology comprises radiation oncologists organized as the BCCA Provincial Radiation Therapy Program located at four regional centres (Cancer Centre for the Southern Interior, Kelowna (CCSI); Fraser Valley Cancer Centre, Surrey (FVCC); Vancouver Cancer Centre (VCC) and Vancouver Island Cancer Centre, Victoria (VICC)).

OUR RESEARCH FOCUS

The majority of radiation oncologists are clinical faculty with limited protected time for research. Despite this limitation, the faculty are actively involved in primarily clinical research, usually through the conduct of Phase I,II or Phase III clinical trials. The majority of clinical trials are funded through co-operative groups such as NCIC, NSABP, though industry sponsored trials are becoming more common. Involvement in basic and translational research is primarily through collaboration with scientists and other clinicians at UBC or UVic. There is a growing interest in health services research and this will be a major focus in the coming years.

The final area of research development will be in technology development and medical physics, in association with the medical physicists at BCCA.

RESEARCH KEYWORDS:

Radiation Oncology, Radiotherapy, Physics, Brachytherapy, Clinical trials, Outcomes research

TRAINING

A) COURSE INSTRUCTORS

UBC PHYS 534 Radiotherapy Physics I: Cynthia Araujo, Alistair Baillie, Wayne Beckham & Sergei Zavgorodni

UBC PHY 535 Radiotherapy Physics II: B. Clark et al

UBC PHY 539 Radiation Dosimetry: Cheryl Duzenli, E. Gete, T. Popescu

UBC PHY 404 Introduction to Medical Physics (6 lecture hrs therapy physics): C. Duenli & I. Spadinger

UBC PHYS 432 Introduction to Medical Physics: Will Ansbacher, Wayne Beckham & Derek Wells

BCIT Radiography Technologist Program – Physics Course: S. Hussein, B. Clark

SUMMARY OF TRAINEES AND DEGREES COMPLETED

<i>Total No. of Current Students</i>	<i>Residents</i>	<i>Physics Residents</i>	<i>Post-graduate Fellows</i>	<i>Undergraduate Medical Students</i>
51	11	2	7	31

CURRENT STUDENTS – DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>
MD		
Valeri Goutsouliak	Mira Keyes	
Jo Martin	Peter Lim	Jul 04
Graham MacDonald	Peter Lim	Sep 04
Andrew Bates	Peter Lim	Aug 04
Miguel Panades	Ivo Olivotto	Jun 04
MSc		
Karl Bush	Tony Popescu	
Miao Zhang	V. Moiseenko	

TRAINEE AWARDS - EXTERNAL

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Lily Kerby	Graeme Duncan	James Wall Hay Scholarship
David Voduc	Mira Keyes	ASCO Young Investigators Award
Alanah Bergman	C. Duzenli	Michael Smith Foundation 2002-05

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
McKenzie, Michael	Study Committee, NCIC CTG SC.19 study Member, Symptom Control Committee, NCIC CTG Reviewer, Canadian Medical Association Journal
Pickles, Tom	President-Elect Canadian Association of Radiation Oncology (Sep, 2003 – Sep, 2005) Executive member GU Radiation Oncologists of Canada (2000 -) Executive member National Cancer Institute of Canada GU Clinical Trials Group (Apr, 2004 -) Executive member Canadian Urology Oncology Group (CUOG) (Apr, 2004 -)
Mitchell Liu	NCIC – FVC Lung representative

Lorna Weir	Local (BC) principal investigator NSABP Member of Board of Directors, Canadian Breast Cancer Foundation (BC/Yukon) and Chair of Medical Advisory Committee
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MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects in 2004</i>	<i>Total Value</i>	<i>No. of New Research Projects in 2004</i>	<i>Total Value</i>
48	n/a	17	n/a

CURRENT RESEARCH – RADIATION ONCOLOGY

Clinical Trials - Fraser Valley Cancer Centre	
1. A phase III study of regional radiation therapy in early breast cancer (MA20) <i>PI: W Kwan; NCIC</i>	
2. Randomized trial comparing intermittent vs. continuous androgen suppression for patients with prostate-specific-antigen progression in the clinical absence of distant metastases following radiotherapy for prostate cancer (PR7) <i>PI: W Kwan; NCIC</i>	
3. A trial of a soy beverage for subjects without clinical disease with rising prostate-specific antigen after radiation for prostate cancer (Soy) <i>PI: W Kwan; NCIC</i>	
4. A randomized trial of Strontium-89 with or without Cisplatin for the palliation of bone pain secondary to hormone refractory prostate cancer (Strontium) <i>PI: W Kwan; Prostate Cancer Research Foundation of Canada</i>	
5. A comparison of acute oral mucositis between morning and afternoon radiotherapy in patients receiving radiation treatments for cancer of the head and neck (HN3) <i>PI: C Leung, F Wong; NCIC</i>	
6. A randomized trial of concomitant radiation, cisplatin, and tirapazamine (SR259075) vs. concomitant radiation and cisplatin in patients with advanced head and neck cancer (EFC4690) <i>PI: C Leung; Sanofi</i>	
Clinical Trials – Vancouver Cancer Centre	
7. A randomized phase II study comparing androgen suppression and pelvic EBRT followed by a high dose 3-dimensional conformal boost vs. androgen suppression and pelvic EBRT followed by a ¹²⁵Iodine brachytherapy implant boost for patients with intermediate and high risk localized prostate cancer (ASCENDE-RT Phase 2) <i>PI: J Morris; Aventis, Amersham Health</i>	
8. A clinical trial comparing adjuvant clodronate therapy vs. placebo in early stage breast cancer patients receiving systemic chemotherapy and/or hormonal therapy or no therapy (BRB34) <i>PI: L Weir; NSABP</i>	
9. A pilot study to explore prophylactic cranial radiation in patients with stable or responding her2neu + metastatic breast cancer after first or second line chemotherapy plus herceptin (BRTCRAD) <i>PI: L Weir; CBCF</i>	

10. A phase III randomized trial comparing intermittent vs. continuous androgen suppression for patients with prostate-specific antigen progression in the clinical absence of distant metastases following radiotherapy for prostate cancer (GUPR07) PI: T Pickles; NCIC
11. A trial to evaluate the efficacy of maintaining hemoglobin levels above 120G/L with erythropoietin vs. above 100G/L without erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer (GOCX4) PI: F Wong; NCIC
12. Trial of a soy beverage for subjects without clinical disease with rising prostate-specific-antigen after radical radiation for prostate cancer (GUSOY) PI: W Kwan, G Duncan; Lotte & John Hecht Memorial Foundation
13. Study of neoadjuvant docetaxel plus neoadjuvant/adjuvant hormone therapy and locoregional radiation therapy for high-risk localized adenocarcinoma of the prostate (GUTBDOC) PI: M McKenzie; Aventis
14. A phase III trial of radiation therapy with or without casodex in patients with prostate-specific-antigen elevation following radical prostatectomy for pT3N0 carcinoma of the prostate (GURT9601) PI: M McKenzie; NCIC-RTOG
15. Treatment time study for head and neck cancer (HN3) PI: J Hay; NCIC
16. A randomized trial of concomitant radiation, cisplatin, and tirapazamine vs. concomitant radiation and cisplatin in patients with advanced head and neck cancer (HNTPTIRA) PI: F Sheehan; Sanofi
17. A dosimetry and dose escalation study of Lymphorad™-131; Iodine I 131 labeled B lymphocyte stimulator in subjects with relapsed multiple myeloma following autologous stem cell transplant (LYTLR131) PI: J Morris; Human Genome Sciences, Inc.
18. Efficacy and safety of subsequent treatment with Y-ibritumomab tiuxetan vs. no further treatment in patients with stage III or IV follicular non-Hodgkin's lymphoma having achieved partial or complete remission after first line chemotherapy (LYTZEV) PI: T Pickles; Berlex
19. A randomized, open label, comparative study of standard whole brain radiation therapy with or without RSR13 in patients with brain metastases (MOTRSR13) PI: R Ma; Allos Therapeutics
20. A phase I dosimetry and dose escalation study of Lymphorad™-131 (LR131; Iodine I 131 labeled B lymphocyte stimulator) in patients with relapsed or refractory multiple myeloma (MYTLR-131) PI: J Morris; Human Genome Sciences, Inc.
21. A phase III randomized trial comparing total androgen blockade vs. total androgen blockade plus pelvic irradiation in clinical adenocarcinoma of the prostate (PR3) PI: M McKenzie; NCIC
22. A randomized phase III double-blind study of ondansetron and dexamethasone vs. ondansetron and placebo in the prophylaxis of radiation induced emesis (SC 19) PI: M McKenzie; NCIC

Clinical Trials - Cancer Centre of the Southern Interior	
23. Randomized, double-blind, placebo-controlled study to evaluate the impact of maintaining hemoglobin levels using epoetin-alfa in limited disease small cell lung cancer (LD SCLC) subjects receiving combined chemotherapy and radiation therapy (LEGACY) PI: I Mohammed; Ortho	
24. A phase III trial of observation +/- tamoxifen vs. radiotherapy +/- tamoxifen for good-risk duct carcinoma in-situ (DCIS) of the female breast (MA26) PI: I Mohammed; NCIC	
25. Double-blind, phase III, placebo-controlled study of methylnaltrexone (MNTX) for relief of constipation due to opioid therapy in advanced medical illness (MNTX) PI: G Fyles	
26. A phase III randomized trial comparing intermittent vs. continuous androgen suppression for patients with prostate-specific-antigen progression in the clinical absence of distant metastases following radiotherapy for prostate cancer (PR7) PI: M Reed; NCIC	
27. A phase III comparison of prophylactic cranial irradiation vs. observation in patients with locally advanced non-small cell lung cancer (NSCLC) (RTOG 0214) PI: I Mohammed	
28. A phase III double-blind, placebo-controlled randomized comparison of megesterol acetate (MEGACE) vs. an N-3 Fatty Acid (EPA) enriched nutritional supplement vs. both for treatment of cancer cachexia and anorexia (SC18) PI: G Fyles; NCIC, CTG, SC	
29. A randomized, phase III, double-blind study of ondansetron and dexamethasone vs. ondansetron and placebo in the prophylaxis of radiation-induced emesis (SC19) PI: D Hoegler; NCIC	
30. A multi-center, double-blind, placebo-controlled, parallel-design trial of the efficacy and safety of sub-cutaneous tetradoxin (tectin) for moderate to severe inadequately controlled cancer-related pain (WEX014) PI: G Fyles; Covance	
Clinical Trials - Vancouver Island Cancer Centre	
31. A phase III study of regional radiation therapy in early breast cancer (MA20) PI: I Olivotto; NCIC	
32. Phase III trial of observation +/- tamoxifen vs. radiotherapy +/- tamoxifen for good-risk duct carcinoma in-situ (DCIS) of the female breast (MA26) PI: P Truong; NCIC	
33. A phase III randomized trial to evaluate the effect of raising hemoglobin using erythropoietin in anemic patients receiving concurrent radiation and cisplatin for cervical cancer (CX4) PI: H Kader; NCIC	
34. A randomized phase III study of concomitant and adjuvant temozolomide and radiotherapy for newly diagnosed glioblastoma multiforme (CE3) PI: H Pai; NCIC	

35. A randomized trial of short- vs. long-acting LHRH agonist preparation prior to transperineal implantation of the prostate PI: E Berthelet; ACURA For a summary see Vancouver Island Cancer Centre
36. Prospective evaluation of the implantation of fiducial markers as a treatment planning tool for external beam radiotherapy in prostate cancer PI: E Berthelet; Vancouver Island Research Advisory and Development Committee (VIRAD), Vancouver Island Prostate Cancer Research Foundation For a summary see Vancouver Island Cancer Centre
37. Prospective evaluation of the implantation of fiducial markers as a treatment planning tool for external beam radiotherapy in prostate cancer - Ultrasound Component PI: E Berthelet; Resonant Medical Montreal For a summary see Vancouver Island Cancer Centre
38. Does scar massage improve pain and function after breast cancer surgery? A randomized controlled study. PI: P Truong; CBCF
39. Trial of soy beverage for subjects without clinical disease with rising prostate-specific-antigen after radical radiation for prostate cancer PI: W Kwan, J Lim; Hecht Foundation
40. Can salivary crystal morphology correctly predict for the presence of breast cancer? A pilot study. PI: J Lim
41. ASCEND RT PI: WJ Morris, E Berthelet; Acura
42. A pilot study of IMRT in patients with head and neck cancer PI: S Larsson
43. High dose-rate breast brachytherapy: A new option in breast conserving treatment? PI: H Kader; CBCF
44. A feasibility study to evaluate 3-dimensional conformal radiation therapy for accelerated partial breast irradiation PI: I Olivotto; CBCF
45. Local management of early primary breast cancer in the geriatric patient with radiofrequency ablation PI: I Olivotto, H Kader; CBCF
46. Study of adjuvant RT in early breast cancer comparing use of breast IMRT to conventional wedge techniques PI: I Olivotto; CIHR
47. The effects of different treatment modalities on the immune response to prostate cancer PI: C Ludgate; Prostate Cancer Research Foundation
48. A pilot study to evaluate the feasibility of self-directed aerobic exercise and its effect on fatigue in prostate cancer patients undergoing radical external beam radiotherapy BCCA PI: P Truong; ACURA opened June 2004

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

No of peer-reviewed papers	No of books and book chapters	No of presentations	No. of poster abstracts	Patent Applications
46	0		2	0

SOCIOBEHAVIOURAL RESEARCH CENTRE**BC CANCER AGENCY**

Telephone: 604-877-6000 ext. 2193

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Richard Doll	MSW, MSc.	Provincial Leader Cancer Rehabilitation Director, Sociobehavioural Research
		Adjunct Professor, Psychology, SFU; Adjunct Professor, Health Care & Epidemiology, UBC
Joanne Stephen	PhD	Researcher
Maria Barroetavena	PhD	Researcher
		Adjunct Professor, Health Care and Epidemiology, UBC
Merissa Myles	BA	Research Assistant
Research Associates:		
Ellen Balka	PhD	Professor, Communication, SFU
Lynda Balneaves	RN, PhD	Asst. Prof, Nursing, UBC
Marilyn Borugian	PhD	Post Doctoral Fellow, BCCA
Susan Cadell	PhD	Asst. Prof, Social Work, UBC
Gwen Chapman	PhD	Associate Prof, Nutrition, UBC
Lyren Chiu	RN, PhD	Asst. Prof, Nursing, UBC
Lori d'Agincourt-Canning	PhD	Post Doctoral Fellow, BCCA
Gillian Fyles	MD, PhD	Medical Leader
Greg Hislop	MD, PhD	Senior Epidemiologist
Donna Jeffery	PhD	Asst. Prof, Social Work, UVIC
Arminée Kazanjian	Dr Soc	Professor, Health Care & Epidemiology, UBC
Anne Leis	PhD	Associate Prof, Epidemiology & Community Health, USask
Wolfgang, Linden	PhD	Professor, Psychology, UBC
Cynthia Mathieson	PhD	Prof of Psychology & Director, Centre for Population Health Services Research, UBC - Okanagan
Greg Miller	PhD	Asst. Prof, Psychology, UBC
Maxine Mueller	RN, PhD	Regional Professional Practice & Academic Leader, Nursing, BCCA
Gary Poole	PhD	Instructor, Health Care & Epidemiology, UBC

OUR RESEARCH FOCUS: Our *vision* is a patient-centred cancer care system that integrates evidence-based knowledge of psychological, social, cultural and behavioural dimensions into all aspects of the cancer control continuum – from prevention to diagnosis to treatment to survival or palliative care – in order to improve the quality of life for patients and families. We support this mission through translational research focused on psychosocial interventions, cross-cultural care, palliative care and lifestyle behaviours.

Psychosocial Research investigates the benefits of psychosocial oncology such as counseling, support groups, expressive therapies and mindfulness meditation – in improving patient and family quality of life, and improving the 'care' in the cancer care system.

Cross-Cultural Research is an underdeveloped area of research and understanding. With British Columbia's ethnic diversity and vulnerable populations, we aim to increase our understanding about the way culture affects patients' health behaviours; their experience of cancer, and their interaction with the cancer care system. This knowledge will be translated into the planning and implementation of culturally competent, equitable and quality care interventions.

Palliative Care Research focuses on improving health care and quality of life for patients in the palliative and end-of-life stages by early identification and management of suffering associated with cancer. The research examines physical, psychosocial and spiritual aspects of this stage of life, and identifies resources that will enhance quality of life during this experience. We are also focussing on translating new research knowledge into improved clinical practice, and health system improvement.

Lifestyle Research focuses on the development of practical interventions aimed at helping patients to adopt improved lifestyle behaviours, thereby lowering the risk of recurrence and improving the quality of survival.

We have developed a number of partnerships with research associates, academic researchers, policy and decision-makers, clinicians, and patients and families in order to ensure knowledge exchange, synthesis, translation, dissemination, and uptake. These interactions are key to the development of research understanding with broad clinical and health services application regionally, provincially and nationally.

RESEARCH KEYWORDS:

Sociobehavioural, cross-cultural, lifestyle, palliative and end-of-life, cultural competence, health disparities, health inequities, vulnerable populations, international health, behavioural sciences, biostatistics, health technology, psychosocial and cognitive behavioural interventions, psycho-oncology, patient navigation, rural health care, ethics, collaborative communities, cancer rehabilitation, psychosocial screening tool, self-administered stress management training, access to health care, health care interpreters, breast cancer, brain cancer, smoking cessation, culturally diverse populations, Palliative Outcome Scale, POS, Crisis Response Team for Palliative Care, nutrition and cancer, food decision making, telehealth, telemedicine, therapeutic touch, Mindfulness Based Stress Reduction, MBSR, knowledge translation, transfer, dissemination, synthesis, collaboration, cancer rehabilitation, complimentary and alternative medicine, ethnocultural, ethnicity, rehabilitation therapy, complimentary and alternative therapy

TRAINING

Course Instruction

MSW Course – School of Social Work and Family Studies SOWK 570C - 001

Course Title: Directed Studies in Social Work – Psychosocial Oncology: Grief, Loss and Survivorship Instructor: Susan Cadell

Instructors from BCCA: Gina MacKenzie, Glenda Christie, Sarah Sample, Nancy Downes, Michael Boyle, Lindsay Downie, Kathy Brandon, Karen Flood, Maria Cristina Barroetavena

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Richard Doll	Member, Canadian Strategy for Cancer Control
	Policy Committee Chair, Canadian Association of Provincial Cancer Agencies
	Chair, Supportive Care Policy Advisory Committee, Canadian Association of Provincial Cancer Agencies
	Advisory Board Member, Institute of Cancer Research, CIHR
Maria Cristina Barroetavena	<ul style="list-style-type: none"> • Member, BCCA/UBC Ethical Review Committee • Chair Scientific Committee, CAPO 2004 Conference • Member, AMSSA Health Committee • Member, 2005 Multicultural Health Fair Organizing Committee • Member, Advisory Committee for Achieving Equal Access in Health Care Project • Steering Committee Member, Access to Health Care Interpreting (Affiliation of Multicultural Societies and Service Agencies of BC)
Lorianne d'Agincourt-Canning	Ethics Consultant, Research Ethics Board, BCCA
Gillian Fyles	Executive Member of the Clinical Trials Symptom Control Group, National Cancer Institute of Canada
	Chair, UBC/BCCA PSMPC Research Sub-Committee
	Co-Medical Director, Kelowna Palliative Response Team
	Chair of the Palliative Care Subcommittee, BCCA/UBC Pain & Symptom Management
Joanne Stephen	Member of the Medical Advisory Board, Canadian Breast Cancer Foundation

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Total Value</i>	<i>No. of New Research Projects in 2004</i>	<i>Total Value</i>
29	\$7, 877,899	16	\$2, 125,979

CURRENT RESEARCH PROJECTS – SOCIOBEHAVIOURAL RESEARCH

Psychosocial Research
<p>1. P-Scan: Development and evaluation of a psychosocial screening tool for the BCCA <i>PI: MC Barroetavena; Co-I: J Stephen, C Poon; BCCA; 2003-2004;</i> The goal of the P-Scan research is to create a psychometrically sound tool that is quick and easy to complete for all patients entering the cancer care system.</p>
<p>2. Improving access to psychosocial/supportive care: an investigation of the potential of technology <i>PI: R Doll; Co-I: J Stephen, C Poon</i> \$17, 500 Canadian Strategy for Cancer Control January 2004 – May 2004. This project identified a range of technological applications for psychosocial/supportive care for cancer patients and caregivers through a review of the literature and key informant interviews. A report was made to the Canadian Strategy for Cancer Control, which includes recommendations for clinical</p>

application.
<p>3. Patient Navigation in Cancer Care <i>PI: R Doll, Co-I: J Stephen, G Hislop, B Poole, MC Barroetavena; CBCI, CBCF, CSCC (CAPCA); 2003-2004; Σ \$53,000</i> This research project developed a conceptual model for patient navigation and pilot tested evaluation tools in the Vancouver Island Health Authority South, and the West Kootenay Boundary region. Work is now underway to collaborate with national stakeholders to report on patient navigation in Canada.</p>
<p>4. National Workshop: The Wellness Model for electronic support groups <i>PI: R Doll Co-I: J Stephen, G MacKenzie; June 2004; \$17, 000 Canadian</i> <i>Strategy for Cancer Control</i> National workshop hosted by BCCA researchers to explore the potential of developing on-line support groups in Canada. Special presentation by Dr. Mitch Gollant of the Wellness Community and Dr. Janine Giese-Davis from Stanford University in California.</p>
<p>5. Information needs and information seeking behaviours of young women with breast cancer <i>PI: J Stephen, Co-I: F Wong, E Balka; Social Science and Humanities Research Council; 2003-2007; Σ \$50,000</i> This qualitative study explores the question "what role does the internet play in the information seeking behaviour of young women who have or have had breast cancer?" The specific objective is to understand how young women at various stages of cancer meet their information needs and what are the implications for policy and practice.</p>
<p>6. Chemotherapy Anxiety Reduction for Breast Cancer (CARE-BC): An RCT testing effectiveness of self-administered stress management training in five community settings <i>PI: J Stephen; Co-I: R Doll, MC Barroetavena, W Linden, K Khoo, K James, G Christie; CBCF; 2004-2006; \$130,000 per year; Σ \$260,000</i> This study will test the effectiveness of self administered stress management trainging (SSMT) for breast cancer patients treated in community oncology setting in rural and semi-rural British Columbia.</p>

Cross Cultural Research
<p>7. National Workshop: Building Collaborative Communities <i>PI: MC Barroetavena; Co-I: B Stanger, R Doll, L Chiu, A Kazanjian, S Cadell; \$50, 000 CIHR, NCIC, BC Cancer Foundation; February 2004</i> The first national workshop on cross cultural cancer research and care was held in Vancouver, BC. Building Collaborative Communities brought together over 60 national stakeholders, including policy makers, researchers, health professionals and community members to outline priority research areas of communication, complementary and alternative health care, and palliative/end of life care.</p>
<p>8. Psychosocial Needs of Chinese Cancer Patients and their Caregivers <i>PI: MC Barroetavena Co-I: R Doll, C The, L Chiu; \$24,000 BC Medical Services Foundation & Heritage Canada's Multiculturalism Program; January 2004-December 2004</i> The research team is working in close collaboration with a community advisory committee to conduct qualitative research on the psychological, social and cultural needs of Chinese cancer patients and their caregivers.</p>
<p>9. Interpreters in Cancer Care: Communication Issues and Experiences <i>PI: MC Baroetavena, Co-I: B Stanger, S Barcaly, K Malli, S Cadell, V Poruchko, G MacKenzie, M Myles</i> <i>BCCA; January 2004-December 2004</i> Using focus group methodology, this study examines the communication issues</p>

and experiences of Chinese and Punjabi speaking interpreters working in the context of cancer care.

10. PSSCAN Translation into Chinese & Punjabi

PI: MC Baroetavena; Co-I: W Linden; BC Cancer Agency; 2004 – 2005

17% of new patients at the Vancouver Cancer Centre speak a Chinese dialect. In order to use the Psychosocial Screening tool (PSSCAN) with Chinese speaking patients, the tool was translated from English to Chinese and back translated into English to check for cultural sensitivity and accuracy. The translated PSSCAN was reviewed by an expert panel of Chinese speaking patients and health care professionals.

11. Cancer Incidence and Mortality in BC Indo-Canadians

PI: G Hislop Co-I: MC Barroetavena, SR Saroa; BCCA; 2004 – 2005

The main objective of this descriptive study is to determine and compare the relative frequencies of cancer cases, and cancer related deaths, by site among South Asians (Indo-Canadians) in B.C. and to compare this pattern with that for the B.C. general population.

12. Use of Screening Programs by Immigrants

PIs: G Hislop, A Kazanjian, MC Barroetavena; BCCA; 2004 – 2005

Developmental work is underway to ascertain the feasibility of linking the BCCA Cancer Registry with Canadian Immigration data. The purpose of this project is to understand the use of screening programs by immigrants.

13. Overcoming systemic barriers to psychosocial support: Understanding the needs of Chinese cancer patients and their caregivers

PI: MC Barroetavena; Co-PI: R Doll, C Teh, L Chiu;

Vancouver Foundation; 2004-2005; Σ \$24,279

This project is aimed at furthering our understanding of the psychological, social and cultural needs of Chinese cancer patients and caregivers. The main objective of the study is to work in collaboration with the Chinese community to include participants' values and beliefs in the planning of resources.

Palliative Care

14. Palliative Care in a Cross-Cultural Context: A New & Emerging Team (NET) for equitable and quality cancer care for culturally diverse populations†

Co-PI: R Doll, A Kazanjian; Co-I: MC Barroetavena, G Fyles, A Leis and G Johnston; CIHR; 2004-2009; For 2004: \$189,939; Σ \$ 1,400,000

This grant will develop a research and training capacity in the area of cultural and cancer palliative care. The objective is to advance knowledge and translate it into education, training, policies and practices that promote a health system offering equitable care for culturally diverse Canadians and to improve the quality of life of patients and their caregivers.

15. Characterizing Access to End of Life Care Among Culturally Diverse Groups

Co-I: MC Barroetavena, G Johnston

CIHR – Palliative Care in the Cross Cultural Context NET

As part of the larger NET research program, this pilot study builds on data from Nova Scotia and extends to B.C. The goal is to establish cultural indicators and link them into quality, population-based end of life and palliative care data sets. Indicators of culture will be examined as predictors of risk for dying out of hospital. Development of cultural indicators will contribute to an assessment of the role of culture on health practices, service utilization, and morbidity and mortality outcomes for use in Canadian linked End of Life studies.

16. Use of the Palliative Outcome Scale (POS) in Tertiary Palliative Care

PI: G Fyles Co-I: A Kazanjian, MC Barroetavena

CIHR – Palliative Care in the Cross Cultural Context NET

This project will assess the cross-cultural dimensions of quality of life, quality of care and patient and family satisfaction, as measured by the Palliative Outcome Scale (POS) developed by Higgins. The BCCA Pain and Symptom Management/Palliative Care Program in conjunction with the Fraser Health Authority Palliative Care Program is collecting data from tertiary palliative care clinics/units. Information will be used to build a quality of life database.

17. Kelowna Palliative Response Team – Cost Effectiveness/Quality of Life Pilot

PIs: G Fyles, S Broughton, C Mathieson, AM Broemeling and others; NCIC; 2003-2005; \$35,000

The Kelowna palliative response team (PRT) is an after-hours crisis response team for patients and their family members registered with the Kelowna Palliative Care Program who wish to die at home. Pilot research is evaluating the cost effectiveness and quality of life outcomes of PRT.

18. Complementary and Alternative Medicines use by Chinese Canadians in Palliative Care

PI: A Leis; CIHR – Palliative Care in the Cross Cultural Context NET; 2004 – 2005

Using a prospective design, 30 Mandarin and Cantonese speaking cancer patients will be invited to participate in a study assessing their use of complementary and alternative medicines. Findings will be compared with the general population of cancer patients.

Lifestyle**19. Towards an Evidence Based Smoking Cessation Program for BCCA: A report on the evidence and a recommended model**

PI: Joanne Stephen, BCCA, January 2004 – May 2004

The project reviewed international clinical practice guidelines, national smoking cessation strategies and provincial resources for smokers interested in quitting. A recommended model for a provincial Smoking Cessation program in the BC Cancer Agency was developed and will be implemented in collaboration with the Vancouver Coastal Health Authority.

20. The Family Context of Food Decision-making in Diverse Ethnocultural Groups

Co-PIs: G Chapman, B Beagan Co-I: S Sekhton, R Levy-Milne, S Raja, J Enang;

CIHR; 2003 – 2006; \$398, 820

The purpose of this study is to examine how families from three diverse ethnocultural groups make decisions about what they eat, and how those decisions relate to culture, gender, life-stage, and health concerns. The three ethnocultural groups included in the study are Punjabi British Columbians, African Nova Scotians, and European Canadians living in British Columbia and Nova Scotia. Findings from the project will help in the development of future health promotion programs.

Partnership Grants**21. Managing Severe and Persistent Stress in Families of Brain Cancer Patients**

PI: G Miller Co-I: R Doll, R Ma; MSFHR; 2004 – 2006; \$120, 000

The goals of this research project are (1) to document the psychological and

biological consequences of caring for a family member who is being treated for a serious disabling medical illness such as a malignant brain tumour, and (2) to identify personal resources and coping strategies that enable caregivers to manage this demanding experience successfully.				
22. Use of Alternative Therapies by Chinese Living in Canada <i>PI: L Chiu Co-I: R Doll, MC Barroetavena</i> <i>Sociobehavioural Cancer Research Network –NCIC; 2004 – 2005; \$5, 000;</i> Preliminary work underway to develop a full qualitative study on the use of complementary and alternative therapies by 1st and 2 nd generation Chinese Canadians with cancer.				
23. Pallium Integrated Care Capacity Building Initiative <i>PI: J Pereira Co-I: G Fyles and others; including Alberta Cancer Board, University of Alberta, University of Saskatchewan, Manitoba, BC, Inuvik Regional Health, Yukon, BC Cancer Agency, Cancer Care Manitoba; \$4,200,000 Primary Health Care Transition Fund; 2003-2008</i> This research program is focused on promoting excellence in hospice and palliative care across the sectors. A professional community of clinicians, educators and academics are engaged in building Canada's palliative care capacity together via a variety of projects.				
24. Current Status of Psychosocial Oncology Care in Canada <i>PI: A Leis Co-I: R Doll, J Taylor-Brown, E Maunsell; NCIC; 2003-2005; \$35, 000</i> This study is an environmental scan to generate a comprehensive inventory of psychosocial oncology care in Canada.				
25. Cancer and Complementary and Alternative Medicine Team <i>Co-PIs: A Leis, M Verhoof Co-I: R Doll, J Stephen and others; NCIC; 2003 – 2005; \$444, 000</i> National research team on complementary and alternative medicine in cancer. Research team nurtures interdisciplinary collaboration and provides pilot funding for team member projects.				
26. Family Caregiver Coping in End of Life Cancer Care <i>PI: K Stadjuhar Co-I: G Fyles, D Barwich; NCIC; 2004 – 2007; \$310,200</i> The overall research question guiding this study is: Why do some palliative/end of life family caregiver groups cope better than others even when under similarly heavy caregiving demands? Research will be conducted with a focus on knowledge translation for clinical practice, health policy and education.				
27. Quality of Life for Palliative Patients and their Caregivers <i>Co-I: R Cohen, G Fyles, A Leis, P Porterfield, and others; NCIC; 2001 – 2005; \$555, 700</i> A national longitudinal Study was funded to consider the quality of life for patients and their family caregivers. Ongoing data collection continues at the BCCA Centre for the Southern Interior.				
28. Brain Tumour Rehabilitation <i>Co-I: J MacDonald, M Parkinson, MC Barroetavena; BCCA; 2003 - ongoing</i> This Research project examines whether comprehensive interdisciplinary rehabilitation services provided to adults with traumatic brain injuries have benefits to those with low-grade brain tumours and their families.				

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
9	0	15	0	0

HEREDITARY CANCER PROGRAM
BC CANCER AGENCY
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<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Barbara McGillivray	MD Medicine	Medical Geneticist Professor, Medical Genetics, UBC
Cheryl Portigal-Todd	MSc Genetic Counselling	Genetic Counsellor Medical Genetics, UBC
Karen Panabaker	MSc Genetic Counselling	Clinical Coordinator, Genetic Counsellor Clinical Assistant Professor, Medical Genetics, UBC
Lorraine d'Agincourt-Canning	PhD Interdisciplinary Studies	Postdoctoral Research Fellow
Yolanda Ridge	MSc Genetic Counselling	Genetic Counsellor Clinical Instructor, Medical Genetics, UBC

OUR RESEARCH FOCUS: The Hereditary Cancer Program (HCP) is a result of the BC Cancer Agency and the BC Provincial Medical Genetics Program working together to provide information and genetic counselling for individuals and families with a strong history of cancer.

Educating doctors, nurses and other health-care providers in BC about hereditary cancer is an important part of the HCP. As this is still a new field, research about all aspects of hereditary cancer is another key aspect of the program.

RESEARCH KEYWORDS:

Medical and health care ethics, research ethics, ethics and genetics, palliative care ethics, cross-cultural ethics, prenatal diagnosis, biomedical ethics, hereditary cancer syndromes,

TRAINING

Course Instructors

Y. Ridge	UBC Med Gen 550
Y. Ridge	UBC PRIN 401
B. McGillivray	UBC P2P1 – Principle of Human Biology
B. McGillivray	UBC MGEN 550
B. McGillivray	UBC P2P1 – Growth and Development Weeks 1-6
K. Panabaker	UBC PRIN 401
C. Portigal-Todd	UBC PRIN 401

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
B. McGillivray	UBC Department of Medical Genetics Teaching Award for Clinical Teaching (2004)

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Lorriane d-Agincourt-Canning	Ethicist, Clinical Research Ethics Board, BCCA
Barbara McGillivray	Chair, Reproduction, Growth and Development, P2P2
	Member, Behavioural Ethics Board, UBC
	Member, Research Ethics Policy Advisory Board, UBC
	Board Member, Canadian Fanconi Disease Association
	President, National Committee on Ethics in Health Research
	Board Member, BC Medical Legal Society
	Chair, Prenatal Diagnosis Committee, Canadian College of Medical Geneticists
	Member, Public Policy, Canadian College of Medical Geneticists
	Member, Standing Committee on Ethics, CIHR
	Obstetrics Lecturer, UBC CME Update Courses in Family Practice
Karen Panabaker	Member, MSc Genetic Counselling Masters Training Program Advisory Committee
	Co-facilitator/founder, Hereditary Cancer Program Networking Group

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Total Value</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value</i>
3	\$276,667	1	\$47,000

CURRENT RESEARCH PROJECTS - HEREDITARY CANCER PROGRAM

Research Projects
1. Evaluation of telemedicine as a tool in the provision of genetic counselling <i>PI: L d'Agincourt-Canning; Vancouver Foundation; 2004-2005; Σ \$47,000</i>
2. Medical Genetics and Ethics <i>PI: L d'Agincourt-Canning; CIHR; 2003-2006; \$38,000 per year; Σ \$114,000</i>
3. Towards an effective hereditary cancer service program for rural populations: Empirical research to inform policy and program development <i>PI: L d'Agincourt-Canning; CIHR; 2003-2009; For 2004: \$45,000; Σ \$115,667</i> The training program proposes to use quantitative and qualitative methodologies to assess the needs of hereditary cancer families who live in rural communities. Its objectives are: (1) to assess the frequency of hereditary cancer syndromes (breast, ovarian and colon) in selected rural and northern BC populations; (2) to identify current and potential barriers (logistical, social and ethical) to access to genetic and associated clinical services in these populations; (3) to evaluate the impact on health or quality of life of reduced access to genetic services and (4) to develop evidence-based approaches to health policy analysis and design of genetic counselling/testing services for rural and remote communities.

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
4	0	2	0	0

DEPARTMENT OF ADVANCED THERAPEUTICS
BC CANCER RESEARCH CENTRE
Telephone: 604-675-8021

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Marcel Bally	PhD Biochemistry	Head, Advanced Therapeutics Adjunct Professor, Pharmaceutical Sciences, UBC; Clinical Professor, Pathology and Laboratory Medicine, UBC
Donald Yapp	PhD Chemistry	Senior Scientist Adjunct Professor, Pharmaceutical Sciences, UBC
Dawn Waterhouse	PhD Biochemistry, MBA	Cancer Specialist, Advanced Therapeutics
Ellen Wasan	PhD, Pathology and Lab Medicine	Senior Scientist Formulation Scientist, Investigational Drug Program, BCCA

OUR RESEARCH FOCUS: We are a translational research department within the BC Cancer Agency, providing anticancer drug development capabilities which are focused on the critical need to rapidly establish the therapeutic value of emerging intervention strategies through validated assessments in preclinical models of cancer and in patients.

Scientists in Advanced Therapeutics lead two translational research platforms:

1. INVESTIGATIONAL DRUG PROGRAM

The Investigational Drug Program (IDP) (Director: Dr. Dawn Waterhouse) expedites development of new and highly promising anti-cancer therapeutic agents up to the initial stages of clinical trials. IDP works with academic investigators and biotechnology companies. IDP has a wealth of expertise in murine models of human cancer, as well as critical ADME studies (absorption, distribution, metabolism and excretion), and completion of the documentation necessary to apply for a successful Investigational New Drug application (IND) in either Canada or the United States.

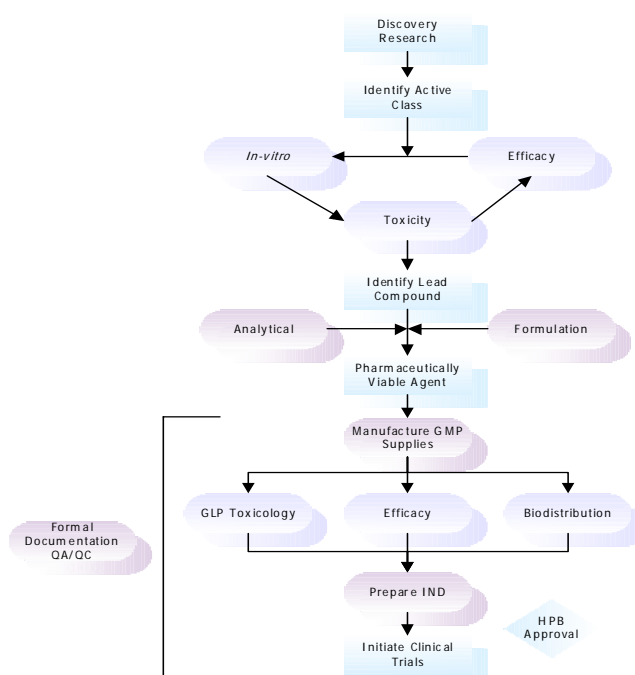


Figure 1 - Development Process for New Therapeutic Agent

2. PHASE I/II CLINICAL TRIALS UNIT

Advanced Therapeutics participates in a rapidly growing Phase I/II/III clinical trials unit at the Vancouver Cancer Centre. These clinical trials are organized in collaboration with colleagues in Medical Oncology, other Canadian cancer treatment centres, co-operative oncology groups (e.g., NCIC) and pharmaceutical and biotechnology companies. Links have been established with US centres such as UCLA and the San Antonio Drug Development Institute.

PROGRESS HIGHLIGHTS DURING 2004:

An Advanced Therapeutics/BC Cancer Agency spin-out company – Celator Pharmaceuticals – initiated a Phase I clinical trial on its pharmaceutical drug product lead candidate, at the BC Cancer Agency and McGill University. Dr Lawrence Mayer, a senior scientist and director of the Investigation Drug Program in Advanced Therapeutics was recruited to the position of President and Head of Research at Celator Pharmaceuticals.

RESEARCH KEYWORDS:

Antiangiogenic agents, in vivo target validation issues, liposomes, myofibroblasts, pharmacokinetic and pharmacodynamic assays, plasma concentration, thalidomide analogues.

TRAINING**A.) Course Instruction**

M Bally UBC Path 500A
M Bally UBC Path 535/635
M Bally UBC Cancer Biology

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
17	5	7	4	1

CURRENT STUDENTS – DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>	<i>Awards/Honours Received</i>
PhD			
N Dos Santos	M Bally	2004	
L Ickenstein	M Bally	2004	
J Shabbits	L Mayer	2004	
BSc			
F Kuan	E Wasan	2004	
J Chow	D Waterhouse	2004	

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
DG Bebb	M Bally	CIHR/Rx&D Fellowship (2002-2004)
N Dos Santos	M Bally	CIHR Industrial Studentship (2001 – 2005)

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Dawn Waterhouse	Canadian Breast Cancer Foundation Postgraduate Breast Cancer Fellowship

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Marcel Bally	Member, Centre for Blood Research, UBC
	Co-Director/Member, Liposome Research Unit

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value</i>
10	\$982,085	4	\$260,792

CURRENT RESEARCH PROJECTS⁷

Advanced Therapeutics
<p>1. <i>Advanced delivery of agents targeting the endoplasmic reticulum in breast cancer</i> <i>PI: S. Berger; Co-I: E. Wasan, D. Waterhouse; CBCRA; 2004-2005; Σ \$85,317</i> The goal is to assess new way to give the drug econazole in tiny lipid bubbles in which it can dissolve. If this approach works, it may lead to a new drug treatment that effectively kills breast cancer cells even when other drugs stop working.</p>
<p>2. <i>Combining conventional therapeutics with molecular targeting strategies for the treatment of breast cancer</i> <i>PI: M Bally; Co-I: K Gelmon, S Chia, P Gill; NCIC; 2002-2005; For 2004-\$108,660; Σ\$326,220</i> This research focuses on two therapeutic agents (i) an ASO targeting bcl-2, an anti-apoptotic signal believed to be an important survival signal; and (ii) a siRNA sequence targeting integrin-linked kinase, which exemplifies a target that is capable of producing pleiotropic effects including stimulating cell growth and cell cycle progression as well as inhibiting apoptosis.</p>

⁷ Key to Abbreviations: PL = Project Leader; PI = Principal Investigator, Co-I = Co-investigator; CBCRA = Canadian Breast Cancer Research Alliance, CIHR = Canadian Institutes of Health Research, MSFHR = Michael Smith Foundation for Health Research, NCIC = National Cancer Institute of Canada; Σ = total amount of project funding committed.

<p>3. Integrin linked kinase inhibition as an approach to treating malignant gliomas <i>PL: B Thiessen; Co-I M Bally, S Dedhar, W Jia; NCIC; 2000-2004; For 2004 – \$205,676; Σ 822,704</i> We will evaluate a molecular pathway that could play a role in malignant glioma progression. We will determine whether integrin linked kinase (ILK) activity is dysregulated in PTEN-mutant glioblastomas and whether inhibition of ILK activity leads to inhibition of glioblastoma growth and progression in cell culture and animal tumour models. We postulate that inhibition of constitutively activated ILK should induce cell cycle arrest and apoptosis of PTEN-mutant tumour cells, especially glioblastomas, a great number of which harbour PTEN mutations.</p>
<p>4. Lipid-based carriers for gene therapy: applications for treatment of cancer <i>CIHR; 2003-2006; For 2004 – \$121,506; Σ \$364,518</i> A key challenge in drug development is the design of carriers that can efficiently deliver molecules in a manner that provides effective treatment of systemic disease. This study is focused on the development of such delivery systems.</p>
<p>5. Liposome/vascular endothelium interactions <i>Co-PI: M Bally, L Mayer; CIHR; 1999-2005; For 2004 – \$144,251; Σ \$797,399</i> This research will explore the development of drug combination products that affect new blood vessel structure and function as well as cancer cell populations within the tumor.</p>
<p>6. Non-invasive monitoring of tumour progression in the Shionogi tumour model for prostate cancer <i>PI : D Yapp; Prostate Cancer Research Foundation of Canada; 2004; Σ \$43,000</i> The primary treatment for advanced cases human prostate cancer is androgen ablation – 80% of tumours will respond and regress. Knowing how a tumour is progressing would enable clinicians to better adapt treatment protocols to a patient's changing needs and possibly improve survival and/or quality of life.</p>
<p>7. A phase I pharmacokinetic and pharmacodynamic study of weekly and twice weekly OSI-774 <i>PI: S Chia; Co-I: S. Glück, CB Gilks, M Hayes, M Bally, K Paton, D Katzenstein; CBCRA/CIHR; 2003-2007; For 2004 – \$70,000; Σ \$280,000; Part of Program 'Translating target discovery into better health outcomes for women with breast cancer' – PL:K Gelmon; Σ1,941,731</i> This study will look at a new drug OSI-774 which acts by blocking the activity of a protein known to be involved in breast cancer development, epidermal growth factor receptor (EGFR). Previous research has suggested that this drug could be useful against breast cancer, but it has not yet been thoroughly studied.</p>
<p>8. Preclinical studies to evaluate utility of inhibition of integrin linked kinase (ILK) in treatment of breast cancer <i>PI: S Dedhar Co-I: M Bally; CBCRA/CIHR; 2003-2006; For 2004 - \$71,200; Σ\$284,800; Part of Program 'Translating target discovery into better health outcomes for women with breast cancer' – PL: K Gelmon; Σ1,941,731</i> This project will investigate three genetic changes to see whether they can be used to predict which cancers will return after treatment and which will respond to anticancer drugs. The group also plans to develop drugs targeted at cells containing these genetic changes, since such drugs would affect only the cancer cells and thus might cause fewer side effects than current treatments.</p>

9. Triggered drug release from thermosensitive liposomes

PI: M Bally; Co-I: E. Wasan; Lotte & John Hecht Memorial Foundation; 2004-2006; For 2004 - \$72,475; Σ \$144,950

Our goal is to optimize the lipid composition and the method of drug encapsulation to achieve desirable physical and biological properties of liposomes for hyperthermia-triggered drug release.

Interdisciplinary**10. Non-invasive monitoring of tumour microenvironment as a tool to optimize anti-cancer therapies**

PI: D Yapp; Cancer Research Society; 2004-2006; For 2004 - \$60,000; Σ \$120,000

The overall goal is to examine whether changes in tumour microenvironment, as a tumour develops or responds to therapy, can be used to guide further treatment strategies. Specific goals are to (i) evaluate tumour hypoxia, perfusion, vasculature, pH and glucose metabolism in the HT-29 model before, during and after treatment with CPT-11, and (ii) evaluate levels of hypoxia, vascular density, proliferation and apoptosis at the cellular level with histology and flow cytometry in the same tumour.

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
20	0	6	2	0

DEPARTMENT OF CANCER CONTROL RESEARCH**BC CANCER RESEARCH CENTRE****Telephone: 604-657-8051/8071**

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Richard Gallagher	MA Medical Sociology	Head, Cancer Control Research Clinical Professor, Health Care and Epidemiology, UBC; Associate Member, Dermatology, UBC; Associate Member, Ophthalmology, UBC; Associate Member, Surgery, UBC
Christopher Bajdik	PhD Health Care & Epidemiology	Research Scientist Clinical Assistant Professor, Health Care & Epidemiology, UBC
John Spinelli	PhD Statistics	Senior Scientist Adjunct Professor, Statistics and Actuarial Science, SFU; Associate Professor, Health Care and Epidemiology, UBC
Marilyn Borugian	PhD Health Care & Epidemiology	Senior Scientist Clinical Assistant Professor, Health Care & Epidemiology, UBC
Mary McBride	MA Genetics	Epidemiologist Clinical Assistant Professor, Health Care & Epidemiology, UBC
Miriam Rosin	PhD Cell Biology	Senior Scientist Clinical Professor, Pathology & Laboratory Medicine, UBC; Professor, Kinesiology, SFU
Nhu Le	PhD Statistics	Senior Scientist Adjunct Professor, Statistics, UBC
Greg Hislop	MD	Senior Epidemiologist Clinical Professor, Health Care & Epidemiology, UBC
Tim Lee	PhD Computing Science	Senior Scientist Adjunct Professor, Computing Science, SFU; Clinical Assistant Professor, Health Care and Epidemiology, UBC

OUR RESEARCH FOCUS: The major effort of the Cancer Control Research (CCR) Program is directed toward reducing cancer incidence and mortality in BC through population-based projects. The program also plays a key role in the BC Cancer Agency's cancer control activities by monitoring the impact of cancer by region of the province, and by assessing the referral trends for the Agency's cancer clinics.

The BC Cancer Registry is part of the Cancer Control Research program. Mary McBride is the scientific director of the Cancer Registry. The Cancer Registry collects data and generates cancer statistics on the BC population. The Registry is the primary source of data for cancer control in BC. It reports on the scope of the cancer problem, provides information to plan programs to reduce mortality and morbidity from cancer, and monitors the effectiveness of such programs.

The registry is used in research. Research-based on population registries avoids one source of potential bias due to non-representative participation and are of better quality than those that use non-population based sources.

The Registry has been in existence since 1969, and has been maintained at the BCCA since 1980. It contains personal and demographic information as well as diagnosis and date of death information on all cases of cancer diagnosed to BC residents.

PROGRESS HIGHLIGHTS DURING 2004:

This has been a very successful year for the CCR research unit in terms of funding, collaboration and output. We have made excellent progress with gene-environment studies, with three underway: prostate, ovarian and non-Hodgkin's lymphoma. As well, the unit expanded its scope to a new tumour site. A new study on the molecular epidemiology of breast cancer, including gene-environment interactions has been funded by CIHR and is now enrolling participants.

A 12-year update on a major cohort study of cancer incidence and mortality in aluminum workers has been completed. CCR researchers expanded the assessment of quantitative dose-response relationships in the industrial environment with the potential benefit of estimating the health impact of improvements to potroom ventilation and other specific improvements within the industry.

The Healthy Aging Study illustrates a deepening of the trend toward significant collaboration with our associates in the Genome Sciences Centre. Dr. Angela Brooks-Wilson is leading the study and Dr. Nhu Le is collaborating on a multidisciplinary effort to identify the genetic factors associated with healthy aging and resistance to age-related diseases.

The international collaborative study of Genes, Environment and Melanoma (GEM) Program, has been very successful, and a request for funding for a further 5 years (2005-2009) has been submitted to the U.S. NIH.

Our contributions to the Interlymph International Collaboration have been incorporated into the first paper produced by the collaboration. It will be submitted to Lancet Oncology in 2005.

One of the major success stories of the past year for our research unit is the funding, international recognition, and major expansion of the BC Oral Cancer Prevention Program, under the direction of Dr. Miriam Rosin. In 2005, this program received NIH support in the amount of US\$ 1,930,339 and Dr. Rosin has also been recognized by the NCI (National Cancer Institute) Specialized Programs of Research Excellence (SPORE). Dr. Rosin's translational research program which involves taking basic research from the laboratory to clinical settings with risk management of patients coincides with the stated goals of the BCCA's strategic plan: to bring to the clinical

care settings novel ideas that have the potential to reduce cancer incidence and mortality, improve survival, and to improve the quality of life. The components of the program include the BC Oral Cancer Translational Program, the Oral Health Network, Oral Dysplasia Clinics, and the Oral Dysplasia Registry.

A major NCIC Program Project Award was submitted for funding this year by Mary McBride. It is a Childhood/Adolescent/Young Adult Cancer Survivorship Research Program, and represents a further new direction for Cancer Control Research. This program involves intensive research into determinants and risk factors for survival and late effects of those treated for cancer in early life.

Cancer Control Research is entering the third year of MSFHR infrastructure funding designed to assist expanding research units in increasing their research capacity. This funding has allowed the department to fund three new staff members who play a vital role in data accumulation, analysis and publication.

RESEARCH KEYWORDS:

Air pollution exposure assessment, descriptive epidemiology of cancer, detection of spatial and temporal cancer clustering, early detection of malignant melanoma using computer vision methods electromagnetic fields and cancer, epidemiology of childhood cancers, identification of occupational and environmental cancer risk factors, modifiable lifestyle factors, statistical genetics.

TRAINING

A.) Course Instruction

C. Bajdik	UBC HCEP 511
C. Bajdik	UBC City-wide course in evidence-based medicine
R. Gallagher	UBC HCE525
J. Spinelli	UBC PATH 548S/ONCO 502
J. Spinelli	UBC HCEC 555
J. Spinelli	UBC HCEP 511
M. Borugian	UBC HCEP 511
M. Borugian	UBC DPAS 410
T. Lee	UBC HCEP 511

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
17	3	10	4	

CURRENT STUDENTS – DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>	<i>Awards/Honours Received</i>
PhD			
T. Donnelly	G. Hislop	2004	

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Christopher Bajdik	Living Science Award, International Biographical Centre, Cambridge, England
	MSFHR Scholar Award (2002-2007)
Marilyn. Borugian	MSFHR Post-doctoral Fellowship (2003-2007)

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Richard Gallagher	External Residency Committee; Dept. of Health & Epidemiology, UBC
	Board of Governors and Past President, Canadian Society for Epidemiology & Biostatistics
	Advisory Committee on Research, National Cancer Institute of Canada
	Population Health Personnel Panel Steering Committee, Michael Smith Foundation for Health Research
	Interim Organizing Board Member, BC Occupational and Environmental Health Network
	DEX Grant Review Panel, Canadian Breast Cancer Research Alliance
	Population and Public Health Panel B-Chairman, Canadian Institutes for Health Research
Christopher Bajdik	Health Services Trainee Evaluation Committee, Michael Smith Foundation for Health Resources
	Grant Review Committee, BC and Yukon Chapter, Canadian Breast Cancer Foundation
John Spinelli	Merit & PSA Committee, Dept of Health Care & Epidemiology, UBC
	Public, Community & Population Health Grants Committee, CIHR
	Chair, Population Health Evaluation Committee, Research Trainee Program, MSFHR
	Epidemiology Review Committee, NCIC
	Priorities and Evaluation Committee, BCCA
	BCCA Research Ethics Board, UBC
Miriam Rosin	Public, Community and Population Health Grants Committee, CIHR
	Epidemiology Review Committee, NCIC
	Priorities and Evaluation Committee, BCCA
	Population Health Review Committee, Research Trainee Program, MSFHR
	UBC, BCCA Ethics Board

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
43	\$10.5 M	9	\$1.5 M

CURRENT RESEARCH PROJECTS – CANCER CONTROL RESEARCH⁸

Cancer Control	
1. <i>Clinical determinants of breast cancer[†]</i> <i>PI: N Le; Co-I: M Deschamps, P Band and G Hislop; CIHR; 2003-2005; For 2004 - \$46,964; Σ \$140,892</i> In principle, the results of this study will contribute to identify the clinical features associated with breast cancer and will improve the screening, follow up and treatment of women presenting these symptoms. The results of this study might lead to the early detection of cancer in women presenting high risk clinical features.	
2. <i>Cohort study of aluminum workers: a 12-year update</i> <i>Co-PI: J Spinelli, N Le, P Demers and R Gallagher; Alcan; 2001-2005; For 2004 - \$127,170; Σ \$381,500</i> We are updating, expanding and improving the original study to better assess quantitative dose-response relationships between exposures at the ALCAN aluminum reduction facility in Kitimat, BC and cancer incidence and mortality from cancer as well as other causes.	
3. <i>Clonal changes in oral lesions of high-risk patients-renewal[†]</i> <i>PI: M Rosin; Co-I: L Zhang, W Lam, M Williams, Epstein, Lee, Berean, Hay, Durham, Hovan, N Le and G Hislop; NIH; 2003-2008; For 2004 - \$385,230 USD; Σ \$2,381,794 CDN or Σ \$1,984,829 USD</i> We continue to develop an approach in which cells collected by scraping the former tumour site with a spatula are analyzed for genetic changes that are indicative of the loss of genes that are normally suppress cancer development. This study that validate the use of this approach to follow patients over time, to look for the evolution of cells in the tissue that might predict tumour development/recurrence.	
4. <i>Development of a carcinogen surveillance program for BC</i> <i>PI: P Demers; Co-I: N Le & K Tescheke; WCB; 2003-2004; Σ \$80,490</i> We will estimate the number of workers exposed to occupational carcinogens in BC, using an approach developed in Finland and data from research studies.	
5. <i>Genes, Environment, Occupation and Cancer (GEOC)</i> <i>PL: R Gallagher; MSFHR; 2003-2006; For 2004 - \$152,276; Σ \$456,828</i> The objective of this research unit is to discover those genetic, environmental and occupational factors and their interactions that define cancer risk and that can inform the development of new strategies for prevention, early detection and treatment.	

⁸ Key to Abbreviations: PI = Principal Investigator, PL = Project Leader; Co-I = Co-investigator; CBCRA = Canadian Breast Cancer Research Alliance; CIHR = Canadian Institutes of Health Research, CPCRI = Canadian Prostate Cancer Research Initiative, MSFHR = Michael Smith Foundation for Health Research, MRC = Medical Research Council; NCIC = National Cancer Institute of Canada; NIH = National Institutes of Health (US); NSERC = Natural Sciences and Engineering Research Council; WCB = Workers Compensation Board; [†] = Inter-departmental project; Σ = total amount of project funding committed.

6. Goodness-of-fit for discrete data and statistical models; biostatistical methods <i>PI: J Spinelli; NSERC; 2001-2006; For 2004 - \$50,000; Σ \$300,000</i> The major goal of this project is to develop tests of fit for discrete distributions and for models used in statistical analysis.
7. Improved methods for haplotype risk estimation in association studies, with specific application to cancer and diabetes <i>PI: J Spinelli; Co-I: B McNeney & J Graham; CIHR; 2004-2006; For 2004 - \$179,499; Σ \$538,497</i> We are developing novel methods which properly take into account the uncertainty in the haplotype inference in estimation and testing of the effects of disease outcome of haplotypes and nongenetic risk factors.
8. Innovative Bayesian methods for biostatistics & epidemiology <i>PI: P Gustafson; Co-I: N Le, A Levy & Y. McNab; CIHR; 2003-2007; For 2004 - \$49,800; Σ \$149,400</i> In principle, the Bayesian approach provides a natural way to describe the uncertainty about risk factor measurements, using probability theory. The goal of this research is to develop and evaluate Bayesian methods for dealing with EIC in case-control analysis. These methods will be tested on both real and simulated data, and they will be compared to existing classical methods.
9. Mechanisms underlying chromosomal instability in mammalian cells <i>PI: M Rosin; NSERC; 2003-2007; For 2004 - \$39,600; Σ \$158,400</i> We will test the hypothesis that one source of elevated chromosome alterations in cells results in reduced ability to correctly repair DNA double-strand break (DSBs) resulting in a higher level of residual damage that leads to complex chromosome changes.
10. Methodologies for health impact assessment and gene identification <i>PI: N Le; NSERC; 2002-2007; For 2004 - \$80,000; Σ \$560,000</i> The objective is to develop statistical theories for improved health impact assessment and gene identification. The development will focus on three areas: spatial statistics, errors in co-variables, and gene identification.
11. Occupational oncology research program[†] <i>PI: N. Le; Co-I: C Bajdik, A Brooks-Wilson, P Demers, R Gallagher, P Rather, J Spinelli & K Teschke; WCB; 2002-2005; For 2004 - \$420,000; Σ \$2,100,000</i> The major goals of this project are to provide data on occupational cancer relevant to the specific industrial and occupational context of BC, and to identify occupational cancer risk factors and potential carcinogens in the workplace with the overall objective of reducing risk.
12. Risk of childhood cancer by SES <i>PIs: M. McBride & J Spinelli; Co-I: M Borugian; EPRI; 2003-2004; For 2004 - \$42,150; Σ \$84,300</i> In the feasibility study, the investigators will assess the availability of study-specific datasets and variables for both BC and Canadian registry cases of childhood leukemia, and the availability of conversion tables. They will also assess the resources required to access the registry and census data required for the study, and costs of analysis.

13. Shift work, light-at-night and melatonin: characterizing a new cancer-related occupational risk factors

PI: M Borugian; Co-I: R Gallagher, N Le and K Aronson;
WCB; 2003-2005; Σ \$29,322

This pilot project will test methods to directly measure light-at-night during a 24-hour, 7-day protocol and to correlate shift work with measurements of light-at-night and melatonin levels. The specific objectives are 1.) to determine the optimal way to wear the luxmeter for direct measurement of 24-hour light exposure patterns, 2.) to characterize light exposure patterns over a 7-day period for workers on different shifts, 3.) to compare light exposure patterns and melatonin levels by shift worked, and determine whether shift worked can predict LAN exposure and/or melatonin levels and 4.) to correlate LAN measurements with self-reported questionnaire data on LAN exposure.

14. Simulation of a population-based genetic testing program for cancer susceptibility[†]

PI: C Bajdik; Co-I: R Gallagher, J Spinelli, D Horsman and D Huntsman;
CIHR; 2003-2005; For 2004 - \$72,641; Σ \$145,282

We will create a simulation model of cancer family history for people with germ line mutations in cancer susceptibility genes, and estimate the sensitivity, specificity and post-test likelihoods associated with family history as a predictor of carrier status for various cancer susceptibility genes and finally estimate the number of carriers that are eligible for a population-based genetic testing program.

15. Solar and artificial UV radiation and risk of non-Hodgkin's lymphoma[†]

PI: J Spinelli; Co-I: R Gallagher, N Le, and J Weber;
MRC/CIHR; 2000-2004; For 2004 - \$113,919; Σ \$455,677

The objectives of this proposal are to determine 1) whether exposure to organochlorines (OC) is related to risk of NHL, 2) whether ultraviolet radiation (UVR) exposure is related to risk of NHL, 3) if prior medical history, particularly with respect to factors related to immune stimulation and suppression, is related to the risk of NHL, 4) whether variation in specific genes leads to increased or decreased susceptibility to NHL, and 5) whether there are interactions between genetic susceptibility and OC and UVR exposure.

16. Sun exposure, vitamin D, and prostate cancer[†]

PI: R Gallagher; Co-I: M Borugian, M Pollack, A Brooks-Wilson, and J Spinelli;
CIHR; 2003-2007; For 2004 - \$162,981; Σ \$490,908

We will determine whether there is an inverse relationship between ultraviolet radiation exposure and risk of prostate cancer and whether there is evidence of a dose-response relationship between exposure and risk.

Interdisciplinary**17. Assessment and validation of new and novel prognostic and predictive factors in breast cancer with tissue microarrays[†]**

PI: S. Chia; Co-I: C Bajdik, K Gelmon, B Gilks, D Huntsman and J Ragaz;
NCIC/CBCRI; 2002-2004; For 2004 - \$235,081; Σ \$705,243

This study attempts to assess and validate potentially new and novel prognostic and predictive markers in breast cancer in a large scale and efficient manner. Knowledge of additional prognostic markers or specific predictive markers will aid in refining relapse risk and determining the group of women most in need of adjuvant therapies and selecting the most appropriate therapies for them.

18.	<p>Cancer genomics: A multidisciplinary approach to the large-scale high-throughput identification of genes involved in early stage cancers-Project 4: Oral Premalignancies[†] <i>PI: V Ling, C Eaves, M Marra; Co-I: M Rosin & others;</i> <i>Genome Canada; 2001-2005; For 2004 - \$464,263; Σ,\$1,649,057</i> The goal of this proposal is to identify recurrent alternations in high-grade oral premalignant lesions and tumours and select those that are frequent in progressing low-grade lesions but infrequent (or absent) in non-progressing lesions.</p>
19.	<p>Child and adolescent cancer: late effects and health utilization <i>PI: M McBride; Co-I: K Goddard, P Rogers and J Spinelli;</i> <i>CIHR; 2001-2004; For 2004 - \$310,778; Σ \$932,334</i> The first goal of this project is to assess the relative risks of selected late and chronic physical conditions of cancer survivors in comparison to large, population-based comparison groups of young adults of the same age-gender distribution as the case group.</p>
20.	<p>Children's oncology group chair's grant <i>PI: P. Rogers; Co-I M McBride; NIH; 2003-2008;</i> <i>For 2004 - US\$193,546; Σ US\$967,730</i> The major long-term goal of this project is to participate in COG Trials.</p>
21.	<p>Clinical implications of EMSY gene amplification events[†] <i>PI: D. Huntsman, Co-I: C Bajdik and K Gelmon;</i> <i>CIHR; 2004-2007; For 2004 - \$35,852; Σ \$113,812</i> EMSY is a newly described gene that interferes with the function of the BRCA2 breast cancer susceptibility gene. For this research unit, we will determine whether EMSY amplification is an independent marker for poor prognosis through the study of 6,500 breast cancer cases. This study will also determine whether EMSY amplification like BRCA2 mutations play a greater role in male breast cancers than breast cancers in women.</p>
22.	<p>Does insulin resistance increase risk of prostate cancer?[†] <i>PI: R Gallagher; Co-I: M Borugian, AS Whittemore, L Kolonel, A Wu, I Oakley-Girvan; CPCRI; 2003-2006; Σ\$49,895</i> We will analyze indicators of insulin resistance using serum prospectively collected from a healthy cohort of men some 10 years ago. Serum from each of these men will be matched with serum from 4 men in the cohort who have not developed prostate cancer. Several indicators of insulin resistance including insulin level, C-peptide level and C-peptide/fructosamine level will be measured.</p>
23.	<p>Double stranded break surveillance genes and susceptibility to non-Hodgkin's lymphoma[†] <i>PI: A Brooks-Wilson; Co-I: J Connors, R Gascoyne and J Spinelli;</i> <i>NCIC; 2004-2007; For 2004 - \$218,857; Σ \$656,572</i> The study will conduct genetic testing on 750 people with non-Hodgkin's lymphoma and 750 healthy people and look for differences between the two groups. The study will focus on those genes known to be involved in repairing genetic damage within a cell, since it may be that malfunctions in this repair system are involved in the development of non-Hodgkin's lymphomas. In addition to individual genes, the study will also look for patterns of genetic differences that are more common in the lymphoma patients than in the healthy people.</p>

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| <p>24. Evaluation of a LED MD fluorescent visualization device as a tool to facilitate the identification of high-risk oral premalignant lesions (OPLs) and early cancer
 <i>PI: M Rosin; Co-I: L Zhang and M Williams;</i>
 <i>LED Medical Diagnostics; 2004-2005; Σ \$200,000</i>
 Evaluation of a LED MD fluorescent visualization device as a tool to facilitate the identification of high-risk oral premalignant lesions (OPLs) and early cancer.
 This grant was used to evaluate the VELScope as a fluorescence-visualization device, for facilitating clinical evaluation of oral mucosa in patients with oral lesions.</p> |
| <p>25. Genomics, Genetics and Gerontology (G3): A multi-disciplinary team for the study of healthy aging[†]
 <i>PI: M. Marra; Co-I: A Brooks-Wilson, J Connors, S Jones, N Le and G Meneilly;</i>
 <i>CIHR; 2003-2007; For 2004 - \$292,500; Σ \$1,170,000</i>
 We will study genetic factors that underlie healthy aging and resistance to common age-related diseases such as cancer, cardiovascular disease and pulmonary disease. Genetic variants found to be associated with healthy aging, or associated with protection against specific common age-related diseases will be useful as prognostics in the tailoring of individual disease prevention programs.</p> |
| <p>26. Identifying groups of genetically-related cancers[†]
 <i>PI: C Bajdik; Co-I: A Brooks-Wilson and S Jones;</i>
 <i>Canadian Cancer Etiology Research Network; 2003-2004; Σ \$20,228</i>
 The objective of this study is to identify groups of cancers that are related genetically. A group will be defined as cancers for which there is published evidence of an association with the same gene. The study will perform a manual search of the "online Mendelian Inheritance in Man" (OMIM) database to identify genes that are associated with cancer risks. Independently, a computerized search of OMIM will be performed. This two-pronged strategy will allow us to compare the results of the searches, iteratively modify the computer search algorithm and identify the strengths and weaknesses of it.</p> |
| <p>27. Investigation of risk factors for P53 protein abnormality in cutaneous malignant melanoma
 <i>Co-PI: R Gallagher and LD Marrett, Cancer Care Ontario</i>
 <i>NCIC; 2000-2004; For 2004 - \$32,787; Σ \$98,361</i>
 <i>Grant #: CCS RG 011101 National Cancer Institute of Canada</i>
 Investigation of risk factors for p53 protein abnormality in cutaneous malignant melanoma. A sub-project of "A Model for Genetic Susceptibility: Melanoma".</p> |
| <p>28. Liver cancer control among North American Chinese
 <i>Co-PI : G Hislop and V Taylor; NIH; 2002-2006;</i>
 <i>For 2004 - US\$94,497; Σ US\$377,988</i>
 The major goal of this project is to increase the proportion of less acculturated Chinese adults who have been tested for HBV and, therefore, either have been vaccinated, are screened for liver cancer, or know they are immune to the disease.</p> |

<p>29. <i>Molecular anatomy of head and neck cancer, a genomic/proteomic approach: Whole genome array CGH of progressing oral dysplasia</i>[†] <i>Co-PI: W Lam, M Rosin and L Zhang; NIH; 2004-2008;</i> <i>For 2004 - US\$270,000; Σ US\$1,080,000</i> The goal of this project is to identify and catalogue genetic alterations and protein changes associated with development stages of oral cancer and to identify list of candidate genes that drive the transformation of oral premalignant lesions to tumours for further study and validation as molecular targets for novel early detection and treatment design.</p>
<p>30. <i>Molecular epidemiology of breast cancer</i>[†] <i>Co-PI: K. Aronson and J Spinelli; Co-I: C Bajdik, A Brooks-Wilson and others; CIHR; 2004-2009; For 2004 - \$285,002; Σ \$1,425,011</i> The goals of this project are 1.) to determine breast cancer risk associated with relevant gene-environment interactions with control for confounders and 2.) to determine breast cancer risk associated with environmental factors according to various relevant breast cancer sub-groups (defined by ER status, PR status, HER-2/neu, etc.) with control for confounders.</p>
<p>31. <i>Occupational risk identification for ovarian cancer-renewal</i> <i>Co-PI: J Bert, R Gallagher, B Lang and N Le; WCB; 2004-2006; For 2004 - \$112,000; Σ \$336,000</i> The purpose of this research is to identify potential carcinogens in the BC work environment for ovarian cancer.</p>
<p>32. <i>Organochlorines, ultraviolet radiation and gene-environment interactions in non-Hodgkin's lymphoma</i>[†] <i>Co-PIs: A Brooks-Wilson, J Connors, R Gascoyne and J Spinelli; NCIC; 2003-2006; For 2004 - \$563,333; Σ \$2,253,332</i> The major goals of this project are: to determine whether exposure to organochlorine compounds and the degree of ultraviolet radiation exposure, or a combination of genetic and environmental factors are related to the risk of NHL.</p>
<p>33. <i>Proteomic assessment of women being diagnosed with breast cancer</i>[†] <i>Co-PI: K Gelmon and A Karsan; Co-I: J. Spinelli and others; CBCF; 2003-2004; For 2004 - \$55,516; Σ \$111,032</i> Proteomic assessment of women being diagnosed with breast cancer.</p>
<p>34. <i>Simulation of a genetic testing program for hereditary non-polyposis colorectal cancer</i>[†] <i>PI: C Bajdik; Co-I: R Gallagher, D Horsman, D Huntsman and J Spinelli; CIHR; 2003-2006; For 2004 - \$149,985; Σ \$449,685</i> The main objectives of this study are to create a simulation model of cancer incidence in the relatives of people with germline mutations in HNPCC genes and to estimate the sensitivity, specifically and post-test likelihoods associated with family history as a predictor of carrier status for HNPCC genes, and estimate the number of carriers who are eligible for a provincial genetic testing program.</p>

<p>35. Study of cancer risks among nurses in BC <i>PI: H Ward; Co-I: R Gallagher, N Le, P Ratner, J Spinelli and K Teschke; WCB; 2001-2005; For 2004 - \$365,170; Σ \$1,825,850</i> The objective of this proposed study is to provide a feasible approach to developing the RN cohort registry and testing hypotheses on occupational cancer risks for nurses. The person-years estimates for this cohort have sufficient power to ascertain the relative risk for nurses developing a relatively rare cancer, such as leukemia. The results of this study will allow the WCB to target prevention efforts to high risk groups of registered nurses and other health care workers.</p>
<p>36. Toward effective patient-professional communication in cancer care <i>PI: S Thorne; Co-I: G Hislop; NCIC; 2001-2004; For 2004 - \$70,393; Σ\$409,916</i> Patterns and themes specific to communication in cancer care will be documented, analyzed and interpreted. Data will be obtained from focus groups and interviews with volunteer cancer patients representing a wide range of demographic, disease, and contextual situations (approximately 250 persons). The findings from this phase of the research will be synthesized into preliminary principles and guidelines for communication from a consumer perspective which will be used as a basis for discussion in interviews with selected health care professionals.</p>
<p>37. Treatment decision making and quality of life in East/South-East Asian women with ductal breast carcinoma in situ (DCIS) <i>Co-PI: G Hislop and S Wong; CBCRA; 2004-2005; Σ \$45,141</i> The goal of this study is to use data collected from focus groups to develop/refine decision making and quality of life measures to be included in a large scale survey of Caucasian and Asian women who are diagnosed with breast cancer.</p>
<p>International Collaborations</p>
<p>38. A model for genetic susceptibility: melanoma <i>Co-PI: R Gallagher with M. Berwick, Sloan-Kettering Institute; Co-I: Armstrong, Millikan, Gruber, Anton-Culver, Rebbeck; NIH; 1999-2004; For 2004 - \$1,280,000; Σ \$6,400,000</i> Melanoma provides a unique model for studies of gene-gene and gene-environmental interaction in the development of cancer. This population-based case control study will look at the relation risk of developing melanoma due to germline mutations or polymorphism in cell cycle genes, due to polymorphism in the melanocortin receptor gene, MC1R, a major pigmentary gene, allelic variation in the DNA repair genes and analyze the interactions among genetic variants and their association with solar UV radiation.</p>
<p>39. Canadian component: International case control study of radio frequency fields and cancer of the brain, salivary gland and leukemias <i>PI: D Krewski; Co-I: M McBride; CIHR/Canadian Wireless Telecommunications Association; 2001-2006; For 2004 - \$131,975; Σ \$659,877</i> The major long-term goal of this project is epidemiologic assessment of risk of brain tumours with exposure to radiofrequency fields or cell phones.</p>

<p>40. Case control study of cell phones and brain cancer <i>Co-PI: M McBride; CIHR; 2002-2006; For 2004 - \$164,969; Σ \$659,877</i> IARC, in an attempt to elucidate the role of radiation exposures in the etiology of selected adult cancers, has developed a research protocol for a multi-site population-based case-control study in collaboration with investigators from 13 countries.</p>
<p>41. Childhood leukemia and socioeconomic status <i>Co-I: M. Borugian, M. McBride and J Spinelli; 2003 – 2004; Electric Power Research Institute (CA); Σ\$US29,900;</i> The major goal of this project is to determine whether there is a relationship between socioeconomic status and risk of childhood leukemia and whether there is evidence of selection bias on socioeconomic status in a previous study of EMF exposure and childhood leukemia.</p>
<p>42. Optical systems for in vivo molecular imaging of cancer[†] <i>PI: R Richards-Kortum, U of Texas Austin; Co-PI: C. MacAulay, M Rosin and others; NIH; 2003-2008; For 2004 - US\$317,998; Σ US\$9,708,197</i> <i>Bioengineering grant:2003-2008: (Bioengineering Research Partnerships):</i> Optical systems for <i>in vivo</i> molecular imaging of cancer. Richards-Kortum et al. \$1,893.176 p.a. (Total: \$9,708.197) The major goal of this project is to integrate development of optical imaging systems and contrast agents with advances in functional genomics.</p>
<p>43. Selection bias and wire coding <i>Co-PI: M McBride and J Spinelli; Co-I: G. Mezei; US Electrical Power Research Institute; 2004-2007; For 2004 - \$97,536; Σ \$292,610</i> The goal of this proposal is to evaluate the role of selection bias in the observed epidemiological association between exposure to extremely low frequency magnetic field (ELF-MF) and childhood leukemia.</p>

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
23	1	13	12	1

DEPARTMENT OF CANCER ENDOCRINOLOGY
BC CANCER RESEARCH CENTRE
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<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Yuzhuo Wang	PhD Anatomy	Senior Scientist Adjunct Professor, Division of Urology, Surgery, UBC
Cheryl Helgason	PhD Biochemistry	Senior Scientist Assistant Professor, Surgery, UBC; Associate Member, Microbiology and Immunology, UBC
Peter W Gout	PhD Biochemistry	Honorary Senior Scientist Emeritus Scientist, Cancer Endocrinology, BCCRC
Juergen Vielkind	PhD Genetics	Senior Scientist & Director, Tumour Tissue Repository to June 2004) Associate Professor Emeritus, Pathology & Lab Medicine, UBC

OUR RESEARCH FOCUS: Our research is focused on the prevention, early diagnosis and treatment of prostate cancer. Our main objective is to delineate biochemical, 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. In addition to the studies on prostate cancer, gene expression profiling during embryonic development and stem cell commitment is an important area of investigation. The major focus of this work is on pancreas development as a means to devise appropriate strategies for generating a replenishable supply of glucose-responsive, insulin-secreting cells from embryonic stem or pancreas progenitor cells. Such studies are also likely to provide important insights into the molecular mechanisms that go awry during the development of pancreas cancer.

PROGRESS HIGHLIGHTS DURING 2004:

- A large research grant was awarded from the US Department of Defense to study a novel therapeutic use for the drug sulfasalazine in a novel animal model developed by YZ Wang.

RESEARCH KEYWORDS:

Androgen independence, anti-cancer agent, cancer tissue xenograft models, dendritic cell function, diabetes, embryonic stem cells, gene expression profiling, immune regulation, immunology and immunotherapy of prostate cancer immunosuppressant, knockout models, metastasis, molecular signatures/biomarkers, novel drugs, pancreas development, prostate cancer stem cells, sulfasalazine.

TRAINING**A.) Course Instruction**

C Helgason	UBC Micro 430
C Helgason	UBC MEDI 502
C Helgason	UBC Surgery 500
YZ Wang	UBC OBST 506

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
14	3	5	5	1

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
A Tien	C Helgason	CIHR/MSFHR Transplantation Studentship
M Wesa	C Helgason	Faculty of Medicine Summer Studentship

SELECTED PERSONAL AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Cheryl Helgason	MSFHR Scholarship 2003-2008
	CIHR New Investigator Award 2001-2006

SELECTED CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Cheryl Helgason	Member, Experimental Medicine Graduate Studies Program, UBC
	Member, Genetics Graduate Studies Programs, UBC
	Member, Editorial Board, Experimental Hematology
	Member; Michael Smith Foundation for Health Research Biomedical Trainee Evaluation Committee
	Member; CIHR Doctoral Research "A" (Biomedical) Awards Committee

MAJOR PROGRAMS & PROJECTS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Project</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Project</i>
10	\$6.2 M	2	\$1.3 M

CURRENT RESEARCH PROJECTS

Cancer Endocrinology	
1. Dendritic cell development and function in a mouse model of systemic lupus erythematosus <i>PI: C Helgason; CIHR; 2001- 2004; For 2004 - \$41,722; Σ \$269,246</i> The goal of this project was to determine the role of the SH2-containing inositol-5-phosphatase SHIP in regulating dendritic cell development and function. Understanding how dendritic cells with specific functional properties are generated will allow us to use them more effectively for immunotherapeutic purposes.	
2. Development of a function-blocking peptide for treatment of cancer <i>PI: PW Gout and Co-PI: YZ Wang; CIHR; 2005; Σ \$150,000</i> The goal of this project 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.	
3. New in vivo model of low-grade human prostate cancer (PCa) – potential applications for molecular analysis and diagnostic screening <i>PI: YZ Wang; NCIC; 2003-2006; For 2004: \$136,800; Σ \$483,951</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.	
4. Novel approach for prostate cancer therapy: application of a unique xenograft model <i>PI: YZ Wang and Co-PI: PW Gout; US Department of Defense; 2004-2007; For 2004 - \$149,600; Σ US\$448,800</i> We have developed a novel method for establishing xenograft animal models of both low-and higher grade human prostate cancer (PCa) with which to investigate experimental therapies. The goal of this study is to see if use of sulfasalazine can lead to the arrest of growth of human PCa tissue grafts and, in particular, of advanced cancers resistant to current therapies.	
5. Role of regulatory T cells in prostate cancer progression <i>PI: C Helgason; Prostate Cancer Research Foundation of Canada; 2002-2004; For 2004 - \$50,000; Σ \$150,000</i> Immunotherapy approaches that attempt to induce or enhance the immune response against prostate cancer offer an exciting alternative to conventional treatment. However, the success of such strategies has been limited by the lack of identified tumour-specific proteins and the immunosuppression often observed in cancer patients. We will study whether regulatory T (Tr) cells, protect tumour cells from the immune system and examine the possibility that elimination of this cell population will allow the immune system to kill the tumour.	

6. Dendritic cells in autoimmunity and cancer <i>PI: C Helgason; MSFHR Establishment Grant; 2003-2005;</i> <i>For 2004 - \$62,500; Σ\$125,000</i> This establishment grant is to help establish Dr. Helgason as a new investigator and fund on-going work related to studies of dendritic cell development and function in mouse models of prostate cancer.
7. Mechanisms of prostate cancer tumor cell-mediated immunosuppression: Examination of dendritic cell survival, maturation and function in response to prostate cancer <i>PI: C Helgason; US Department of Defense; 2002-2005;</i> <i>For 2004 - US\$125,000; Σ US\$375,000</i> We investigated the mechanisms by which prostate tumor cells alter immunity with a particular emphasis on dendritic cells and regulatory T cells.
Interdisciplinary
8. Development of pre-neoplastic and early-stage human lung cancer xenograft models[†] <i>PI: YZ Wang; Co-I: S Lam, J English; BC Lung Association; 2003-2005;</i> <i>For 2004 - \$25,000; Σ \$50,000</i> The objective of this study is to perform a pilot study to develop in-vivo preclinical models of early stage human lung cancer and pre-neoplastic lesions.
9. Quantitative and comprehensive atlas of gene expression in mouse development <i>PL: P Hoodless and M Marra; Co-I: C Helgason and E Simpson;</i> <i>Genome Canada; 2002-2005; For 2004 - \$4,398,508; Σ \$13,195,524</i> For a summary of this project see Terry Fox Laboratory.
10. Application of Pharmacogenomics for Rational Chemotherapy of Lung Cancer <i>PIs: S Lam & V Ling; Co-I: J English, W Lam, C MacAulay, R Ng, YZ Wang, J Yee; Genome Canada; 2004-2007; For 2004 - \$1,146,696; Σ \$3,440,089</i> For a summary of this project see Cancer Imaging.

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
3	2	6	24	0

DEPARTMENT OF CANCER GENETICS AND DEVELOPMENTAL BIOLOGY
BC CANCER RESEARCH CENTRE
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<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
Wan Lam	PhD Biochemistry	Senior Scientist Clinical 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
Sharon Gorski	PhD Developmental Biology	Scientist
Raymond Ng	PhD Computer Science	Affiliated Scientist Professor, Computer Science, UBC

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. Developing and applying highly sensitive techniques to identify and track mutations in patient biopsies at the genome-wide level;
2. Identifying novel tumor suppressor genes and oncogenes associated with various cancers;
3. 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;
4. Establishing novel models of cancer metastasis, and identifying genes involved in the establishment of organ-specific metastasis;
5. Investigating the family of energy dependent ATP-binding membrane transport proteins associated with chemotherapy resistance, hormone secretion and programmed cell death; and
6. Developing novel cell-based screens to discover new targets and therapeutics against cancer cell invasion and survival, and tumour angiogenesis.

Model systems such as the mouse, the zebrafish, the nematode worm, and the fruit fly are used as a comparative approach to investigate normal developmental and molecular pathways implicated in the cancer process. This approach is highly informative as to how genetic mutations associated with malignant transformation override normal control mechanisms.

PROGRESS HIGHLIGHTS DURING 2004:

- Development of the sub-megabyte tiling resolution (SMRT) whole genome micro-array
- Identification of a new target – the protein integrin linked kinase – for anti-angiogenesis therapy and the arrest of blood vessel-forming endothelial cells.

RESEARCH KEYWORDS:

Apoptosis, autophagy, bioinformatics, *C. elegans*, cancer biology, cell culture developmental biology, *Drosophila*, drug transport, gene discovery, gene expression, genomics, large scale DNA mapping, large scale DNA sequencing, membrane biochemistry, multi-drug resistance, pathogens, programmed cell death, retina, RNAi.

TRAINING

A.) Course Instruction

S Dedhar	UBC Med Gen521/Path 531	Molecular and Cell Biology of Cancer
S Dedhar	UBC Biochem 511	
S Dedhar	UBC Biochem 509	
W Lam	UBC Path 548F	Histopathology
W Lam	UBC Path 548F	Microdissection
W Lam	UBC Path 548C	Bioinformatics
W Lam	UBC Biol 448	Direct Studies

B.) Summary of Trainees and Degrees Completed

Total No. of Current Student	Post-doctoral	Post-graduate	Undergraduate	Clinical
41	29	8	2	0

CURRENT STUDENTS – DEGREES COMPLETED

Name	Supervisor	Date Completed	Awards/Honours Received
PhD			
S. Atwell	S. Dedhar	2004	
P. Lam	V. Ling	2004	
L. Henderson	W. Lam	2004	
K. Cleveland	W. Lam	2004	

Trainee Awards

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
S Atwell	S. Dedhar	NSERC Scholarship
B Coe	W. Lam	MSFHR Grad Studentship
R deLeeuw	W. Lam	MSFHR Grad Studentship
N Filipenko	S. Dedhar	MSFHR Postdoctoral Award
C Garnis	W. Lam	MSFHR Grad Studentship
M Ho	V. Ling	MSFHR Masters Award
M Lo	V. Ling	CIHR Doctoral Res Award
C Tan	S. Dedhar	CIHR Scholarship
G Vatcher	V. Ling / W. Lam	MSFHR Postdoctoral Award

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Victor Ling	MSFHR Scholar (2001-2005)
Shoukat Dedhar	MSFHR Distinguished Scholar (2001-2005)
Marco Marra	NCIC/Terry Fox Young Investigator Award
	MSFHR Scholar (2001-2005)
	Honorary Degree, Doctor of Science, SFU
	Honorary Degree, Doctor of Laws, University of Calgary

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Victor Ling	Council Member, Canadian Institutes of Health Research
	Member, Premiers Advisory Council of Science and Technology
Shoukat Dedhar	Chair, NCIC Grant Panel B (to 2004)
	Member, OCRN Translational Research Grants Panel (to 2004)
	Chair, Scientific Professional Staff Association, BCCA
	Chair & Organizer of EMT 2005 International Conference on Epithelial-Mesenchymal Transformation in Vancouver, BC
Wan Lam	Graduate Advisor, Pathology, UBC
	Member, NCIC Grant Panel J
	Member, CIHR Genomics Panel
	Member, OCRN Translational Research Panel
	Member, 2004 World Congress of Lung Cancer Organizing Committee

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
21	\$10.1 M	8	\$2.8 M

CURRENT RESEARCH PROJECTS⁹

Cancer Genetics & Developmental Biology	
1.	<p><i>ABC transporters and clinical response to therapy - renewed</i> <i>PI: V. Ling; NCIC; 2004-2010; For 2004 – \$150,000; Σ\$750,000</i> The research objective 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 goal is to identify the molecules that cause it. Another goal is to continue work on the TAPL transporter to determine its role in cancer prevention.</p>
2.	<p><i>Cell extra-cellular matrix interactions in differentiation and oncogenesis</i> <i>PI: S. Dedhar; NCIC; 2003-2008; For 2004 – \$150,000; Σ\$754,250</i> The research goal to study ILK to learn how it controls attachment of cells to ECM, how it stops cells from dying and how it encourages cells to become cancerous.</p>
3.	<p><i>Functional role of calreticulin in integrin-mediated regulation of cell adhesion</i> <i>PI: S Dedhar; CIHR; 2000-2004; For 2004 - \$86,980; Σ\$391,647</i> The research objective is to determine how calreticulin regulates integrin function through 'inside-out' signaling.</p>
4.	<p><i>A genomic approach to identifying novel targets for early detection and intervention of prostate cancer</i> <i>PI: W Lam; USA Dept of Defense New Invest. Award; 2001-2004; For 2004 - US\$74,968; ΣUS\$224,905</i> The objective of this grant is to perform genome-wide scanning of PINs and cancers for genetic changes.</p>
5.	<p><i>Regulation of E-Cadherin expression and Wnt signaling by integrin linked kinase (ILK)</i> <i>PI: S. Dedhar; CIHR; 2003-2006; For 2004 - \$69,161; Σ182,903</i> This research aims to study the process whereby cancer cells spread to distant organs, called epithelial to mesenchymal transformation. The study will investigate factors regulating the activity of a key protein <i>E Cadherin</i> which holds epithelial cells together.</p>

⁹ Key to Abbreviations: PI = Principal Investigator, PL = Project Leader; Co-I = Co-investigator; CBCRA = Canadian Breast Cancer Research Alliance; CIHR = Canadian Institutes of Health Research, CPCRI = Canadian Prostate Cancer Research Initiative, MSFHR = Michael Smith Foundation for Health Research, MRC = Medical Research Council; NCIC = National Cancer Institute of Canada; NIH = National Institutes of Health (US); NSERC = Natural Sciences and Engineering Research Council; WCB = Workers Compensation Board; ⁺ = Inter-departmental project; Σ = total amount of project funding committed.

6.	<p><i>The role of sister of p-glycoprotein in liver function</i> <i>PI: V Ling; CIHR; 2000-2005; For 2004 - \$123,500; Σ\$617,500</i> The goal of this study is to characterize the role of the protein, sister of p-glycoprotein (sPgp), in bile formation and excretion. sPgp is closely related to p-glycoprotein which is associated with multidrug resistance.</p>
Interdisciplinary Research	
7.	<p><i>Cancer Genomics: A multi-disciplinary approach to the large scale high-throughput identification of genes involved in early stage cancers[†]</i> <i>PIs: V Ling, C Eaves & M Marra; Co-PIs: K Humphries, D. Huntsman, S Jones, W Lam, S Lam, P Lansdorp, C MacAulay, M Rosin, M Sadar, I Tai, J Vielkind; Genome BC/Canada; 2001-2005; For 2004 - \$5,592,811; Σ\$16,778,433</i> 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>
8.	<p><i>Genome wide synthetic clones for use in diagnostic probes and high density genomic hybridization assays</i> <i>PIs: W Lam, C. MacAulay; CIHR Proof of Principle; 2004; \$99,855</i> The goal of this study is to further develop the method of synthetically producing DNA clones for the whole genome tiling resolution DNA microarray developed in Dr. Wan Lam's laboratory.</p>
9.	<p><i>Genomic profiles of lung cancer that predict prognosis and response to adjuvant chemotherapy</i> <i>PI: M-S Tsao, OCI; Co-I: W Lam; OCN; 2004-2007; \$175,520 to W Lam; For 2004 - \$175,520; Σ\$526,560;</i> The goal of this study is to make whole genome profiles from lung cancer patients of the Ontario Cancer Institute using the whole genome tiling resolution DNA microarray.</p>
10.	<p><i>Integrin linked kinase inhibition as an approach to treating malignant glioma</i> <i>PI: B Thiessen; Co-PI: S Dedhar; Terry Fox New Frontiers Initiative; 2000-2004 For 2004 - \$274,000; Σ \$10,960,000</i> The research objectives are to study the role of ILK activation in brain cancers and to determine inhibitors to ILK may block brain cancer progression.</p>
11.	<p><i>New molecular targets in mantle cell lymphoma[†]</i> <i>PL: R Gascoyne; PIs: J Connors, D Horsman, W Lam; Lymphoma Research Foundation; 2004-2007; For 2004 - US\$98,000 ΣUS\$2,174,409</i> For a summary of this project see Pathology and Laboratory Medicine</p>
12.	<p><i>New technologies for surveillance of biowarfare agents and identification of engineered virulence genes</i> <i>PIs: R Fernandez, UBC, W Lam; CBRN Research & Technology Initiative; 2003-2007; For 2004 - \$86,250; Σ\$345,000</i> The objective of this research is to develop a two-dimensional DNA display technology for mutation detection in pathogens.</p>

- | | |
|-----|--|
| 13. | <p>Novel molecular prognostic makers and potential therapeutic targets in non-small cell lung cancer</p> <p>PI: M-S Tsao, OCI; Co-I: W Lam; NCIC; 2004-2009; \$150,000 to W Lam; For 2004 - \$150,000; Σ\$750,000</p> <p>Dr. Tsao will identify specific genetic changes that have potential as predictors of lung cancer outcomes in patients. They will investigate the genetic changes in 600 lung cancer cell samples from patients and will use genetically altered animals to discover whether treatment aimed at some of these genes will stop lung cancers from growing.</p> |
| 14. | <p>Pharmacogenomics of non-small cell lung cancer[†]</p> <p>PIs: S Lam & V Ling; Co-PI: J English, W Lam, C MacAulay, R Ng, J le Riche; YZ Wang, J Yee; Genome Canada; 2004-2007; For 2004 - \$1,143,363; Σ\$3,430,090</p> <p>The research goal is to use the whole genome BAC CGH microarray to generate predictive genomic signatures of chemotherapy response in non-small cell lung cancer (NSCLC) patients, and to use a novel human tissue xenograft system to create a platform for innovation that facilitates the development of more effective drugs for the treatment of NSCLC.</p> |
| 15. | <p>Preclinical studies to evaluate utility of inhibition of integrin linked kinase (ILK) in treatment of breast cancer[†]</p> <p>PIs: K Gelmon; Co-PIs: S. Dedhar, M Bally; CBCRA/CIHR; 2003-2006; For 2004 - \$142,400; Σ\$569,600 [part of Translating target discovery into better health outcomes for women with breast cancer program; Σ1,941,731]</p> <p>The project objectives are to evaluate ILK small molecule inhibitors in cell culture and mouse models of human breast cancer.</p> |
| 16. | <p>Role of integrin linked kinase in prostate cancer progression</p> <p>PI: P Rennie; Co-PI: S Dedhar; NCIC; 2001-2006; For 2004 - \$145,000; Σ\$725,000 [part of Terry Fox Foundation Program Project on Prostate Cancer Progression]</p> <p>The research objectives are to determine the signaling pathways and consequences of ILK activation for prostate cancer progression, and to evaluate inhibitors of ILK as therapeutics for prostate cancer.</p> |
| 17. | <p>Solid Tumor Progression-Research Unit</p> <p>Director: C Roskelley, UBC; Co-I: S Dedhar, M Roberge; MSFHR; 2003-2006; For 2004 - \$150,000; Σ\$450,000</p> <p>Surgery, radiation and chemotherapy are routinely used for treating solid tumours. However, very few therapies effectively counter metastatic progression (spread to other areas of the body), which is the major cause of death associated with cancer tumours. This unit aims to develop and evaluate novel compounds that show promise of halting or reversing tumour spread.</p> |
| 18. | <p>Validation and Development of Comparative Genomic Hybridization Arrays for Clinical Use in Cancer[†]</p> <p>PIs: D Horsman, W Lam; Co-PIs: C. MacAulay, R Ng, J Squire; Genome BC/Canada; 2004-2007; For 2004 - \$768,589; Σ2,305,769</p> <p>This project is an extension of the Cancer Genomics program, with the objective of introducing a high resolution, partially automated and competitively priced technology to assess DNA dosage alterations in cancer.</p> |

19.	Whole genome array CGH of progressing oral dysplasia[†] <i>PIs: M Rosin & W Lam; NIDCR, NIH; 2004-2008;</i> <i>For 2004 - US\$270,000; ΣUS\$1,080,000</i> The objective of this grant is to use genomics to discover a novel genetic marker in order to differentiate progressing low-grade dysplastic lesions from morphologically indistinguishable non-progressing low-grade lesions.
International Collaborations	
20.	Early Detection Research Network[†] <i>PL: A Gazdar, University of Texas SW; Co-I: W Lam, C MacAulay</i> <i>NIH; 2004-2009; For 2004 - US\$25,000; Σ US\$125,000</i> For a summary of this project see Cancer Imaging.
21.	Optical systems for in vivo molecular imaging of cancer[†] <i>PL: R. Richards-Kortum, Rice University; Co-I: W Lam, C MacAulay;</i> <i>NIH; 2003-2008; For 2004 - US\$224,923, ΣUS\$2,000,000</i> For a summary of this project see Cancer Imaging

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
24	1	37	50	0

DEPARTMENT OF CANCER IMAGING
BC CANCER RESEARCH CENTRE
Telephone: 604-675-8081

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Calum MacAulay	PhD Physics	Head, Cancer Imaging
		Clinical Associate Professor, Pathology, UBC; Associate Member, Physics, UBC
Stephen Lam	MD	Senior Scientist & Head, BCCA Lung Tumour Group
		Professor, Medicine, UBC
Haishan Zeng	PhD Medical Physics	Senior Scientist
		Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC; Visiting Professor, Fujian Normal University, China;
Jaclyn Hung	PhD Physics	Senior Scientist
		Clinical Assistant Professor, Pathology and Laboratory Medicine, UBC
Mladen Korbelik	PhD Biology	Senior Scientist
		Clinical Professor, Pathology and Laboratory Medicine, UBC
David Garner	PhD Chemistry	Senior Scientist (on sabbatical)
		Clinical Scientist, Pathology and Laboratory Medicine, UBC; CEO, Perceptronix Inc.
Alexei Doudkine	PhD Chemistry	Research Scientist
Martial Guillaud	PhD Biomedical Engineering	Research Scientist
Pierre Lane	PhD Electrical Engineering, PEng	Research Scientist
		Research Scientist, Digital Optical Imaging Corp.
Annette McWilliams	MBBS, FRACP (Respiratory Medicine)	Research Physician
Jean le Riche	MB ChB, FRCPC (Pathology)	Associate Member
		Former, Head of Pathology, BCCA

OUR RESEARCH FOCUS: We exploit the interaction of light at both the micro- and macro-scopic level to detect, delineate, grade and treat early (predominantly pre-invasive) cancers. We are currently focused on early cancer management issues in Lung, Cervix, Prostate, Breast and Skin. This is achieved by developing novel procedures and improving our understanding of:

1. Automated image analysis of cell preparations
2. In vivo tissue spectroscopy (reflectance, autofluorescence, fluorescence, Raman)
3. Interactive/automated analysis of tissue preparations
4. In vivo tissue imaging (autofluorescence, fluorescence, reflectance)
5. Confocal microscopy
6. Photodynamic therapy
7. Chemoprevention
8. Tissue modeling (static and dynamic)

The department has a special emphasis on enabling the translation of research to clinical usefulness.

RESEARCH HIGHLIGHT 2004 – LUNG CANCER

- The key to effectively managing lung cancer is to detect it early. Since 2000, the use of quantitative computer assisted sputum cytometry in combination with autofluorescence bronchoscopy and spiral thoracic CT scan has been used in an early lung cancer detection program as part of the Lung Health Study. Approximately 1200 subjects have been evaluated. Overall, 60% of subjects have atypia on sputum cytometry and 85% of subjects have small pulmonary nodules that require surveillance. A total of 42 cancers in 34 subjects have been detected, with 75% detected by thoracic CT scan and 25% detected by autofluorescence bronchoscopy (CT occult). Nearly 80% of detected cancers were Stage 0/I, early enough that the chance of cure is very high. The use of sputum cytometry in combination with CT scan and autofluorescence bronchoscopy increased the detection of subjects with cancer from 3% with CT scan alone to 5%.

RESEARCH KEYWORDS:

Automated image analysis, cancer biology, cancer chemoprevention, light-tissue interaction, molecular genetics of pre-invasive lung cancer, optical properties of biological tissues, quantitative microscopy, sex differences in lung cancer.

TRAINING

A.) Course Instruction

C MacAulay UBC Phys 404
H Zeng UBC Phys 543
J Hung UBC Bio 448

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
10	3	2	5	

CURRENT STUDENTS - DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>	<i>Awards/Honours Received</i>
PhD			
I Cecic	M Korbelik	2004	MSFHR PhD Trainee
J Lindblad	C MacAulay	2004	
MSc			
D Lau	H Zeng	2004	

SELECTED CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Stephen Lam	President, International Photodynamic Association
	Member, Advisory Council on Lung Cancer, NCIC
Mladen Korbelik	Chair, Graduate Student Supervisory Committee
	Member, Graduate Student Committee, Dept. of Pathology
Haishan Zeng	Grant Review Committee Member (Medical Physics and Imaging Committee), CIHR
	Chief Scientist and Vice President, SpectraVu Medical Inc.

MAJOR RESEARCH PROGRAMS & PROJECTS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
20	\$4.2 M	6	\$1.7 M

CURRENT RESEARCH PROJECTS¹⁰

Cancer Imaging
<p>1. Confocal and tomographic reconstruction microscopy- renewal <i>PI: C MacAulay and P Lane; CIHR; 2002-2005; For 2004 - \$137,504; Σ \$412,512</i> The hypothesis to be examined in this project is that by replacing the mechanical diaphragms of a conventional microscope with one or more digital micromirror devices (DMDs) one can construct a microscope capable of improved confocal fluorescence imaging as well as 30D imaging of absorbance stained material. The DMD is a reflective spatial light modulator manufactured by Texas Instruments. It consists of a 1024-by-768 array of movable micromirrors on 17 micromillimeter centers.</p>
<p>2. Genetic alteration in lung cancer development-gender difference? <i>PI J Hung; CIHR; 1999- 2004; For 2004 - \$25,000; Σ\$132,500</i> The primary aim of this project is to study heavy smokers, both female and male to identify the molecular and genetic changes which lead to lung cancer, and to determine whether these differ in men and women.</p>

¹⁰ Key to Abbreviations: PL = Project Leader; PI = Principal Investigator; Co-I = Co-Investigator; CIHR = Canadian Institutes of Health Research; NCI = National Cancer Institute (US); NCIC = National Cancer Institute of Canada; NIH = National Institutes of Health (US);

<p>3. Near-infrared fluorescence spectroscopy and imaging for skin cancer detection and evaluation <i>PI: H Zeng and H Lui; Canadian Dermatology Foundation; 2003-2004; Σ \$30,000</i> There are three aims for this project: 1) to quantify the NIR fluorescence properties of normal and diseased skin; 2) to understand the origin of skin NIR fluorescence changes at the tissue (microscopic) level; and 3) to determine if the differences in skin NIR fluorescence properties can differentiate skin cancer from other skin diseases. Suggestions will be given for future clinical studies, but building a clinical system will not be the aim of this project.</p>
<p>4. PDT and immunotherapy of solid tumors <i>PI: M Korbelik; CIHR; 1993-2007; For 2004 – \$97,620; Σ \$672,252</i> This study will exploit photoreactive drug-based therapeutic intervention elicits the development of immune response against treated tumor which contributes to the eventual eradication of the malignant lesion. We will optimize the procedure to expose (photodynamic therapy or PDT) to cancer cells to PDT in vitro to obtain PDT generated cancer vaccines.</p>
<p>5. Pre-invasive and stage 1A lung cancer biomarkers identified through random peptide phage display <i>PI J Hung; CIHR; 2004- 2007; For 2004 – \$48,304; Σ \$119,030</i> This project will identify protein abnormalities produced by cancer genes in early clinical stage 0 (pre-invasive) and 1A (early invasive) squamous lung cancers. The identification of such panel of protein markers in pre-invasive and invasive lung squamous carcinoma represents ideal biomarkers for the early detection of such lesions in the sputum and in bronchial biopsies of individual with or at risk for lung cancer.</p>
<p>6. Raman spectroscopy for non-invasive diagnosis: application in skin cancer detection and evaluation <i>PI: H Zeng, H Lui and M Chen; NCIC; 2004-2007; For 2004 – \$69,168; Σ \$208,004</i> When light strikes tissues, some of it bounces off in such a way that it loses its light energy, a process called "Raman scattering." The amount of energy lost depends on characteristics of the tissues, and can be measured in minutes to complete the procedure and were not useful in patients. This study will use a device that rapidly measures Raman scattering and compare the utility of their device on about 1,500 suspected skin cancers.</p>
<p>7. Rapid raman spectroscopy for non-invasive skin cancer diagnosis <i>PI: H Zeng; Canadian Dermatology Foundation; 2004-2005; Σ \$25,000</i> Our primary objectives are aimed at a detailed understanding of the optical spectroscopic properties of skin cancer: (1) to characterize the specific Raman, fluorescence, and reflectance features of skin cancer using visible and near infrared light and to test the diagnostic utility of these modalities alone and in combination; (2) to develop diagnostic algorithms for spectroscopic skin cancer diagnosis; (3) to evaluate the effect of secondary changes to skin cancers such as necrosis, inflammation, and ulceration on spectroscopic signals; and (4) to elucidate the biophysical origins of the these optical signals.</p>

<p>8. Relevance of complement activation in photodynamic therapy-mediated eradication of solid tumors <i>PI: M Korbelik; NCIC; 2003-2006; For 2004 – \$105,689; Σ \$276,278</i> The goal is to study how an impaired complement system in an animal model – a chain reaction in which several proteins become activated – can be activated and how it might affect cancer treatments. The objective will be to test ways to make activation of the complement system contribute to cancer cell destruction without causing other effects.</p>
<p>9. Tomographic reconstruction microscopy <i>PI: C MacAulay and P Lane; CIHR; 1999-2007; For 2004 - \$40,495; Σ \$332,303</i> Our goal is to improve early cancer detection and diagnosis capability by using a novel 3-D device to measure internal quantitative information of biological samples instead of 2-D images acquired by conventional optical microscopes. The project will use a 3-D imaging platform called Optical Computed-Tomography, a novel optical scanning technique, and involvement of pathologists.</p>
<p>10. Visible to near infrared fluorescence Excitation-Emission Matrix (EEM) spectroscopy system for skin characterization and diagnosis <i>PI: H Zeng and H Lui; CIHR; 2003- 2005; For 2004 - \$48,671; Σ \$152,410</i> This study will investigate interesting fluorescence properties from melanin, a skin chromophore responsible for UV protection and for skin colour. We will build a new device to study skin autofluorescence properties in the longer wavelength, short wave and near infrared bands. This new device may be particularly beneficial to the diagnosis of pigmented skin lesions.</p>
Interdisciplinary
<p>11. Genome wide synthetic clones for use in diagnostic probes and high density genomic hybridization assays[†] <i>PI: W Lam and C MacAulay; CIHR; 2004; Σ \$99,855</i> The objectives of this project is to verify the identity of the amplified fragment pools (AFPs) generated from the 37,000 BAC clones, to produce synthetic genomic arrays and assay for consistency of SGA production and hybridization, and to prove the utility of SGA on analyzing clinical materials.</p>
<p>12. Novel xenograft models of early stage human lung cancer and preneoplastic lesions[†] <i>PI: S Lam, J English, YZ Wang;</i> <i>Canadian (BC) Lung Association; 2003-2005; For 2004 - \$25,000; Σ \$50,000;</i> For a summary of this project see Cancer Endocrinology.</p>
<p>13. Onco-LIFE endoscopic light source and video camera <i>PI: S Lam and A McWilliams; Xillix Technologies Inc.; 2003-2004; Σ \$106,000</i> Pivotal study designed to collect clinical data that will confirm the safety and effectiveness of fluorescence imaging with the Onco-LIFE Endoscopic Light Source and Video Camera when used as an adjunct to white light imaging for the detection and localization of tissue suspicious for moderate or severe dysplasia, carcinoma in situ or invasive lung cancer. Clinical data gathered is intended to be utilized for regulatory submissions.</p>

<p>14. Pharmacogenomics of non-small cell lung cancer[†] <i>PL: S Lam and V Ling; Co-I: J English, W Lam, C MacAulay, R Ng, YZ Wang, J Yee and others; Genome Canada; 2004-2007; For 2004 - \$1,146,696; Σ \$3,440,089</i> The goal of this project is to use the whole genome BAC CGH microarray to generate predictive genomic signatures of chemotherapy response in non-small cell lung cancer (NSCLC) patients, and to use a novel human tissue xenograft system to create a platform for innovation that facilitates the development of more effective drugs for the treatment of NSCLC.</p>
<p>International</p>
<p>15. Markers for Risk Assessment / Early Detection of Lung and Breast Cancer <i>PL: A Gazdar, University of Texas SW; Co-I: S Lam; NIH - NCI; 1999-2004; For 2004 - US\$36,532, ΣUS\$175,973</i> This collaborative population-based early detection study will use molecular analyses on specimens from heavy smokers who have developed sputum atypia or bronchial dysplasia. The objective is to develop knowledge of the role of molecular markers for risk assessment and early diagnosis</p>
<p>16. Optical Systems for in-vivo molecular imaging of cancer[†] <i>PL: RR Richards-Kortum, University of Texas Austin; Co-I: S Lam, W Lam, S Jones, M Korbelik, P Lansdorp, M Marra, C MacAulay & M Rosin; NIH - NCI; 2004-2009; For 2004 - US\$271,633; ΣUS\$1,358,169</i> The goal of this project is to integrate development of optical imaging systems and contrast agents with advances in functional genomics. We will develop molecular-specific, optically active contrast agents that can be applied topically. We will also develop inexpensive, rugged and portable imaging systems to monitor the three-dimensional profile of targeted biomarkers. These contrast agents and imaging systems will have broad applicability to many types of cancer; here, we will develop and test agents and imaging systems for the cervix, oral cavity and the lung tumors.</p>
<p>17. Partnership for Research in Optical Coherence Tomography <i>PI: J Izatt, Duke University; Co-I: C MacAulay, S Lam and H Zeng; NIH; 2000-2004; For 2004 - US\$166,504; ΣUS\$666,018</i> This project presents a multidisciplinary approach to advance the state of the art in diagnostic anatomical and functional medical imaging in situ at the micron scale. This will be achieved by developing fundamental advances in the technology of Optical Coherence Tomography, and by employing these advances for novel clinical applications. Our proposed Partnership includes biomedical engineers and clinicians from five institutions with demonstrated leadership in the transfer of optical diagnostic technologies to clinical practice.</p>
<p>18. Participant in University of Texas SPORE in Lung Cancer[†] <i>Director: J Minna; Co-I: D Banerjee, S Lam, C MacAulay; NIH - NCI; 2003-2008; For 2004 - US\$9,715; ΣUS\$450,762 total award</i> The strategic goal of the specialized program of research excellence (SPORE) is to identify and understand the molecular hallmarks of lung cancer, and to translate this information into the clinic for early detection, prognosis and selection/development of new treatments for lung cancer.</p>

19. Phase II trial of ACAPHA in former smokers with IEN

PL: A. Gazdar, University of Texas SW; Co-I: S Lam, R Buncher, M You, JC LeRiche, C MacAulay, M Guillaud and A McWilliams;

NIH; 2002-2007; For 2004 - \$942,075; Σ US\$4,710,376

The goal of this project is to evaluate the efficacy and safety of a novel food supplement – ACAPHA, in former smokers with bronchial intraepithelial neoplasia (IEN) in a doubleblind, randomized, placebo controlled clinical trial. The results will provide new information on the efficacy and safety of a novel botanical food supplement for chemoprevention of lung cancer. It will also provide new information on the use of novel biomarkers as surrogate endpoints for assessing the effect of chemoprevention.

20. Program project: Chemoprevention of lung cancer

PI: MW Anderson, U of Cincinnati; Co-I D Banerjee, M Guillaud, S Lam, JC LeRiche, C MacAulay and A McWilliams;

NIH; 2003-2008; For 2004 - US\$432,277; Σ \$2,161,385

This project is designed to test the hypothesis that a selective combination of chemopreventive agents (budesonide, green tea extracts, myo-inositol and difluoromethylornithine) can prevent the progression and formation of preneoplastic lesions in the respiratory epithelium. BCCA contributes to develop confocal microendoscopy as a non-biopsy method to assess the effect of chemopreventive agents.

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
15	1	18	42	3

DEPARTMENT OF MEDICAL BIOPHYSICS**BC CANCER RESEARCH CENTRE**

Telephone: 604-675-8030

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Ralph Durand	PhD Biophysics	Head, Medical Biophysics Associate Vice-President, Research, BCCA; Honorary Professor, Pathology and Laboratory Medicine, UBC; Associate Member, Physics and Astronomy, UBC; Director, Interdisciplinary Oncology Program, UBC
Aly Karsan	MD	Senior Scientist, Hematopathologist, Dept. of Pathology, BCCA Associate Professor, Pathology and Laboratory Medicine, UBC
Andrew Minchinton	PhD Radiation Biology	Senior Scientist Honorary Assistant Professor, Pathology and Laboratory Medicine, UBC
Peggy Olive	PhD Biochemistry	Senior Scientist Adjunct Professor, Physics and Astronomy, UBC; Honorary Professor, Pathology and Laboratory Medicine, UBC

OUR RESEARCH FOCUS: Radiation therapy is a cornerstone of treatment for many patients' tumours. Improving radiation and drug treatment of solid tumours is an important focus in the Department, but now our focus also includes studies into the biology and vasculature of solid tumours as well as methods of treating tumours and predicting their response to treatment.

Over the past 30 years, classical radiobiology research on new types of radiotherapy including pions has been supplanted by experiments with radiation sensitizers and hypoxic cell cytotoxins, development of probes for hypoxic cells and multilayer cultures for drug studies, characterization of low dose radiation effects and multimodality therapies. New models for tumour perfusion and chromatin conformation have been developed, as have assays for DNA damage and repair.

PROGRESS HIGHLIGHTS DURING 2004

- First data published from a translational research study in which the outcomes of patients with cervical cancer was predicted in the laboratory based on biopsies obtained during therapy¹¹

¹¹ Durand, R. E. and Aquino-Parsons, C. *Int. J. Radiat. Oncol. Biol. Phys.* 58: 555-560, 2004.

- The pivotal role of PMB-Jk signaling was elucidated in the role of new blood cell development and regulation by Notch4¹²
- A novel new 3-dimensional model was described and validated to allow determination of chemotherapeutic drug penetration into solid tumours¹³
- A marker for DNA damage and repair shown to be exploitable for rapid determination of tumour cell response to drugs and radiation, with the eventual potential of guiding and individualizing tumour therapy¹⁴.

RESEARCH KEYWORDS:

Angiogenesis, apoptosis, assays-tumour sensitivity, bioreductive cytotoxins, chromatin organization, comet assay, DNA damage, endothelial biology, experimental chemotherapy, experimental radiotherapy, flow cytometry, image cytometry, immunohistochemistry, oxygenation, radiation biology, radiobiology, radiosensitizers, radiosensitization, spheroids, stem cell differentiation, tumour biology, tumour hypoxia, tumour response assays.

TRAINING

A.) Course Instruction

A Karsan	UBC MEDG 521/PATH 531
A Karsan	UBC PHAR545
R Durand	UBC PHYS 405/436
R Durand	UBC PATH548/ONCO 502
R Durand	BCCA-Radiobiology to Radiation Oncology Residents
P Olive	UBC PHYS 405/436
P Olive	UBC PATH548/ONCO 502
P Olive	BCCA-Radiobiology to Radiation Oncology Residents
A Minchinton	UBC PHYS 405/436
A Minchinton	BCCA-Radiobiology to Radiation Oncology Residents

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
25	7	13	4	1

CURRENT STUDENTS – DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>	<i>Awards/Honours Received</i>
PhD			
K Bennewith	R Durand	2004	CIHR Studentship
B Larrivee	A Karsan	2004	HSFC Studentship
T Reistsema	P Olive	2004	
S Sobhanifar	P Olive	2004	
K Leong	A Karsan	2004	CIHR Studentship/DoD Award

¹² MacKenzie, F *et al*: *J Biol Chem* 279:11657-63, 2004 & Nosedá, M *et al*: *Mol Cell Biol* 24:8813-22, 2004.

¹³ MacKenzie, F *et al*: *Blood*, 104:1760-8, 2004.

¹⁴ Olive, P.L. *et al*: *Inter. J. Radiat. Oncol. Biol. Phys.* 58:331-335, 2004 & Olive, P.L. *et al*: *Cancer Res.* 64: 5363-5369, 2004.

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
A Kyle	A Minchinton	CIHR Doctoral Research Award
A Kyle	A Minchinton	MSFHR Trainee Award

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Aly Karsan	MSFHR Scholar Award (2001-2006)
	Heart & Stroke Foundation Visiting Scientist Award

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Ralph Durand	Member, NCIC Advisory Committee on Research
	Chair, CIHR Cancer B Panel
	Ad Hoc Reviewer, National Institutes of Health grant panel
Andrew Minchinton	Member, MSFHR Research Trainee Program Panel
	Pathology and Laboratory Medicine Graduate Awards Committee
	Canadian Breast Cancer Foundation (BC & Yukon) Grants Committee
	Canadian Breast Cancer Foundation (Ontario) Grants Committee
Peggy Olive	Vice-President Elect, International Association for Radiation Research
	Member, Panel SC15, NCRP Lunar Missions Radiation Risk Evaluation
	Organizing Committee, 8 th International Workshop on Radiation Damage to DNA
	Editorial board member: <i>Mutagenesis</i> ; <i>IJRB</i>
	Member, Canadian Association for Radiation Oncology task force on translational research
Aly Karsan	Member, NCIC Panel B
	Member, Editorial Board, Experimental Hematology
	Member, UBC MD/PhD Advisory and Admissions Committee
	External reviewer, UK-MRC, CIHR, HSFC

RESEARCH PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
21	\$2.5 M	6	\$899,143

CURRENT RESEARCH PROJECTS¹⁵

Medical Biophysics
<p>1. Angiogenesis in ischemia PI: A Karsan; Heart & Stroke Foundation; 2001-2004; For 2004 - \$95,000; Σ \$380,000 The goal is to study molecular mechanisms of neovascularization in ischemia</p>
<p>2. Applications of the comet assay in cancer biology PI: P Olive; NCIC; 2000-2005; For 2004 - \$112,623; Σ \$563,115 This project further develops the comet method as a versatile technique for measuring DNA damage in tumour and normal tissues. The ultimate goal is to understand how tumours and normal tissues respond to therapeutic interventions.</p>
<p>3. Control of cell proliferation in solid tumours and implications for therapy PI: R Durand; CIHR; 2003-2007; For 2004 - \$129,325; Σ \$567,779 This project examines tumour cell growth in patients during their treatment. The aim is to determine how many and how well each patient's tumour cells respond to therapy, which in turn provides the ability to individualize therapy and to offer timely suggestions of different treatment options for some patients.</p>
<p>4. DNA repair complexes and tumour responses to ionizing radiation PI: P Olive; NCIC; 2004-2007; For 2004 - \$149,920; Σ \$449,760 A cell's sensitivity to radiation is known to be related to its ability to repair the damage to its DNA caused by radiation. The repair of radiation-caused DNA damage is carried out by substances called repair complexes, which can be identified under a microscope. This study will investigate the possibility that the rate at which these complexes disappear after radiation treatment is related to the cell's ability to repair the damage.</p>
<p>5. Lipopolysaccharide signaling in endothelial cells PI: A Karsan; CIHR; 2003-2008; For 2004 - \$111,479; Σ \$557,395 The major goal of this project is to understand endothelial signaling in response to Toll-like receptor activation.</p>
<p>6. Maintenance support for a flow cytometry facility PI: R Durand; CIHR; 2001-2006; For 2004 - \$54,000; Σ \$270,000 This grant subsidizes flow-cytometry and cell-sorting core costs for users.</p>
<p>7. Mechanisms of ischemic neovascularization PI: A Karsan; Heart & Stroke Foundation; 2004-2009; For 2004 - \$108,470; Σ \$542,350 This project will try to determine whether Notch activation in endothelial cells plays a role in arteriogenesis by promoting endothelial transformation to smooth muscle cells.</p>

¹⁵ Key to Abbreviations: PI = Principal Investigator, Co-I = Co-investigator; CBCF = Canadian Breast Cancer Foundation, CIHR = Canadian Institutes of Health Research, MSFHR = Michael Smith Foundation for Health Research, NCIC = National Cancer Institute of Canada; Σ = total amount of project funding committed.

<p>8. Mechanisms of tumour angiogenesis PI: A Karsan; NCIC; 2003-2006; For 2004 - \$144,110; Σ \$432,330 The purpose of this grant is to understand the role of Notch signaling in tumor angiogenesis.</p>
<p>9. Micro-regional assessment of the anticancer activity of trastuzumab (Herceptin) PI: A Minchinton; CBCF; 2004-2006; For 2004 - \$96,899; Σ \$193,798 This project studies the role of extravascular penetration in the activity of Herceptin.</p>
<p>10. Micro-regional effects of pyrimidine analogues in tumours PI: A Minchinton; CIHR; 2004-2007; For 2004 - \$143,854; Σ \$431,562 This project examines the role extravascular penetration plays in the activity of pyrimidine analogues.</p>
<p>11. Molecular mechanisms of endothelial survival/apoptosis PI: A Karsan; Heart & Stroke Foundation; 2003-2006; For 2004 - \$91,176; Σ \$273,258 This project is to determine whether Notch4 can protect endothelial cells from death triggered by glucose, homocysteine and oxidized lipids.</p>
<p>12. Motuporamines as anticancer agents PI: A Minchinton; CIHR; 2004; Σ \$100,000 The grant examines the clinical usefulness of motuporamines as anticancer drugs.</p>
<p>13. Quantitation of hypoxic tumour cells PI: P Olive; CIHR; 2003-2008; For 2004 - \$104,107; Σ \$543,481 This project examines tumor hypoxia in xenografts and clinical samples using flow cytometry and fluorescence imaging with chemical and endogenous markers for hypoxia.</p>
<p>14. Tumour blood flow and response to therapy PI: R Durand; NCIC; 2002-2005; For 2004 - \$165,872; Σ \$497,617 This project aims to refine our understanding of the nature of tumour hypoxia in experimental and clinical tumours, while concurrently exploring new strategies to both define and eliminate hypoxia in the clinic.</p>
<p>15. Tumour cell environment and resistance to treatment PI: P Olive; CIHR; 2002-2005; For 2004 - \$98,359; Σ \$321,647 This project examines potential mechanisms for multicellular resistance to treatment with emphasis on intracellular calcium and cell signaling.</p>
<p>16. Tumour microenvironment: extravascular drug diffusion PI: A Minchinton; NCIC; 2001-2004; For 2004 - \$128,391; Σ \$385,174 Using complementary <i>in vivo</i> and <i>in vitro</i> techniques, this project examines the role the tumour microenvironment plays in determining the distribution and penetration of anticancer agents.</p>

Interdisciplinary				
17. Cardiovascular and respiratory stem cell plasticity				
PL: J Galipeau, Jewish Gen Hosp, Montreal; Co-I: A Karsan, P Lansdorp, P Liu, L Megeney, J Stewart; CARE/NET-CIHR, Stem Cell Network, Heart & Stroke Foundation; 2004-2009; For 2004 - \$300,000; Σ \$1,500,000 The goal of this large interdisciplinary project is to study the use of adult stem cells as repair material for damaged hearts, lungs, and blood vessels.				
18. Endothelial to mesenchymal transformation[†]				
PI: A Karsan, Co-I: P Hoodless; CIHR; 2003-2008; For 2004 - \$116,075; Σ \$580,375 The major goal of this project is to understand how the cardiac cushion develops using the process of endothelial to mesenchymal transition				
19. Evaluation of sotrasterol sulphate for use in therapeutic angiogenesis				
PIs: A Karsan, R Anderson, UBC; CIHR; 2003-2004; Σ \$98,682 The purpose of this project is to confirm the proangiogenic properties of this newly-discovered compound <i>in vivo</i> .				
20. Proteomic assessment of women being diagnosed with breast cancer				
Co-PI: K Gelmon, A. Karsan; Co-I: M Hayes, J Spinelli, D Harrison, P Switzer, P Hassell, M Stilwell; CBCF; 2003-2004; For 2004 - \$55,516; Σ \$111,1032 The purpose of this project is to identify serum biomarkers for breast cancer.				
21. Solid tumour progression research unit				
PL: C. Roskelley, UBC; Co-I: S Dedhar, R Anderson, A Karsan, A Minchinton, M Roberge; MSFHR; 2003-2007; For 2004 - \$149,914; Σ \$599,656 This research unit aims to develop and evaluate novel compounds that control or prevent solid tumour metastasis. This research will encompass the development of cell-based screening assays to identify key molecules involved in three processes underlying tumour spread: tumour cell invasion, metastatic apoptosis and endothelial cell sprouting, compound development and pre-clinical testing.				

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
14	4	216	3	0

CANADA'S MICHAEL SMITH GENOME SCIENCES CENTRE
BC CANCER RESEARCH CENTRE
Telephone: 604-675-8150

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Marco Marra	PhD Genetics	Director Associate Professor, Medical Genetics, UBC; Adjunct Professor, Molecular Biology and Biochemistry, SFU; Associate Member, Michael Smith Laboratories, UBC; Cross-appointment: Cancer Genetics & Developmental Biology
Steven Jones	PhD Genetics	Head, Bioinformatics Assistant Professor, Medical Genetics, UBC; Adjunct Professor, Molecular Biology and Biochemistry, SFU; Associate Member, Michael Smith Laboratories, UBC
Angela Brooks-Wilson	PhD Medical Genetics	Head, Cancer Genetics Assistant Professor, Medical Genetics, UBC
Isabella Tai	MD, PhD Physiology	Senior Scientist Assistant Professor, Gastroenterology, UBC; Associate Member, Vancouver Coastal Health Sciences Centre
Jacqueline Schein	MSc Genetics	Head, Mapping
Gregg Morin	PhD Biochemistry	Head, Proteomics
Robert Holt	PhD Pharmacology	Head, Sequencing Adjunct Professor, Genetics Graduate Program, UBC; Adjunct Professor, Psychiatry, University of Alberta; Assistant Professor, Psychiatry, UBC
Marianne Sadar	PhD Biochemistry	Program Leader, Prostate Cancer Research, BCCA Assistant Professor, Surgery, UBC; Associate Member, Dept of Pathology and Laboratory Medicine, UBC
Sharon Gorski	PhD Dev. Biology	Research Scientist Cross-appointment: Cancer Genetics & Developmental Biology
Asim Siddiqui	PhD Bioinformatics	Group Leader, Bioinformatics, Genome Sciences Centre
Stephane Flibotte	PhD Physics	Senior Scientist
Martin Krzywinski	MSc Physics	Scientist

OUR RESEARCH FOCUS: The primary mandates of Canada's Michael Smith Genome Sciences Centre (GSC) are to become an internationally-recognized state-of-the-art facility specializing in high-throughput genome research activities and to apply genomics and bioinformatics tools and technologies to cancer and disease research. Genome research activities include large-scale DNA sequencing, bioinformatics, whole genome mapping, gene expression assays, BAC rearrays, large-scale high-throughput transcript cloning, proteomics and technology development.

Specialized groups at the GSC focus on cancer genetics (polymorphism discovery and genotyping), programmed cell death, gastrointestinal cancers, prostate cancer, protein-protein interactions, gene expression regulation, brain disorders and mental illness, quality assurance, training, and project management.

The facility was designed specifically for flexibility and high throughput with a particular emphasis on efficiency and rapid scale-up. Research is carried out on the latest instrumentation, with data collected and analyzed on one of the most innovative and flexible bioinformatics computing facilities in the world.

PROGRESS HIGHLIGHTS DURING 2004:

- BC Biotech Alliance Innovation and Achievement Award for sequencing of the SARS coronavirus genome; March 2004
- Dr. Gregg Morin joins the Genome Sciences Centre as Head, Proteomics in April 2004
- Dr. Marianne Sadar and her team of twelve join the Genome Sciences Centre in June 2004. Her research is focused on prostate cancer therapies that will delay or prevent tumour progression and emergence of hormone independence.

RESEARCH KEYWORDS:

Apoptosis, association studies, autophagy, bioinformatics, breast cancer, *C. briggsae*, *C. elegans*, cancer susceptibility, comparative genomics, comparative genome hybridization, complex disease, DNA sequencing, *Drosophila*, gene discovery, gene expression and data analysis, gene expression profiling, gene prediction, gene regulatory control, genome mapping, genome instability, genome sequence analysis, genomics, genotyping, large-scale fingerprinting, lymphoma, pathogenomics, physical mapping, microsatellite, non-Hodgkin lymphoma cancer and aging, population-based genetics, programmed cell death, protein-protein interactions, proteomics, protein structure, psychiatric genomics, molecular cloning, retina, RNAi, cell culture, SAGE, SNP discovery, single nucleotide polymorphism, system design and analysis, software architecture, software design and construction, software development process, software project management, target validation, telomerase, telomeres, vectors of infectious disease.

TRAINING

A.) Course Instruction

A Brooks-Wilson	UBC MEDGEN 505
A Brooks-Wilson	UBC MEDGEN 520
A Brooks-Wilson	UBC MEDGEN 545
A Brooks-Wilson	UBC HCEP 511
I Tai	UBC ISCI 4481
I Tai	UBC Medicine P2P2
I Tai	UBC Program Based Learning – Liver and Biliary System
M Marra	UBC ISCI 4481 – Medical Innovation and Healthcare Politics
M Marra	UBC MEDGEN 505
R Holt	UBC MEDGEN 505
R Holt	UBC Neuroscience 501
S Jones	UBC MEDGEN 505

B.) Summary of Trainees & Awards

<i>Total No. of Current Student</i>	<i>Postdoctoral Fellow</i>	<i>Graduate Student</i>	<i>Undergraduate</i>	<i>Clinical</i>
49	11	22	14	2

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
E Pleasance	S Jones	MSFHR PhD Scholar (2002-2005), NSERC Postdoc Scholarship (2002-2004), CIHR Doctoral Award (2004-2005)
J Halaschek-Weiner	A Brooks-Wilson	Austrian Science Fund PDF Fellowship (2004-2005)
M Griffith	M Marra	MSFHR Jnr Scholar (2004-2006), NSERC Postdoc Scholarship (2004-2005), UBC Grad Entrance Scholarship (2004-2005)
O Griffith	S Jones	MSFHR MSc Scholar (2003-2005), NSERC Postdoc Scholarship (2003-2005)
P Sipahimalani	A Brooks-Wilson	UBC Grad Fellowship (2004-2005)
S Chittaranjan	M Marra	MSFHR Snr Scholar (2004-2005)
S Montgomery	S Jones	MSFHR Snr Scholar (2004-2007)
S Quayle	M Sadar	MSFHR PhD Scholar (2002-2005)

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Marco Marra	Terry Fox Young Investigator Award, NCIC
	Honorary Degree, Doctor of Science, SFU
	Career Investigator Award, MSFHR (2001-2006)
Steven Jones	Outstanding Alumni Award for Academic Achievement, SFU
	Career Investigator Award, MSFHR (2003-2005)
Isabella Tai	Faculty Scholar, Dept of Medicine, UBC (2003-2005)
	CIHR/CAG Fehring Research Fellowship (2002-2004)
Robert Holt	Member, CIHR Behavioural Sciences B Committee
	Career Investigator Award, MSFHR (2004-2006)
Caroline Astell	Voted as one of the 50 Women of the Year, Ms. Magazine
Stephen Montgomery	Best Overall Winner, BCNET Coolest Application Contest,
Obi Griffith	Voted as one of the 25 Best and the Brightest, Macleans Magazine

SELECTED CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Marco Marra	Member, Biomedical Research Trainee Evaluation Committee, (MSFHR)
	Member, College of Reviewers, Canada Research Chairs Program, (CIHR)
	Member, Genome Research Review Committee, (NHGRI)
	Canadian Scientific Representative, NHGRI International Sequencing Consortium
Steven Jones	Founding Director, CIHR/MSFHR Bioinformatics Training Program
	Director of Bioinformatics, Genome BC Bioinformatics Platform
	Member, Task Force, national Consultation on Access to Scientific Research Data (NCASRD)
	Member, International Regulome Consortium, OHRI
	Member, Committee for Development of HPC in BC, BCNET
	Member, Scientific Advisory Committee, Genome BC
Angela Brooks-Wilson	Member, 2004 CIHR New Investigators Meeting Priority and Planning Committee
	Member, CIHR Institute of Cancer Research Advisory Board
	Member, Genome BC Ethics Advisory Committee
	Member, Interlymph Collaborative Research Group and Interlymph Genetic Polymorphisms Working Group
Marianne Sadar	Lead Representative, Joint Program Committee, Vancouver Centre of Excellence for Prostate Cancer Research

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
49	\$38.1 M	17	\$10.9 M

CURRENT RESEARCH PROJECTS¹⁶

Genome Sciences
<p>1. Bioinformatics of mammalian gene expression <i>PI: S Jones; Co-I: M Marra; Genome Canada; 2002-2006;</i> <i>For 2004 - \$1,677,458; Σ \$6,709,834</i> The objective is to discover, by bioinformatics techniques, regulatory elements in mammalian genes.</p>
<p>2. Bovine genome project: Full insert cDNA sequencing plan – Competition II award <i>PI: M Marra, R Holt, S Jones, S Moore, U of Alberta;</i> <i>Genome Canada; 2004-2007; \$5,128,062 to GSC;</i> <i>For 2004 - \$2,198,574; Σ \$6,595,723</i> The sequencing of the bovine genome will help lay the groundwork for breakthroughs that will benefit both human health and agriculture. The objective is to carry out full insert - cDNA sequencing as part of NIH/USDA Bovine Genome Sequencing Project.</p>
<p>3. Bovine genome project <i>PI: S Moore, U of Alberta; Co-I: M Marra, S Jones, B Benkel;</i> <i>ASRA; 2001-2004; For 2004 - \$125,000; Σ \$500,000</i> The objective is to construct a BAC physical mapping resource to support bovine genomics.</p>
<p>4. Cancer Genomics – Genome Canada Competition I award† <i>PI: M Marra, C Eaves, V Ling; Co-I: K Humphries, S Jones, S Lam, W Lam, P Lansdorp, C MacAulay, M Rosin, M Sadar, J Vielkind]</i> <i>Genome Canada; 2001-2006; \$500,850 to GSC;</i> <i>For 2004 - \$3,348,182; Σ \$16,778,433;</i> 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>

¹⁶ Key to abbreviations: PI = Principal Investigator, Co-I = Co-investigator; ASRA = Alberta Science and Research Authority, CBCF = Canadian Breast Cancer Foundations; CIHR = Canadian Institutes of Health Research, MSFHR = Michael Smith Foundation for Health Research, NCIC = National Cancer Institute of Canada; NIH = National Institutes of Health (US), † = Inter-departmental project; Σ = total amount of project funding committed.

<p>5. Comparative and functional genomics of the human pathogen <i>Cryptococcus neoformans</i> – Genome Canada Competition II award <i>PI: J Kronstad, UBC; Co-I: R Brunham, S Jones, M Marra, C. Nelson</i> <i>Genome Canada; 2002-2005; \$1,079,279 to GSC;</i> <i>For 2004 - \$359,759; Σ \$1,917,000</i> The objective is to perform whole genome shotgun sequencing and genome annotation of the fungal pathogen <i>Cryptococcus neoformans</i>.</p>
<p>6. Cloning and characterization of <i>inx</i>s and <i>echinus</i>, two genes involved in programmed cell death in <i>Drosophila</i> <i>PI: M Marra; NSERC; 2002-2007; For 2004 - \$32,424 ; Σ \$162,120</i> The objective is to clone and characterize two genes involved in programmed cell death in the fruit fly, <i>Drosophila melanogaster</i>.</p>
<p>7. Creation of a publicly available SAGE dataset from NIH approved human ES cell lines <i>PI: C Eaves, M Marra; NIH/NCI/SAIC; 2003-2005;</i> <i>For 2004 - US\$110,000; Σ \$330,000 USD</i> The objective is to construct and analyze 11 SAGE libraries from NIH approved human embryonic stem cell lines, and to make the SAGE dataset publicly available via the internet.</p>
<p>8. Development of a mass spectrometry-based method of full-length sequencing of proteins <i>PI: J Kast; Co-I: S Jones; CIHR; 2003-2006; \$54,000 to GSC;</i> <i>For 2004 - \$94,462; Σ \$283,386</i> The study will develop a novel method to determine the individual state of each protein in high throughput, combining the expertise of two groups working on the analysis of the genome and the proteome.</p>
<p>9. Development of a potential new therapy for androgen independent prostate cancer <i>PI: M Sadar; Health Canada; 2001-2006; For 2004 - \$100,000; Σ \$500,000</i> The aim of this proposal is to determine if the expression of a specific modified protein (ARn) within prostate cancer cells is able to inhibit tumour growth and prevent the progression of the tumour to androgen (testosterone) independence.</p>
<p>10. Development of ESP for structural and functional oncogenomics <i>PI: C Collins; Co-I: M Marra;</i> <i>NIH/NHGRI; 2004-2007; For 2004 \$0; Σ \$1,877,096</i> The objective is to develop end sequence profiling (ESP) to determine the structural organization of tumours.</p>
<p>11. Discovery of new drug candidates for the prevention of hormone refractory prostate cancer <i>PI: M Sadar; Co-I: R Anderson;</i> <i>US Army, Dept of Defense Prostate Cancer Research Program; 2004-2007;</i> <i>For 2004 - \$162,000; Σ \$486,000 USD</i> The objective is to discover new drug candidates for the prevention of hormone refractory prostate cancer</p>
<p>12. Dissecting chemotherapy resistance in colorectal cancer using a genome-wide approach <i>PI: I Tai; Canadian Society for Intestinal Research; 2003-2005;</i> <i>For 2004: \$25,000; Σ \$85,000</i> The objective is to identify genetic markers of chemotherapy resistance from colorectal cancer.</p>

<p>13. Expression profiles of cells and tissues in <i>C. elegans</i> – Genome Canada Competition II award <i>PL: D Baillie; Co-I: M Marra, D Moerman, S Jones, F Ouellette, C Wahlestedt, E Sonnhhammer, R Olafson, A Vas Gomes and T Burglin</i> <i>Genome Canada; 2002-2006; \$706,426 to GSC;</i> <i>For 2004 - \$750,000; Σ \$3,000,000</i> The goal is to examine the <i>C. elegans</i>, a soil nematode, after identifying genes that are similar in both humans and worms. By discovering the function of the genes in worms and their expression, the study hopes to understand the equivalent gene functions in humans. This work will in turn help understand not only genetic defects involving the malfunction of a single gene, but also the way in which genes and their products interact with developing cells, tissues and organs.</p>
<p>14. Genes with major effects on life span in <i>C. elegans</i> <i>PIs: D Riddle, Co-I: M Marra; MNH/NIA; 2000-2005;</i> <i>For 2004 - \$106,500; Σ \$532,500</i> The objective is to construct, sequence and analyze SAGE libraries from long-lived <i>C. elegans</i> mutants.</p>
<p>15. Genetic variation in isoniazid metabolism genes: Effect on and use for prediction of Hepatotoxicity <i>PIs: A Brooks-Wilson, F Marra; Co-I: V Cook, K Elwood, M Fitzgerald</i> <i>BC Lung Association; 2004-2006; For 2004 - \$ 22,500; Σ \$45,000</i> The objective is to determine response rate of isoniazid-treated patients and controls, to determine the spectrum of genetic variation in CES1 and CES2 patients with severe hepatotoxicity and estimate allele frequencies for genetic variants in NAT2, CES1 and CES2 in TB-relevant population groups in Vancouver.</p>
<p>16. Genome British Columbia Bioinformatics platform – Genome Canada Competition I & II awards <i>PI: S Jones; Genome British Columbia / Genome Canada; 2001-2006;</i> <i>For 2004 - \$1,759,011; Σ \$8,795,055</i> The objective is to provide bioinformatics related to high-throughput DNA sequencing and DNA mapping including technical advice, support and capacity.</p>
<p>17. Genome British Columbia Sequencing and Mapping platform – Genome Canada Competition I and II, Applied Health & other awards <i>PI: M Marra; Genome Canada; 2001-2007;</i> <i>For 2004 - \$6,065,119; Σ \$24,260,478</i> The objective is to provide high-throughput DNA sequencing and DNA mapping including technical advice, support and capacity.</p>
<p>18. Genome wide analysis reveals a novel gene involved in chemotherapy resistance in colorectal cancers <i>PI: I Tai; CDHF/CAG; 2004-2006; For 2004 - \$60,000; Σ \$120,000</i> The major goal of this project is to examine the role of a novel gene with a potential to contribute to chemotherapy resistance.</p>
<p>19. Genomic and proteomic analysis of androgen independent prostate cancer <i>PI: M Sadar; Co-I: M Marra, S Jones, YZ Wang, R Holt, K Meehan;</i> <i>NIH; 2004-2009; \$455,000 to GSC; For 2004 - \$266,500; Σ \$1,332,500</i> The goal is to develop an in vivo model using hollow fibers to retrieve uncontaminated packages of prostate cancer cells (tumours) that can be used for subsequent molecular biology analyses of the progression of prostate cancer to androgen independence.</p>

<p>20. Full length cDNA sequencing MGC Project <i>PI: M Marra; NIH/NCI/SAIC; 2000-2004; For 2004 - \$2,041,603; Σ \$6,124,809</i> The GSC will conduct full-length cDNA sequencing and targetted clone recovery.</p>
<p>21. Improvements in BAC fingerprinting and end sequencing <i>PI: M Marra; Co-I: S Flibotte, D Fuhrmann, S Jones, M Krzywinski, A Marziali and J Schien</i> <i>NIH/NHGRI; 2003-2006; For 2004 - \$1,987,019; Σ \$5,961,059</i> The objective is to undertake the development and implementation of both laboratory and bioinformatics' procedures to enhance the efficiency and reduce the costs of BAC fingerprint mapping and BAC end sequencing.</p>
<p>22. Innovative approaches to cancer susceptibility <i>PI: A Brooks-Wilson;</i> <i>CFI/BC Knowledge Development Fund; 2003-2004; Σ \$299,166</i> The objective is to put in place a large-scale, high-throughput variant detection and genotyping capability to support Dr. Brooks-Wilson in establishing an independent cancer genetics program.</p>
<p>23. Large scale genome sequencing/validation and improvement of whole genome assemblies <i>PI: R. Wilson; Co-I: S. Jones; NIH; 2003-2006;</i> <i>For 2004 - \$141,065; Σ \$423,197</i> The major goals of this project are for the GSC to verify the sequence of human and mouse and to validate and improve the whole genome assemblies.</p>
<p>24. Mammalian gene collection <i>PI: M Marra; NCI-FCRDC/SAIC; 2004-2007;</i> <i>For 2004 - US\$1,857,478; Σ US\$5,572,434</i> The objective is to support efforts to acquire clones representing human and mouse genes missing from the Mammalian Gene Collection project.</p>
<p>25. Molecular characterization of autophagic cell death <i>Co-PI: G Morin, S Gorski; NCIC; 2004-2008; For 2004 - \$129,016; Σ \$374,927</i> The objective is to identify genes and pathways involved in the autophagic cell death process.</p>
<p>26. Novel genomic approach to studying DNA copy number variation in schizophrenia and bipolar disorder <i>Co-PI: R Holt, W Honer; CIHR; 2004-2006; For 2004 - \$9,657; Σ \$94,087</i> The objective of this study is to investigate abnormalities in DNA copy number in schizophrenia and bipolar disorder using array comparative genome hybridization.</p>
<p>27. Quantitative and comprehensive atlas of gene expression in mouse development – Genome Canada Competition II award <i>PL: P Hoodless & M Marra; Co-I: R Strausberg, E Simpson, G Riggins, S Jones, C. Helgason; Genome Canada; 2002-2006; \$4,578,549 to GSC;</i> <i>For 2004 - \$3,298,881; Σ \$13,195,524</i> In an effort to thoroughly understand the genes that regulate mouse development, this project aims to develop an "atlas" of genes which are expressed at various stages of mouse development in different types of tissue. Since disease may result from a failure in the regulation of genes, an understanding of how gene expression is controlled in mice will provide an important insight into the disease process in humans.</p>

<p>28. Role of autophagy in breast cancer <i>PI: S Gorski; US Department of Defense; 2005-2006; Σ \$100,419 USD</i> Our main objectives are to test the concepts that alterations in the autophagy process are related to the causation and/or progression of human breast cancer, or a breast cancer subtype, and that modulation of autophagy can affect the efficacy of breast cancer treatments.</p>
<p>29. SAGE sequencing of mouse genome to develop an atlas of gene expression <i>PI: M Marra; NCI/SAIC; 2003-2006; For 2004 - \$433,333; Σ \$1,300,000</i> The goal is to carry out SAGE gene expression profiling of tissues selected from time points throughout mouse development.</p>
<p>30. Sequencing the mouse genome (Xenopus full-length cDNA sequencing) <i>PI: R Wilson; Co-I: M Marra; NIH/NHGRI; 2003-2004; Σ \$1,040,000</i> The GSC will conduct full-length cDNA sequencing in support of the Xenopus Full-length Sequencing Project.</p>
<p>Interdisciplinary</p>
<p>31. Bioinformatics training for health research <i>PI: S Jones; Co-I: D Baillie, P Heiter, F Brinkman, J Bryan, A Condon, A Gupta, F Ouellette, F Pio; CIHR; 2002-2008; For 2004 - \$306,854; Σ \$1,841,125</i> The objective is to train bioinformatics' graduate students and post-doctoral fellows.</p>
<p>32. Bioinformatics training program supplementary award <i>PI: S Jones; Co-I: D Baillie, P Heiter, F Brinkman, J Bryan, A Condon, A Gupta, F Ouellette, F Pio; MSFHR; 2002-2006; For 2004 - \$75,000; Σ \$300,000</i> The objective is to train bioinformatics' graduate students and post-doctoral fellows.</p>
<p>33. Canadian longitudinal study of aging: Developmental activities phase I <i>PIs: S Kirkland, P Raina, C Wolfson, Lady Davis Inst for Med Res (Montreal); Co-I: A Brooks-Wilson and 141 others; CIHR; 2004-2005; For 2004: \$974,000; Σ \$1,744,000</i> The objective is to collect data on the process of aging, through longitudinal studies.</p>
<p>34. Double stranded break surveillance genes and susceptibility to non-Hodgkin lymphoma <i>PI: A Brooks-Wilson; Co-I: J Connors, R Gascoyne, J Spinelli; NCIC; 2004-2007; For 2004: \$149,531; Σ \$444,593</i> This project will perform haplotype-based association studies in a case/control collection of hundreds of blood DNA samples from NHL patients and hundreds from controls, to determine whether genetic variation in any of the six key DNA repair genes affects susceptibility to NHL. The identification of genetic factors that predispose to NHL will be useful in the development of panels of diagnostic tests to help identify individuals at-risk for this cancer.</p>
<p>35. Genomics, Genetics & Gerontology (G3): A multidisciplinary team for the study of healthy aging <i>PI: M Marra, A Brooks-Wilson; Co-I: S Jones, N Le, J Connors, G Meneilly; CIHR; 2003-2008; For 2004 - \$231,969; Σ \$1,159,844</i> This project will study genetic factors that underlie healthy aging and resistance to common age-related diseases such as cancer, cardiovascular disease and pulmonary disease. Genetic variants found to be associated with healthy aging, or associated with the protection against specific common age-related diseases will be useful as prognostics in the tailoring of individual disease prevention programs.</p>

<p>36. Genomic tools for diagnosis and evaluation of mental retardation <i>PI: J Friedman, M Marra; Co-I: R Holt, J Schein, S Jones and others;</i> <i>Genome Canada; 2004-2007; Σ \$885,460 to GSC;</i> <i>For 2004: \$855,760; Σ \$5,558,297</i> The goals is to develop an alternative to karyotyping to identify chromosomal abnormalities in people with mental retardation. The project will evaluate a new testing method to identify chromosome abnormalities 100 times smaller than those detectable by karyotyping.</p>
<p>37. Identifying new genes causing spinocerebellar ataxias with an integrated clinical, molecular genetic and bioinformatics approach <i>PI: B. Leavitt; Co-I: R Holt, F. Ouellette, B. Casey</i> <i>National Organization for Rare Disorders; 2004-2005; Σ US\$39,991</i> The long term goal is to improve the care for people with hereditary forms of spinocerebellar ataxias.</p>
<p>38. Molecular epidemiology of breast cancer <i>PI: K Aronson, Queen's U; Co-I: P Ayotte, C Bajdik, A Brooks-Wilson, C Lohrisch, H Richardson, S Sengupta, J Spinelli;</i> <i>CIHR; 2004-2009; For 2004: \$248,997; Σ \$1,244,988</i> The goal of this study is to determine if breast cancer risk is associated with PAH and light at night exposures, genetic factors, and the interaction between genetic and environmental factors, and to determine if breast cancer risk is different according to the type of breast cancer.</p>
<p>39. Occupational risk identification for ovarian cancer <i>PI: N Le; Co-I: C Bajdik, A Brooks-Wilson, J Spinelli, R Gallagher, P Demers</i> <i>WCB; 2004-2005; Σ \$112,505</i> The purpose of this research is to identify potential carcinogens in the BC work environment for ovarian cancer.</p>
<p>40. Occupational oncology research program <i>PI: N. Le; Co-I: A. Brooks-Wilson, J Spinelli, R Gallagher, P Demers, C Bajdik;</i> <i>WCB; 2002-2004; For 2004 - \$204,450; Σ \$408,900</i> The major goals of this project are to provide data on occupational cancer relevant to the specific industrial and occupational context of BC, and to identify occupational cancer risk factors and potential carcinogens in the workplace with the overall objective of reducing risk.</p>
<p>41. Optical systems for in vivo molecular imaging of cancer <i>PL: R Richards-Kortum, Rice University; Co-I K Adler-Storthz, S Jones, S Lam, C MacAulay, M Marra, W Lam, P Lansdorp, et al</i> <i>NIH; 2004-2009; \$172,900 to GSC; For 2004 - \$2,074,000; Σ \$10,370,000</i> The goal of this project is to integrate development of optical imaging systems and contrast agents with advances in functional genomics. We will develop molecular-specific, optically active contrast agents that can be applied topically. We will also develop inexpensive, rugged and portable imaging systems to monitor the three-dimensional profile of targeted biomarkers. These contrast agents and imaging systems will have broad applicability to many types of cancer; here, we will develop and test agents and imaging systems for the cervix, oral cavity and the lung tumors.</p>

<p>42. Organochlorines (OC), ultraviolet radiation (UVR) and gene-environment (G/E) interactions in non-Hodgkin's lymphoma (NHL) <i>PI: J Spinelli; Co-I: A Brooks-Wilson, N Le, J Connors, R Gallagher, JP Weber, R Gascoyne;</i> <i>NCIC; 2003-2006; For 2004: \$189,222; Σ \$563,333</i> The major goals of this project are: to determine whether exposure to organochlorine compounds and the degree of ultraviolet radiation exposure, or a combination of genetic and environmental factors are related to the risk of NHL.</p>
<p>43. Prevalence of human papillomavirus in British Columbia <i>Co-PI: A Brooks-Wilson, G Ogilvie; Co-I: J Maticic, R Moore, J Lo and L St. Germain]</i> <i>Merck Frosst Canada Ltd; 2004-2006; For 2004: \$99,000; Σ \$198,548</i> This study will determine the prevalence of individual types of Human Papillomavirus in British Columbia and will be useful for the optimization of vaccine programs in the province.</p>
<p>44. Proteomics associated with the progression of prostate cancer to androgen independence <i>PI: M Sadar, J. Vielkind; Health Canada; 2001-2006;</i> <i>For 2004 - \$100,000; Σ \$500,000</i> SELDI-TOF-MS and 2D PAGE analysis of the proteome of prostate cancer cells during progression to androgen independence.</p>
<p>45. SARS: A scientific collaborative to support public health response through vaccination <i>PL: D Skowronski; Co-I: R Brunham, D Patrick, T Booth, D Scheifele, M Petric, B Pourboholoul, C Astell, L Babiuk, Y Av-Gay, W Bowie, M Krajden, S Jones, M Marra, M Naus, V Remple, J Russell, C Richardson, R Tellier, R Meyesers, A McGeer, T Tam and . Drebot; CIHR: 2003-2004; Σ \$500,000</i> The major goal is to develop vaccine candidates for testing in Phase One human trials.</p>
<p>46. SAVI (SARS Accelerated Vaccine Initiative) <i>PL: B Finlay, R Brunham; Co-I: M Marra, C Astell et al;</i> <i>BC Government/MSFHR; 2003-2004; For 2004 - \$1,300,000; Σ \$2,600,000</i> The major goal is to develop vaccine candidates for testing in Phase One human trials.</p>
<p>47. Sun exposure, vitamin D and prostate cancer <i>PI: R. Gallagher; Co-I: A. Brooks-Wilson, J Spinelli, M Borugian, M Pollack, G. Chambers; CIHR; 2003-2006; For 2004 - \$163,636; Σ \$490,908</i> This project will determine whether there is an inverse relationship between ultraviolet radiation exposure and risk of prostate cancer and whether there is evidence of a dose-response relationship between exposure and risk.</p>
<p>48. Vancouver Centre of Excellence in prostate cancer research <i>Co-PI: M Sadar; L Goldenberg, Prostate Centre, VGH;</i> <i>Health Canada; 1999-2004; \$1,500,000 to BCCA;</i> <i>For 2004 - \$1,000,000; Σ \$5,000,000</i> The goal of this project is to study the proteomics of early development of prostate cancer using Ciphergen's SELDI Protein Chip technology.</p>

International
<p>49. Genomics approach to the identification of the genetic and environmental components underlying berry quality in grapevine: GRAPEgen</p> <p><i>PLs: S Lund, JM Martinez-Zapater; Collaborators: M Marra, S Jones, R Olafson, P Bowen, J Bohlmann;</i></p> <p><i>Genome Spain/Genome Canada; 2004-2007; \$890,195 to GSC;</i></p> <p><i>For 2004 - \$1,044,827; Σ \$3,134,481</i></p> <p>The aims of this study is to understand how genes control berry ripening in different growing environments and to develop new varieties through breeding programs that exploit the natural variation inherent in Vitis.</p>

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
26	9	39	152	7

TERRY FOX LABORATORY
BC CANCER RESEARCH CENTRE
Telephone: 604-675-8125

<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Allen Eaves	MD, PhD, FRCPC, FACP	Director, Terry Fox Laboratory Professor, Medicine, UBC; Professor, Pathology and Laboratory Medicine, UBC
Ryan Brinkman	PhD Genetics	Senior Scientist Assistant Professor, Medical Genetics, UBC
Connie Eaves	PhD Immunology	Deputy Director & Senior Scientist Professor, Medical Genetics, UBC
Donna Hogge	MD, PhD Exp. Pathology, FRCPC	Senior Scientist
Pamela Hoodless	PhD Biochemistry	Clinical Prof., Hematology, UBC Senior Scientist Assistant Professor, Medical Genetics, UBC; Assistant Professor, Genetics, UBC
Keith Humphries	MD, PhD Medical Genetics	Senior Scientist
Robert Kay	PhD Biochemistry	Professor, Medicine, UBC Senior Scientist
Gerald Krystal	PhD Protein Chemistry	Professor, Medical Genetics, UBC Senior Scientist Professor, Pathology and Laboratory Medicine, UBC
Peter Lansdorp	MD, PhD Exp. Hematology	Senior Scientist
Dixie Mager	PhD Med. Biophysics	Professor, Medicine, UBC Senior Scientist
Clayton Smith	MD, FRCPC	Professor, Medical Genetics, UBC Senior Scientist Clinical Associate Professor, Medicine, UBC; Director, Leukemia/Bone Marrow Transplantation Program of BC
Fumio Takei	PhD Immunology	Senior Scientist Professor, Pathology and Laboratory Medicine, UBC
Xiaoyan Jiang	MD, PhD Mol. Biology	Research Scientist Assistant Professor, Medical Genetics, UBC
Andrew Weng	MD, PhD Mol Genetics and Cell Biology	Senior Scientist Clinical Scientist, Pathology, BCCA; Asst. Professor, Pathology & Laboratory Medicine, UBC

OUR RESEARCH FOCUS: The Terry Fox Laboratory (TFL) was created in 1981 as a joint undertaking between the British Columbia Cancer Agency, the B.C. Cancer Foundation, the University of British Columbia and the National Cancer Institute of Canada. Since 1981, TFL has grown to over 140 researchers, including 67 students and postdoctoral fellows. TFL researchers enjoy a unique interactive relationship with the clinical staff of the BCCA and the Vancouver Hospital and Health Sciences Centre (VHHSC). This makes possible ready access to an enormous variety of human material on a daily basis for fundamental experimentation and investigation, and provides novel opportunities for the rapid movement of new methodology from bench to bedside.

The current emphasis of the TFL is on the development of new technologies and their use to address fundamental questions in the control of cell growth and differentiation, aging, and gene regulation with particular focus on hematology/oncology.

A range of state-of-the-art equipment and facilities exist to support the research of TFL and its collaborators. In no particular order these include:

- facilities for recombinant DNA technology and DNA sequencing
- preparation and isolation of monoclonal antibodies
- expression of recombinant proteins
- protein purification and characterization
- light and fluorescence microscopy
- cytogenetic analysis and a specialized media preparation service
- transgenic and gene targeting facility
- flow cytometry core facility, and
- Level 3 biohazard containment facility

PROGRESS HIGHLIGHTS DURING 2004

- A discovery that a protein called E2F4 plays a critical role in the early development of B-cell lymphocytes was reported. The discovery may turn out to be important in understanding how cell proliferation and development is coordinated and aid efforts to increase the number bone marrow stem cells available for transplantation.
- A discovery that the protein SHIP also ensures that macrophages in the body's immune system do not overact to inflammation-inducing conditions, in response to bacterial and viral attacks. This knowledge could play an important role in developing strategies to treat allergies, auto-immune disorders and to control septic shock in hospital patients.
- A discovery of a gene *Rtel*, which appears to be essential in preventing genetic instability caused by the loss of the length of telomeres at the ends of chromosomes which is a natural effect of aging cells.

RESEARCH KEYWORDS:

Bone marrow transplantation, breast cancer stem cells, cell adhesion molecules, developmental biology, embryogenesis, image analysis in biological sciences, leukemia, mutagenesis, myeloproliferative and myelodysplastic syndromes, gene therapy, gene transfer, hematology, hematopoietic stem cells, human endogenous retroviruses, human leukemia hematopoiesis, mammalian genome structure and evolution, natural killer cells, normal and leukemic stem cell biology, quantitative fluorescence in situ hybridization techniques, signal transduction, transgenic mice, telomere biology, recombinant proteins.

TRAINING**A.) Course Instruction**

D Hogge UBC Medicine II: Blood & Lymphatics
 D Hogge UBC Pathology 548R
 P Hoodless UBC MEDG 545
 P Hoodless UBC MEDG 521
 K Humphries UBC Pathology 500
 R Kay UBC MEDG 545
 D Mager UBC MEDG 545
 D Mager UBC MEDG 420
 D Mager UBC MEDG 530
 F Takei UBC Oncology 502

B.) Summary of Trainees and Degrees Completed

<i>Total No. of Current Student</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
100	23	33	42	2

CURRENT STUDENTS – DEGREES COMPLETED

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>
PhD		
J Rupert	P Hoodless	2004
B Guilbault	R Kay	2004
R Marwali	F Takei	2004

TRAINEE AWARDS

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Afshin Raouf	C Eaves	CIHR Fellowship
Andrea Tegzes	C Eaves	NSERC Industrial Scholarship (2004-2006)
Andrew Muranyi	D Hogge	UGF Fellowship, UBC Graduate Fellowship (2004-2005)
Arefeh Rouhi	D Mager	NSERC & MSFHR Master's Trainee Award (2003-2005)
Bob Argiropoulos	K Humphries	Leukemia Research Fund Fellowship Award (2004-2006)
Bradford Dykstra	C Eaves	NCIC TFF Research Studentship (2003-2007)

David Kent	C Eaves/ M Marra	Stem Cell Network Graduate Studentship (2004-2005)
Frann Antignano	G Krystal	NSERC Studentship & M SFHR Junior Graduate Studentship (2004-2006)
Hideaki Ohta	Alumni	University of Osaka Fellowship (2001-2004)
Iris Cheung	P Lansdorp, A Rose	CIHR Canada graduate scholarship-doctoral award (2003-2006), MSFHR Doctoral Award (2004-2005)
Koichi Hirose	Alumni	MSFHR Fellowship (2003-2006)
Kristen McKnight	P Hoodless	NSERC Fellowship (2004-2007)
K Lucke	C Eaves	German Government Fellowship (2004-2006)
Linnea Veinotte	F Takei	MSFHR Senior Graduate Studentship (2001-2003)
Lisa Dreolini	F Takei	NSERC Studentship (2003-2005)
Louie N Van de Lagemaat	D Mager	CIHR doctoral award (2004-2007)
Mark Romanish	D Mager	Edward Squires Memorial Scholarship (2004-2005)
Matthew Greenwood	Alumni	Stem Cell Network Graduate Studentship (2003-2005)
Melanie Kardel	C Eaves	NSERC Studentship (2003-2005)
Michael Rauh	G Krystal, AW Chow	CIHR MD/PhD Program Studentship (2000-2007)
Michelle Bowie	C Eaves	CIHR & Stem Cell Network Studentship (2003-2005)
Motoi Maeda	Alumni	MSFHR Postdoctoral Fellowship (2003-2006)
Pavie Vrljicak	P Hoodless	UGF Graduate Fellowship (2004-2005)
Peter Eirew	C Eaves	Stem Cell Network Graduate Studentship
Sean Kennedy	C Eaves	NSERC Studentship (2003-2005)
Yun Zhao	Postdoc	Leukemia Research Fund Fellowship (2004-2006)

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
Clayton Smith	MSFHR Senior Scholar Award (2003-2008)
	Canada Research Chair Award
Connie Eaves	Robert L. Noble Prize Award for Excellence (2003-2004)
Pamela Hoodless	MSFHR Scholar and Incentive Award (2001-2006)
	CIHR New Investigator Scholar Award (2002-2007)

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
Allen Eaves	Chairman of MITACS Board of Directors
	President of Stemcell Group of Companies
Connie Eaves	Chairman and Supervisor, Management Committee of the Joint Animal Facility, BCCA
	Member, Faculty of Medicine Nominating Committee, UBC
	Member, Canada Research Chairs Internal Review Committee
	Member, Advisory Committee for the UBC Life Sciences Institute
	Chair and Member, International Society for Experimental Hematology Awards Committee
	Associate Scientific Director and Member of the Board of the Stem Cell Network
	Member, Clinical Trials Network Committee of the Canadian Bone Marrow Transplant Group
	Delegate, Leaders' Forum for Health Research in Canada, MSFHR, Ottawa, ON, Set 29-30
Keith Humphries	Chair, Canadian Council of American Society for Gene Therapy
	Vice-President, International Society for Experimental Hematology
	Director, Transgenic and Gene Targeting Facility, BCCA
	Member, NCI-USA Program Project Review Team, Jan 2004
	Member, National Heart, Lung and Blood Institute Program Project Review Committee, May 2004
	Member, National Heart, Lung and Blood Institute Special Emphasis Committee Panel, Dec 2004
	Member, Leukemia Research Fund of Canada Scientific Review Panel
	Member, SCOR Grant Panel of the Leukemia and Lymphoma Society of America
Robert Kay	Member, Medical Genetics Graduate Program Advisory Committee
	Member, Genetics Graduate Program Advisory Committee
Gerald Krystal	Organizer, 12 th International Conference on Second Messengers and Phosphoproteins, Montreal, August 2004
Peter Lansdorp	Director, Cryogenic Lab, Terry Fox Laboratory, BCCA
	Member, ASH Scientific Committee on Stem Cells
	Invited Advisory Board Member, International Society of Stem Cell Research (ISSCR)
	Special Emphasis Panel, National Heart, Lung and Blood Institute, Washington DC
Dixie Mager	Member, Radiation Safety Committee, BCCA
Fumio Takei	Member, Grant Panel A, Immunology, NCIC
	Member, Scientific Advisory Committee, 12 th International Congress of Immunology
Clayton Smith	Director, Leukemia/Bone Marrow Transplant Program of BC, BCCA
Xiaoyan Jiang	Adjunct Professor, Shanghai Institute of Medical Genetics, School of Medicine, Shanghai Jiaotong University

MAJOR PROJECTS & PROGRAMS (NEW PROJECTS MARKED WITH ASTERISK)

<i>No. of Active Research Projects</i>	<i>Annual Value of Research Projects</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value of New Research Projects</i>
43	\$9.0 M	9	\$1.9 M

CURRENT RESEARCH PROJECTS¹⁷

Terry Fox Laboratory			
1. Analysis of mammalian natural killer cell receptor genes	<i>PI: D Mager; CIHR; 2001-2004; For 2004 - \$40,214; Σ \$120,642</i> The long term aim of this research is to understand the functions and molecular evolution of genes encoding mammalian natural killer cell receptors.		
2. Activation and proliferation of purified hemopoietic stem cells	<i>PI: P Lansdorp; NIH; 2002-2005; For 2004 - USD \$198,586; Σ \$595,758</i> This project will propose to further examine the role of telomerase and telomeres in hematopoiesis. This project will test the hypothesis that replication history of hematopoietic stem cells is traceable by examining telomere length.		
3. Disease mechanisms in chronic myeloid lymphoma (CML)	<i>PI: A Eaves; Co-PIs: C Eaves and X Jiang; NCIC; 2003-2006; For 2004 - \$150,000; Σ \$454,250</i> This grant will study CML stem cells, since controlling or destroying these cells is necessary if CML is to be cured. The grant will look at how the speed of CML cell multiplication is controlled; what properties of these cells cause leukemia to develop or a relapse to occur; and whether new drugs developed from their results can be effectively tested.		
4. Dependence of stem cell self-renewal on cultural variables	<i>PI: C Eaves; Stem Cell Network; 2003-2005; For 2004 - \$161,800; Σ \$323,600</i> The goal of this project is to study how varying the environment under which cells are grown will change the expression of different genes to better control stem cell growth and differentiation.		
5. Effects of retroelements on mammalian genes	<i>PI: D Mager; CIHR; 1999-2010; For 2004 - \$85,785; Σ \$943,636</i> The goal of this research is to understand how mobile genetic elements ("jumping DNA") in human and mouse genomes affect gene regulation and genome rearrangement processes. This project will also examine the role that mobile elements may play in determining the qualities that distinguish humans from our closest relative, the chimpanzee.		
6. Gene therapy for sickle cell anemia and β-thalassemia (Gene transfer and stem cell biology in sickle cell disease and supplement)	<i>Co-PI: C Eaves and K Humphries; NHLBI/NIH; 2000-2005; For 2004 - US\$43,727; Σ US\$218,636</i> The objective is the successful preclinical development of a strategy and procedure will achieve effective gene therapy for sickle cell disease (SCD). The project's ultimate objective is the complete and sustained reconstitution of the bone marrow of SCD patients.		

¹⁷ Key to Abbreviations: PI = Principal Investigator, Co-I = Co-Investigator, CBCF = Canadian Breast Cancer Foundation, CIHR = Canadian Institutes of Health Research, MSFHR = Michael Smith Foundation for Health Research, NCIC = National Cancer Institute of Canada; Σ = total amount of project funding committed.

<p>7. The function of activin-like signaling in early mouse development: determination of the anterior primitive streak and node <i>PI: P Hoodless; NCIC; 2001-2005; \$120,138 to P Hoodless; Σ \$360,414</i> The goal of this study is to gain new insights into the function of molecular signaling pathways, especially activin-like proteins, involved in early mammalian development at a stage when the cells of the embryo start to differentiate into the head and the body.</p>
<p>8. Flow cytometry high throughput screening of the hematopoietic system of transgenic mice <i>PI: C Smith; NIH; 2000-2004; For 2004 - \$375,000; Σ \$1,500,000</i> This project supports the rapid characterization and sorting of different cell types of the blood system in mouse models.</p>
<p>9. HOXB4 target-genes specifying hematopoietic stem cell renewal <i>PI: K Humphries; Stem Cell Network; 2003-2005; For 2004 - \$198,423; Σ \$396,846</i> This project will determine the target genes of specific transcription factoris in rare cell types with the goal of identifying key transcript subsets that correlate with enhanced HSC self-renewal capacity.</p>
<p>10. Mechanisms and functions of activin/nodal signaling in early mouse embryogenesis <i>PI: P Hoodless; MSFHR; 2001-2004; For 2004 - \$62,500; Σ \$187,500</i> This grant will support the set-up of Dr. Hoodless' laboratory as a MSFHR scholar.</p>
<p>11. Molecular characterization of a novel gene (Ahi-1) in normal and leukemic hematopoiesis <i>PI: X Jiang; NCIC; 2004-2006; \$?</i> The overall goal of this project is to understand the molecular mechanisms of aberrant gene regulation and function that contribute to the development of human leukemia. This investigation will focus on characterizing normal functions and potential leukemogenic activities of a new candidate oncogene; Ahi1 (Abelson helper integration site 1) that was recently identified. The long term goal is to elucidate how NK cells differentiate from their progenitors and mature into functional NK cells.</p>
<p>12. Manipulation of proliferative abnormalities in acute myeloid leukemia (AML) stem cells <i>PI: D Hogge; Cancer Research Society Inc.; 2003-2005; For 2004 - \$57,000; Σ \$114,000</i> The overall goal of this project is to further characterize the molecular basis for proliferative abnormalities in AML cells in order to facilitate the identification of targets for novel therapeutic agents.</p>
<p>13. Molecular biology of the initiation of T-cell transformation by RasGRP1 and Ras GTPases <i>PI: R Kay; Cancer Research Society, Inc; 2004-2006; For 2004 - \$60,000; Σ \$120,000</i> This project will use a murine model to investigate mechanistic links between normal and malignant development of T-cells and to identify activating mutations in Ras GTPases that frequently occur in T-cell acute lymphoblastic leukemia</p>

<p>14. NK cell differentiation <i>PI: F Takei; CIHR; 2003-2007; For 2004 - \$128,027; Σ \$320,068</i> The goal of this study is to compare a generation of NK cells from primitive blood forming cell sin newborn mice and adult mice and find out why this process takes a long time. The long term goal is to elucidate how NK cells differentiate from their progenitors and mature into functional NK cells.</p>
<p>15. Optimization of the use of diphtheria toxin-growth factor fusion proteins for the treatment of acute leukemia <i>PI: D Hogge; CIHR; 2004-2006; For 2004 - \$34,377; Σ \$68,754</i> This proposal will study the level of expression of the target receptors on different leukemia samples and the proliferative activity the leukemia cells from these samples to determine if these features will predict response to the DT-GF molecules. The grant will also determine if combining the DT-GF molecule with another drug which targets leukemia cells will be more effective than either drug alone.</p>
<p>16. A phase I study of DT388IL3 fusion protein inpatients with relapsed and refractory acute myeloid leukemia <i>PI: D Hogge; Leukemia Research Fund of Canada; 2004-2006; For 2004 - \$43,500; Σ \$87,000</i> The goal of this study is to assess dosage and toxicity of a sterilized recombinant diphtheria fusion protein – DT388IL3 – in a clinical trial of patients with acute myeloid leukemia.</p>
<p>17. Regulation of cell adhesion mediated by LFA-1 and ICAMS <i>PI: F Takei; CIHR; 2001-2005; For 2004 - \$47,612; Σ \$529,085</i> The goal of this study is to understand how a protein called LFA-1 involved in cell-cell binding acts to initiate the cascade of events to guide 'killer lymphocyte' cells of the immune system to attack diseased cells.</p>
<p>18. The role of novel oncogene (Ahi-1) in the development of leukemia <i>PI: X Jiang; Cancer Research Society; 2003-2005; For 2004 - \$60,000; Σ \$120,000</i> The overall goal of this research program is to understand the molecular mechanisms of aberrant gene regulation and function that contribute to the development of human leukemia ultimately, leading to the development of more effective, molecularly targeted therapies.</p>
<p>19. Regulation of natural killer cell receptor genes <i>PI: D Mager; CIHR; 2004-2010; For 2004 - \$100,926; Σ \$605,561</i> Our goal is to elucidate the mechanisms that generate functional diversity of NK cells – the white blood cells considered to be the first line of immune defense against virus-infected and cancer cells. Specifically the receptors that recognize MHC class-I molecules, and to employ this knowledge to develop ways to use the body's immune system against cancer.</p>
<p>20. Receptors on NK and NKT cells <i>PI: F Takei; CIHR; 2003-2005; For 2004 - \$359,653; Σ \$719,306</i> This grant will study NKT cells in more detail. In particular, the grant will find out NKT cells' role in the immune system, whether they use the same receptors as NK cells to recognize healthy cells, and what factors stimulate their activity.</p>
<p>21. RasGRPs and TCR selection <i>PI: R Kay; CIHR; 1992-2004; For 2004 - \$56,897; Σ \$421,181</i> The goal is to develop cDNA library screening strategies to identify novel oncogenes, and determine the roles of the selected oncogenes in normal and malignant T cell development.</p>

<p>22. Role of RasGRP1 in BCR-induced deletion of immature B cells <i>PI: R Kay; CIHR; 2004-2008; For 2004 - \$117,336; Σ \$821,347</i> Our goal is to understand the molecular mechanism by which Ras GRP1 increases the sensitivity of immature B cells to survival signal suppression and induction of cell death. Insight into regulation of B cell activation vs. deletion is critical to ensure effective immune response to foreign antigens while avoiding auto-immunity.</p>
<p>23. Replicative shortening of telomeres in human cells <i>PI: P Lansdorp, S Poon; CIHR; 2000-2006; For 2004 - \$113,500; Σ \$661,736</i> Our goal is to investigate the role of the human RTEL (regulator of telomere length) protein in the growth of normal and malignant cells. The objective of this study is to understand the role of telomeres in aging and cancer by addressing specific questions about the molecular mechanisms of telomere loss.</p>
<p>24. The role of Ahi-1 in human leukemogenesis <i>PI: X Jiang; Leukemia Research Fund; 2004-2006; For 2004 - \$50,000; Σ \$100,000</i> The overall aim of this project is to gain new insights into the pathogenesis of human leukemia that will ultimately lead to the development of a new rationally designed, molecularly targeted therapies by delineating the normal functions and transforming properties of a new candidate oncogene (Ahi-1).</p>
<p>25. Role of GPCRs in hemopoiesis and leukemogenesis <i>PI: R Kay; Co-applicants: K Humphries; Medical Research Council; 1999-2004; For 2004 - \$117,336; Σ \$586,680</i> The research project will select and perform functional analyses of GPCRs, heterotrimeric G proteins and small GTP activators, to determine their mechanisms of oncogenesis.</p>
<p>26. The role of SHIP in hemopoietic cell proliferation, activation and transformation <i>PI: G Krystal; NCI; 2000-2005; For 2004 - \$149,266; Σ \$746,330</i> The goal of the project is to carry out structure: function studies with the Src homology 2-containing -inositol 5' phosphatase, SHIP, to determine which of its domains are critical for its ability to regulate mast cell and macrophage responses to extracellular signals, to further identify SHIP's binding partners and to elucidate SHIP's role in normal and abnormal hemopoiesis.</p>
<p>27. The role of SHIP in hemopoiesis and innate immunity <i>PI: G Krystal; NCIC; 2004-2009; For 2004 - \$150,000; Σ \$900,000</i> This grant will investigate the SHIP protein, its effects on our cells, and how its activity is controlled. The grant will also look for molecules whose activity is regulated by SHIP and determine SHIP's role in early blood cell development and effects on immune system activity.</p>
<p>28. Role of GTPase activators in early thymocyte development <i>PI: R Kay; UBC Interim Funding HeRRO Program; 2003-2004; Σ \$20,000</i> The goal of this bridging grant was to continue the support characterization of RasGTPases in thymocyte development, now continued with CIHR support.</p>
<p>29. Stem cell centre - infrastructure operating funds <i>PI: P Lansdorp; CFI; 2003-2006; For 2004 - \$41,500; Σ \$124,500</i> Partial infrastructure operating funds for the stem cell centre project.</p>

<p>30. Stem cell and gene regulation <i>PI: A Eaves; Co-PIs: C Eaves, D Hogge, P Hoodless, K Humphries, R Kay, G Krystal, P Lansdorp, D Mager, C Smith, H Sutherland and F Takei; MSFHR Research Unit; 2003-2006; For 2004 - \$250,000; Σ \$1,000,000</i> Studies will focus on defining molecular pathways that govern stem cell renewal, viability, their development into specific types of cells (such as bone and blood) and their ability to multiply in a variety of body tissue. Researchers are particularly interested in understanding how inherited and acquired gene mutations may influence these processes and contribute to the development of cancer.</p>
<p>31. Stem cell centre <i>PI: P Lansdorp; CFI; 2002-2005; For 2004 - \$1,258,398; Σ \$3,775,195</i> This project will address new questions in stem cell biology and explore emerging possibilities for the use of stem cells in regenerative medicine. The centre will comprise of three laboratories: a stem cell sorting and analysis laboratory, a gene vector laboratory and a Good Manufacturing Practice (GMP) Stem Cell Processing Laboratory.</p>
<p>32. A systemic approach to modeling, capturing, analyzing and disseminating flow cytometry data <i>PI: R Brinkman; CIHR; 2004-2005; Σ \$5,536</i> The goal is to implement a systemic approach to modeling, capturing, analyzing and disseminating flow cytometry data, not only for high throughput studies, but for general flow cytometry as well. This proposal will implement a systemic approach to modeling, capturing, analyzing and disseminating flow cytometry data, not only for high throughput studies, but for general flow cytometry as well.</p>
<p>33. TGFβ signal transduction pathways in developmental programs <i>PI: P Hoodless; CIHR; 2003-2008; For 2004 - \$58,500; Σ \$176,875</i> The goal of this project is to develop a better understanding of how the TGFβ signaling pathway is capable of regulating a wide diversity of cell-cell communications involved in proliferation, differentiation and apoptosis. Our strategy is to compare and contrast the functional role of Smad signaling pathways in two developmental programs, early embryonic patterning and hemopoiesis.</p>
<p>34. Use of Celera database to facilitate mammalian genomic studies <i>PI: D Mager; CIHR; 2002-2005; For 2004 - \$6000; Σ \$18,000</i> Access to the Celera database of the human genome is essential required for many of the mammalian genome studies underway.</p>
<p>Interdisciplinary</p>
<p>35. Cancer Genomics – Genome Canada Competition I award <i>Co-PI: V Ling, M Marra, C Eaves; Co-I: K Humphries, S Jones, S Lam, W Lam, P Lansdorp, C MacAulay, M Rosin, J Vielkind; Genome Canada; 2001-2006; For 2004 - \$3,355,767; Σ \$16,778,835</i> See summary of project in Cancer Genetics section.</p>
<p>36. Characterization and self-renewal control of normal hematopoietic stem cells <i>PI: C Eaves; NCI; 2002-2007; For 2004 - \$127,108; Σ \$635,540</i> The long-term goal of this project is to develop methods for controlling and manipulating normal hematopoietic stem cell (HSC) expansion.</p>

<p>37. Creation of publicly available SAGE dataset for NIH approved human ES cell lines <i>Co-PI: M Marra and C Eaves; NIH; 2003-2004; Σ \$300,000USD</i> See summary of project in Genome Sciences Centre section</p>
<p>38. Endothelial to mesenchymal transformation <i>Co-PI: P Hoodless, A Karsan; CIHR; 2003-2008; For 2004 - \$58,037; Σ \$290,188</i> The major goal of this project is to understand TNF-induced endothelial apoptosis. Our goal is to understand how a recently identified cell-surface receptors signals the endothelial cells involved in heart development to transform, and to determine whether defective signals from the receptor will cause cardiac defects that the mimic those seen in humans with heart valves and membranous wall problems.</p>
<p>39. HOXB4: a hemopoietic stem cell expanding factor <i>PI: K Humphries, G Sauvageau (University of Montreal); NIH; 2001-2005; For 2004 - \$104,000; Σ \$416,000</i> The goals of this project is to enhance the potential of HSCs to expand in vitro, to develop and test clinically-relevant strategies aimed at achieving a maximal expansion of HSCs in vitro and to identify a HOXB4-containing "HSC-renewal protein complex" and determine the role of the newly identified proteins in HSC self-renewal.</p>
<p>40. Normal and leukemic Hematopoiesis <i>PI: K Humphries; Co-applicants: C Abramovich, J Cashman, C Eaves, P Hoodless, G Krystal and P Lansdorp; NCIC; 2002-2007; For 2004 - \$1,031,205; Σ \$5,238,379 [Group Grant]</i> The overall goal of this project is to determine how normal blood cells become leukemia cells and to apply that information to develop new leukemia treatments. This program included sub-projects on the following: a) Genetic determinants of hematopoietic stem cell function b) Regulation of proliferation versus differentiation during normal and leukemic hemopoiesis</p>
<p>41. A novel transplant protocol for CML <i>PI: A Eaves, C Eaves, M de Lima, MD Anderson; NIH; 2004-2005; Σ \$65,000</i> This project will evaluate three purging methods to selectively eliminate CML stem cells.</p>
<p>42. A quantitative and comprehensive atlas of gene expression in mouse development <i>Co-PI: M Marra and P Hoodless; Co-I: E Simpson, R Strausberg, S Jones, C Helgason & G Riggins; Genome Canada/NIH/NCI/BC Cancer Foundation; 2002-2005; For 2004 - \$1,085,321; Σ \$3,255,964</i> In order to achieve an understanding of mammalian development, this project will construct an atlas of gene expression that will define the normal state for many tissues by determining, in a comprehensive and qualitative fashion, the number and identification of genes expressed throughout the development. The project will focus on individual cell types and tissues rather than on cruder preparations of material containing heterogeneous mixtures of cells/tissues.</p>
<p>43. Telomere length regulation in murine cells <i>PI: P Lansdorp; NCIC; 2002-2007; For 2004 - \$101,759; Σ \$508,795 [Group Grant]</i> The goal of this project is to understand telomere length regulation in the mouse and clarify the relation between telomere length and telomere function.</p>

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
37	3	42	43	0

VANCOUVER ISLAND CANCER CENTRE
BC CANCER AGENCY
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<i>Researcher name</i>		<i>Position & Cross-Appointments</i>
Brian Weinerman	MD	Regional Vice President, Vancouver Island Cancer Centre, BCCA Honorary Clinical Professor, Medical Oncology, UBC
Charlotte Ann Syme	MSc Nursing	Provincial Leader, Pain and Symptom Management/Palliative Care Adjunct Clinical Professor, Palliative Care, UBC; Adjunct Associate Professor, Nursing, UVic
Elaine Wai	MD, MSc Clinical Epidemiology	Radiation Oncologist Clinical Assistant Professor, Radiation Oncology, UBC
Howard Pai	MD	Radiation Oncologist Clinical Assistant Professor, Surgery, UBC
Ivo Olivotto	MD	Head, Radiation Oncology Professor, Surgery, UBC
Paul Blood	MD, PhD Epidemiology	Radiation Oncologist Clinical Assistant Professor, Surgery, UBC
Brad Nelson	PhD Immunology	Director, Trev & Joyce Deeley Research Centre, Vancouver Island Cancer Centre Adj Assoc Professor, Biology & Biochemistry, UVic
Xiaobo Duan	PhD Virology	Research Project Leader

OUR RESEARCH FOCUS: The Vancouver Island Cancer Centre (VICC) is one of the four full service Cancer Centres of the British Columbia Cancer Agency. VICC provides oncology consultations and chemotherapy and radiotherapy treatments for people who live on Vancouver Island and the Gulf Islands. Researchers at the VICC actively lead, and are involved in a range of laboratory, clinical and translational research projects in collaboration with researchers at the BC Cancer Research Centre in Vancouver, at University of Victoria and elsewhere. VICC participates in a large number of clinical trials, which for consistency of reporting, are included as part of the Medical Oncology Division report.

In 2003, through generous funding by the late Trev and Joyce Deeley, the Deeley Research Centre (DRC) was opened at the VICC. Since 2003, the DRC has been set up as a translational research centre that performs 'bench-to-bedside' research for patients on Vancouver Island and throughout the province of BC. Researchers at the DRC study how the immune system responds to cancer and how best to enhance this response for preventive and therapeutic purposes. The DRC is also the home of the Tumour Tissue Repository.

Tumor Tissue Repository (TTR) is housed in the Trev & Joyce Deeley Research Centre. TTR captures and collects molecular data from a growing collection of different cancerous tissues. To build a complete history of the tissue, patient-orientated data such as clinical details of the disease, treatment regimens and disease outcomes will need to be added. Dr Juergen Vielkind will retire as TTRs founding director in 2005, when Dr Peter Watson of the University of Manitoba will take over.

The Tumor Tissue Repository is comprised of two complementary parts, a Processing and Storage Laboratory (TPSL) and a Bioinformatics Clinical Research Database (BCRDB). A BCRDB functional prototype has been established in collaboration with IBM. The TPSL is the laboratory where cancerous tissue samples are collected, analyzed to ensure that they are of research value and stored. DNA, RNA and protein studies will be performed on the samples and data results from these analyses are re-populated into the BCRDB. The database is also designed to capture and securely store patient clinical data and outcomes. The availability of tissue, comprehensiveness of data and availability of new emerging bioinformatics technologies, will represent a research tool to support and direct new research initiatives as well as allow the exploration of data-interactions previously not possible. The final outcome will be an individualized patient therapy.

PROGRESS HIGHLIGHTS DURING 2004

- Recruitment of Dr. Brad Nelson, as Director of the Deeley Research Centre, to establish a laboratory translational research program at VICC

CURRENT AWARDS AND HONOURS

<i>Name</i>	<i>Distinguished Award/Honour</i>
CA Syme	Canadian Association of Nurses in Oncology Award for Excellence in Education
P Blood	Canadian Graduate Scholarship Doctoral Award, CIHR (2004)
	Junior Graduate Studentship, MSFHR/ BC Medical Services Foundation (2004)

SELECT CURRENT CONTRIBUTIONS

<i>Name</i>	<i>Membership/Committee Involvement</i>
CA Syme	President, BC Hospice Palliative Care Association (2003-2006)
	Member, Canadian Hospice Palliative Care Association Standards Committee
E Wai	Member, Vancouver Island Research Advisory and Development Committee
	Member, BCCA Steering Committee for Mapping the Journey of Breast Cancer project
P Blood	Member, BCCA Ethics Review Board
H Pai	Vice President, Capital Informatics Society
	Member, Health Research Initiative Advisory Committee, Uvic
	Chair, Vancouver Island Cancer Care Steering Committee
	Member, Planning & Priorities Committee, Vancouver Island Health Authority
	Member, Vancouver Island South Region Cancer Care Coordinating Committee
	President, Canadian Association of Medical Oncologists

I Olivotto	Chair, Breast Cancer Theme Day WesCan Annual Conference, Victoria, BC
	Chair, Workshop for Validation of Novel Biomarkers in Breast Cancer, CBCRA, Toronto, ON
	Member, Vancouver Island Health Authority Regional Oncology Program Steering Committee
	Founding Member, BC Association of Radiation Oncologist
	Member, Research Advisory Committee, Canadian Breast Cancer Research Partnership
	Chair, Planning Committee, Workshop to develop a validation platform for novel biomarkers in breast cancer

MAJOR PROJECTS & PROGRAMS

<i>No. of Active Research Projects</i>	<i>Total Value</i>	<i>No. of New Research Project in 2004</i>	<i>Total Value</i>
15	\$8.2 M	4	\$2.8 M

CURRENT RESEARCH PROJECTS¹⁸

Vancouver Island Cancer Centre	
1. A pilot study to determine the accessibility and reliability of data on patients treated with DCIS in British Columbia PI: E Wai; Co-I: M MacKinnon, M Hayes and I Olivotto; CBCRA; 2004-2006; Σ \$25,000 The goal of this study is to determine what information is available electronically and on paper about the initial management, follow-up and outcome of all women with ductal carcinoma in situ (DCIS) in BC..	
2. Does scar massage improve pain and function after breast cancer surgery? A randomized control study. PI: P Truong; 2003-2005; CBCF; Σ46,393	
3. Palliative care in cross-cultural context: A NET for equitable and quality cancer care for ethnically diverse populations[†] PL: R Doll; A Kazanjian (UBC); Co-I: CA Syme; CIHR; 2004-2009; \$1,380,000 For a summary of this project see Psychosocial Research.	
4. Overcoming barriers to communication through end of life and palliative transitions PL: P Kirk, F Lau (UVic); Co-I: G Maclean, CA Syme; CIHR; 2004-2009; Σ \$1,380,000 The goal is to create a collaborative, interdisciplinary team and practice community to engage in cross-theme research and training in communication through transitions from curative to end-of-life and palliative care.	
5. Prostate cancer patient internet delivery system of electronic health records PI: H Pai; UVIC/MSFHR; 2004; Σ \$30,000	
6. Does the sequence of radiotherapy and chemotherapy influence outcome in inflammatory breast cancer PI: I Olivotto; Co-I: S Allan, T Shenkier and L Weir; CBCF; 2003-2004; Σ	

¹⁸ Key abbreviations: PI = Principal Investigator; Co-I = Co-Investigator; ACURA = Abbott – CARO Uro-Oncology Research Award; CBCF = Canadian Breast Cancer Foundation BC/Yukon chapter; CBCRA = Canadian Breast Cancer Research Alliance; CIHR = Canadian Institutes of Health Research; VIRAD = Vancouver Island Research Advisory and Development Committee, [†] = Inter-departmental project.

<p>\$19,785 The goal is to determine whether the sequence of clinical intervention for inflammatory breast cancer has a positive effect on the outcome of treatment.</p>
<p>7. A comprehensive testing strategy for the integration of novel biomarkers into early breast cancer care[†] <i>PI: I Olivotto; Co-PIs: B Norris, B Gilkes, D Huntsman, K Gelmon, C Bajdik, P Ravdin and S Taylor; CIHR/Canada Breast Cancer Research Initiative; 2003-2008; Σ \$544,899</i> This project will link the expression of novel biomarkers tested by immunohistochemistry on tissue microarrays with 10-year demographic, staging, treatment and outcome information collected, audited and maintained through Breast Cancer Outcomes unit.</p>
<p>8. What is the risk of hip fracture in men treated with external beam radiation for prostate cancer? A dose/risk analysis utilizing population health data <i>PI: P Blood; Canadian Association of Radiation Oncologists ACURA Research Award; 2004; Σ \$15,390</i> Dose-escalation studies in prostate cancer have shown that increasing the radiation dose to the prostate increases the biochemical rate of control. However, normal tissue tolerance is the major limiting factor in dose-escalation studies. This project will help develop the knowledge and understanding of the long-term effects of radiation on normal tissues to ensure the safety of dose-escalation and to cure prostate cancer with minimal toxicity.</p>
<p>9. A randomized trial of short vs. long acting LHRH agonist preparation prior to transperineal implantation of the prostate <i>PI: E Berthelet; ACURA; 2003-2007; Σ18,500</i> The primary objective of this study is the median time to testosterone recovery in patients receiving long acting or short acting LHRH hormone preparations and TPIP as radical treatment for limited stage prostate cancer. The suppression of testosterone to castrate levels has a definite advantage in terms of prostate volume downsizing, disease control and ease of Brachytherapy, in this patient population. Testosterone recovery is an important endpoint to consider in this patient population since prolongation of testosterone suppression may also delay the return of erectile function.</p>
<p>10. Prospective evaluation of the implantation of fiducial markers as a treatment planning tool for external beam radiotherapy in prostate cancer <i>PI: E Berthelet; VIRAD; Σ \$13,500;</i> The implantation of gold fiducial markers in the prostate allows the quantification of prostate motion during the course of treatment. Moreover, it also permits the application of on line correction to be made to the treatment fields on a daily basis. Although in widespread use around the world and in Canada, further testing is needed in order to assess the benefit of this somewhat invasive technique. If the motion of the prostate can be predicted or anticipated, an algorithm can be developed and the systematic use of fiducial markers may not be necessary in all patients.</p>
<p>11. A pilot study to evaluate the feasibility of self-directed aerobic exercise and its effect on fatigue in prostate cancer patients undergoing radical external beam radiotherapy <i>PI: P Truong; ACURA; Σ \$20,027</i> Fatigue is a common side effect of external beam radiotherapy. Although exercise is a modality that has potential to improve cancer-therapy side effects, its role in reducing radiotherapy-related fatigue is unclear, particularly among prostate cancer patients. In this project we will evaluate: tolerability and</p>

adherence to a self-directed, moderate-intensity aerobic exercise program during radical external beam radiotherapy (EBRT) for prostate cancer; the effect of aerobic exercise on fatigue during and after EBRT; and the effect of aerobic exercise on quality of life, physical fitness, hematologic and biochemical parameters in prostate cancer patients undergoing external beam radiotherapy.	
12. <i>Can salivary crystal morphology correctly predict for the presence of breast cancer</i>	PI: J. Lim; 2004 Salivary Crystal Morphology (SCM) testing is based on the finding that dried human saliva forms crystal patterns that are specific to certain disease states, including cancer. This study will determine if SCM can accurately distinguish women with metastatic breast cancer from healthy women. This test could be a simple, inexpensive and painless tool to improve the detection of breast cancer.
13. <i>Evaluation of Internal Mammary Lymph Nodes</i>	PI: D Mankoff, U of Washington; Co-I: V. Bernstein; NIH; 2001-2006; ΣUS\$2,000,000 The goal is to develop diagnostic roles of PET to identify IMN metastases, and to develop methods for using FDG PET in planning radiotherapy trials.
14. <i>A potential testing strategy for the testing of novel biomarkers into early breast cancer care[†]</i>	PI: B Norris; Co-I: I Olivetto; CBCRA; 2003-2007; Σ544,899. Part of Program 'Translating target discovery into better health outcomes for women with breast cancer' – PL: K Gelmon; Σ1,941,731 This research will assemble 4,500 cases of invasive breast cancer in tissue microarrays linked to 10+ years of clinical outcome information
15. <i>Eliciting autoimmunity to ovarian tumours in mice by genetic disruption of T cell tolerance mechanisms</i>	PI: B Nelson; US DOD; 2000 – 2005; US\$147,707; Σ566,304 The goal of this study is to gain insights into how ovarian cancer cells evade rejection by the T cells of the immune system. The project will generate modified T cells and tested to see if the anti-tumour immune response can be improved.

OUTPUT: PRESENTATIONS, PUBLICATIONS AND PATENT APPLICATIONS IN 2004

<i>No of peer-reviewed papers</i>	<i>No of books and book chapters</i>	<i>No of presentations</i>	<i>No. of poster abstracts</i>	<i>Patent Applications</i>
19	0	16	25	0

PUBLICATIONS

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SUMMARY OF FINANCIAL RESEARCH REVENUES - 2004

The British Columbia Cancer Agency's Research Finances are formally reported as part of the consolidated financial statements of the Provincial Health Services Authority. The PHSA financial year runs April 1st to March 31st, each year.

BC CANCER AGENCY RESEARCH REVENUES

The table of BC Cancer Agency research revenues below reflects realized research revenues – cash in the bank – and not the total value of research grants, contracts and clinical trials awarded to researchers at BC Cancer Agency.

Research Operations

<i>Project / Program Specific Research Funds</i>	2004/05	2003/04
BC Foundations & Agencies	2,263,386	1,898,675
Genome Canada/BC	13,329,966	11,739,392
Canadian Federal Foundations & Agencies	10,848,221	8,970,433
Canadian Industry	2,266,947	1,692,353
Other Canadian Funds	923,590	773,054
<i>Sub-Total Canadian Funding</i>	<u>29,632,110</u>	<u>25,073,907</u>
US and Foreign Foundations and Agencies	11,997,267	9,671,863
Other International Funds	1,183,552	919,875
International Industry	2,707,244	1,477,958
<i>Sub-Total International Funding</i>	<u>15,888,063</u>	<u>12,069,696</u>
<i>Sub-Total Clinical Trial Revenue</i>	<u>5,871,448</u>	<u>2,387,155</u>
TOTAL DIRECT RESEARCH FUNDING	<u>\$51,391,621</u>	<u>\$39,530,758</u>

Note: The capital cost of the new BC Cancer Research Centre (\$27.8 M CFI; \$27.8M BCKDF) is not included in this summary of research operating revenues.