

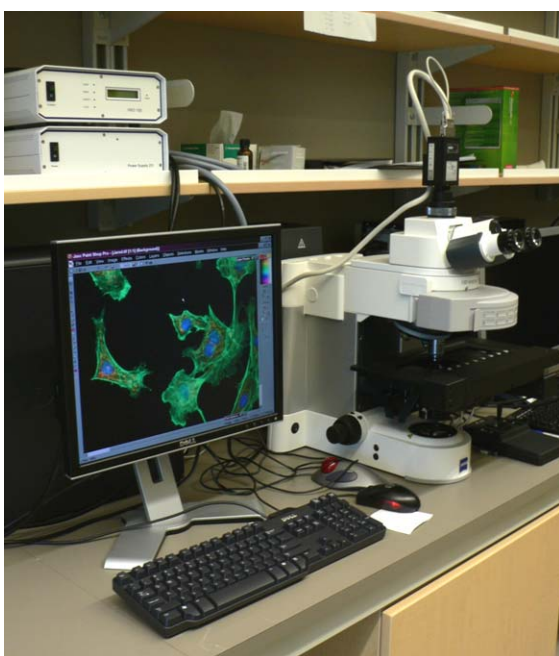
CANCER IMAGING

BCCA CANCER RESEARCH CENTRE

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Our Research Focus:



Researchers in Cancer Imaging exploit the interactions of light with human tissue at macroscopic and microscopic levels to detect, grade and treat early-stage cancers. Our current focus is upon early management processes in lung, cervix, prostate, breast and skin cancers. Specifically, we conduct research to develop and validate innovative equipment and procedures for clinical uses and to improve 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, and
8. Tissue modeling (static and dynamic)

Researchers in Cancer Imaging have developed expertise in translating the tools and procedures developed into clinically useful devices and processes.

Research Highlights 2005 – 2006

Significant progress was achieved in each of the following major initiatives:

- **Cervical Cancer.** In collaboration with Drs. Dianne Miller, Wan Lam and the Genome Sciences Centre, we have completed molecular analysis of over 20 cervical intraepithelial neoplasia (CIN) samples from cervical loop electrosurgical excision procedure (LEEP) subjects, with the goal of developing *in vivo* molecular contrast targets for nanoparticle labeling and improved early detection of cancer. In addition, a spin-off company was created to commercialize some fluorescence reflectance imaging and spectroscopy technology developed for early cervical cancer detection. In collaboration with MD Anderson Cancer Centre and Rice University, Cancer Imaging is also involved in a program to test and transfer cervical screening devices – specifically quantitative cytology and multispectral colposcopic imaging developed at BCCA – to the resource poor regions of the developing world (Nigeria and China) where the incidence of cervical cancer is extremely high.
- **Lung Cancer.** Under Dr. Stephen Lam’s leadership we focused on three major areas of early detection and management of early lung cancer. (1) We used quantitative sputum analysis on over 2000 sputum samples from patients in ongoing lung chemoprevention trials to identify a sputum biomarker which shows a good correlation between changes associated with the p53 oncogene and also with successful lung cancer treatment. (2) Cancer Imaging is developing an optical coherence tomography (OCT) system for live imaging of the lung periphery from the inside, and is developing an endoscopic Raman probe which will have the capability of detecting cancer related biochemical changes *in vivo* and increasing the specificity of early lung cancer detection. (3) In collaboration with Dr. Wan Lam (Cancer Genetics) and others, we identified molecular changes (DNA alterations, levels of RNA expression) associated with early lung cancer and lung cancer treatment response.
- **Oral Cancer.** In collaboration with Dr. Miriam Rosin (Cancer Control Research) and colleagues, we published evidence of the clinical utility of specific oral cancer devices. In association with LED Inc., we continued to commercialize the VELscope, a device for the detection and treatment of oral premalignant lesions (OPLs). LED obtained FDA and Health Canada approval for the device and the VELscope has gone into production. The device is being introduced to dentists in BC and around the world for enhanced oral cancer screening. Quantitative cytology and histology is being used on brushings from the mouth and tissue biopsies identified by use of the VELscope to correctly discriminate between samples with inflammation and trauma.
- **Skin Cancer.** Our goal is to develop non-invasive optical methods for improving the early detection of skin cancers. We developed two new devices: (1) a rapid near infrared (NIR) Raman spectroscopy system for *in vivo* skin biochemical analysis and (2) a NIR autofluorescence imaging system for *in vivo* skin imaging. With these new tools, we discovered unique Raman and NIR fluorescence spectral signatures from melanin, an important skin pigment that absorbs UV and visible light strongly and appears as a dark substance, causing difficulties in interpretation in clinical diagnosis. These new optical signatures in the NIR wavelength range shed new light for non-invasive diagnosis of melanoma and pigmented skin diseases. We are currently accumulating clinical data from various skin lesions and skin cancers in an attempt to develop an optimized algorithm for skin cancer detection.

Key Research Staff

<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
David Garner	PhD Chemistry	Senior Scientist (on sabbatical) Clinical Scientist, Path and Lab Medicine, UBC CEO, Perceptronix Inc.
Martial Guillard	PhD Biomedical Eng.	Research Scientist
Mladen Korbelik	PhD Biology	Senior Scientist Clinical Professor, Path and Lab Medicine, UBC
Stephen Lam	MD	Senior Scientist & Head, BCCA Lung Tumour Group Professor, Medicine, UBC
Pierre Lane	PhD Electrical Eng., 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
Haishan Zeng	PhD Medical Physics	Senior Scientist Clin Asst Prof, Path and Lab Medicine, UBC Visiting Prof, Fujian Normal University, China

Training

A.) Course Instruction

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

B.) Summary of Trainees

<i>Total No. of Current Students</i>	<i>Post-doctoral</i>	<i>Post-graduate</i>	<i>Undergraduate</i>	<i>Clinical</i>
8	2	6	-	-

C.) Current Students - Degrees Completed

<i>Name</i>	<i>Supervisor</i>	<i>Date Completed</i>
MSc		
Brandon Stott	M Korbelik	2005
Xiao Han	H Zeng	2006

D.) Trainee Awards

<i>Name</i>	<i>Supervisor</i>	<i>Award Received</i>
Gerald Li	C MacAulay	CIHR scholarship (2006-2007)

Selected Current Contributions

<i>Name</i>	<i>Membership/Committee Involvement</i>
M Korbelyk	Chair, Graduate Student Supervisory Committee
	Member, Graduate Student Committee, Dept. of Pathology
S Lam	President, International Photodynamic Association
	Member, Advisory Council on Lung Cancer, NCIC

Current Research Projects²

1. Application of pharmacogenomics for rational therapy of lung cancer	
PL: S Lam, V Ling Co-I: J English, W Lam, C MacAulay, R Ng, YZ Wang, J Yee et al. Genome Canada, Merck & Amgen \$2,094,884 (2005) \$1,949,131 (2006) \$6,680,176 (2004-2007)	The goals are (1) to generate predictive genomic signatures of chemotherapy response in non-small cell lung cancer (NSCLC) patients using whole genome BAC CGH and gene expression microarray profiling, and (2) 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.
2. Integration of digital micromirror devices with confocal macroscopy for improved genetic microarray reading and tissue imaging	
PI: B Wilson (U Toronto) Co-I: C MacAulay, TW Yeow (U Waterloo) Canadian Institutes of Photonics Innovation \$40,000 (2005) \$163,000 (2004 – 2009)	The goal is to design, construct and test a novel microarray instrument that will have unlimited dynamic range and image registration.
3. Optical systems for <i>in-vivo</i> molecular imaging of cancer	
PL: RR Richards-Kortum, (U of Texas Austin) Co-I: S Lam, W Lam, S Jones, M Korbelyk, P Lansdorp, M Marra, C MacAulay, M Rosin NIH – NCI US\$500,099 (2005) US\$1,358,169 (2004-2009)	The goal is to integrate development of optical imaging systems and contrast agents with advances in functional genomics through the development of 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.

² Key to abbreviations: PI = Principal Investigator, Co-I = Co-investigator; CIHR* = Funding Institution; \$150,000 (2005-2007) = Total Project Funding for Given Years (*see pages 16-17 for a list of acronyms)

4. Optical techniques and oral pre-cancer management	
<p>PI: M Rosin, C MacAulay, D Garner, M Guillaud, et al. BCCA/ NIH/ NCI \$368,922 (2005) \$1,943,863 (2005-2010)</p>	<p>The goal is to evaluate three innovative, potentially complementary visualization and imaging devices, alone and in combination, for early detection and follow-up of oral premalignant lesions and oral cancer.</p>
5. Optical technologies for cervical neoplasia	
<p>PL: M Follen, RR Richards-Kortum, (MD Anderson Cancer Centre, Rice U) Co-I: C MacAulay, M Guillaud, N MacKinnon NIH – NCI US\$712,397 (2005) US\$1,045,955 (1999-2007)</p>	<p>The goal 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>
6. Participant in University of Texas SPORE in lung cancer	
<p>Director: J Minna (UTexasSW) Co-I: D Banerjee, S Lam, C MacAulay NIH – NCI US\$9,715 (2005) US\$71,919 (2003-2008)</p>	<p>The strategic goal of the specialized program of research excellence (SPORE) is 1) to identify and understand the molecular hallmarks of lung cancer and 2) to translate this information into the clinic for early detection, prognosis and selection/development of new treatments for lung cancer.</p>
7. PDT and immunotherapy of solid tumors	
<p>PI: M Korbelik CIHR \$97,620 (2005) \$97,620 (2006) \$818,682 (1993-2007)</p>	<p>Our goal is to: 1) optimize the procedure for obtaining photodynamic therapy (PDT) generated cancer vaccines, 2) investigate how they induce immune response search for immune adjuvants that may further potentiate their effect, and 3) explore the potential for combining these vaccines with radiotherapy and surgery.</p>
8. Phase II trial of ACAPHA in former smokers with IEN	
<p>PL: A. Gazdar (U of TexasSW) Co-I: S Lam, R Buncher, M You, JC leRiche, C MacAulay, M Guillaud, A McWilliams NIH \$845,564 (2005) US\$4,710,376 (2002-2007)</p>	<p>The goal is to evaluate the efficacy and safety of a novel food supplement – ACAPHA – in former smokers with bronchial intraepithelial neoplasia (IEN) in a double-blind, 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.</p>
9. Pre-invasive and stage 1A lung cancer biomarkers identified through random peptide phage display	
<p>PI: J Hung CIHR \$59,515 (2005) \$59,515 (2006) \$178,545 (2004- 2007)</p>	<p>This goal is to identify protein abnormalities produced by cancer genes in early clinical stage 0 (pre-invasive) and 1A (early invasive) squamous cell lung cancers. The identification of such a panel of protein markers in pre-invasive and invasive lung squamous carcinoma represent ideal biomarkers for the early detection of such lesions in the sputum and in bronchial biopsies of individuals with or at risk for lung cancer.</p>

10. Program project: Chemoprevention of lung cancer	
<p><i>PL: MW Anderson</i> (Cincinnati) <i>Co-I: D Banerjee, M Guillaud,</i> <i>S Lam, JC LeRiche, C</i> <i>MacAulay, A McWilliams</i> NIH US\$1,440,510 (2005) US\$2,161,385 (2003-2008)</p>	<p>This project is designed to test the hypothesis that a selective combination of chemo preventive 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.</p>
11. Raman spectroscopy for non-invasive diagnosis: Application in skin cancer detection and evaluation	
<p><i>PI: H Zeng</i> <i>Co-I: H Lui, M Chen</i> NCIC \$66,168 (2005) \$72,668 (2006) \$208,004 (2004-2007)</p>	<p>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>
12. Rapid raman spectroscopy for non-invasive skin cancer diagnosis	
<p><i>PI: H Zeng</i> <i>Canadian Dermatology</i> <i>Foundation</i> \$25,000 (2005)</p>	<p>Our goals are: (1) to obtain a detailed understanding of the optical spectroscopic properties of skin cancer; (2) 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; (3) to develop diagnostic algorithms for spectroscopic skin cancer diagnosis; (4) to evaluate the effect of secondary changes to skin cancers such as necrosis, inflammation, and ulceration on spectroscopic signals; and (5) to elucidate the biophysical origins of these optical signals.</p>
13. Relevance of complement activation in photodynamic therapy-mediated eradication of solid tumors	
<p><i>PI: M Korbelik</i> NCIC \$81,192 (2005) \$279,013 (2003-2006)</p>	<p>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>
14. Tomographic reconstruction microscopy	
<p><i>PI: C MacAulay</i> <i>Co-I: P Lane</i> CIHR \$50,000 (2005) \$50,000 (2006) \$382,303 (1999-2007)</p>	<p>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 involve pathologists and will use a 3-D imaging platform called Optical Computed-Tomography, a novel optical scanning technique.</p>