BC Cancer Agency scientists make internationally significant discovery, mapping the evolution of breast cancer ‘avatars’

The renewed University of British Columbia Medical Undergraduate Program (MDUP) curriculum launches in August, 2015

Optimization of lab services and implementation of a standard test menu for the province

Dr. Lockwood and his family welcome baby number three to the family!
NEW Introducing the New Survey Tool Solution

This solution is offered at the enterprise level AT NO CHARGE to all end users and will have features that include:

UBC IT’s new enterprise survey tool solution by FluidSurveys/SurveyMonkey is available starting today. The new tool is available to all staff and faculty and is a Canadian hosted solution that meets strict BC privacy legislations and the functional requirements of the UBC community.

- Building powerful surveys, forms, questionnaires and polls
- Friendly drag and drop interface
- Sharing and collaboration between accounts
- All in one solution to collect data online, offline, and via mobile
- Report generation and analytics
- Administrative control

You can start using the new tool by logging in with your campus-wide login information at https://survey.ubc.ca/.
Change, evolution, excellence, and opportunity are processes, a characteristic, and a circumstance that have filled my thoughts over the last number of months and especially recently. Preparation of the Departmental Self Study, participating in and reading the Report of the Department Review, and developing (with the help of many) our response to the Review kept them at the forefront of my thinking. And now, the most recent issue of the Pathology Magazine keeps their profile high for me.

Self Study document preparation (which involved many individuals to whom I am very grateful) clearly and not surprisingly confirmed that the Department is populated by amazingly talented, committed people who collectively are responsible for the excellence that exists in it. This time also highlighted that change and evolution will occur and be required to overcome challenges but also to take advantage of opportunities before us. The Department Review and our response to it emphasized this further. An opportunity exists right now to transform the Department, building upon and further enhancing its excellence across a multi-faceted Clinical-Academic mission and establish it as a model academic unit in an academic health sciences network, the latter of which is an emerging and evolving concept in the UBC Faculty of Medicine. This transformation is enabled by a number of environmental factors that include (but are not limited to) the provincial scope of the UBC Faculty of Medicine, legislated laboratory reform, and the recent commitment of new resources to pathology and laboratory medicine in BC. What is additionally significant about this transformation is that a number of issues and challenges faced by the Department will coincidentally be addressed in whole or in part.

As always, this issue of the Pathology Magazine provides a wonderful overview of the Department and its people. Notably, the content also aligns well with my own current mental preoccupations. From the new MD undergraduate curriculum that is slated to begin soon, to renewal and growth of the Department with the arrival of new members, and to laboratory reform across the province, change seems now to be a constant feature of our working lives and is on prominent display. Evolution, whether in the “adaptation” of cancer cells over time or in the development of the graduate program, is nicely demonstrated.

Excellence (and creativity) across education and research domains and of the people in the Department is also abundantly clear. And, the opportunity to transform ourselves enters the realm of possibilities when consideration of all that we are (as illustrated and described) is combined with a constellation of events in our environment, not the least of which is an injection of new resources into pathology and laboratory medicine in the province. So, please take time to read and enjoy Pathology Magazine, and to ponder a future that is not only different, but also better.
The PROOF Centre

AUTHORS: BRUCE McMANUS, MD, PHD, FRSC, FCAHS, FRCPC, FCAP, FACC
Professor, UBC Department of Pathology & Laboratory Medicine; Co-Director, Institute for Heart + Lung Health; CEO, Centre of Excellence for Prevention of Organ Failure (PROOF Centre), St. Paul’s Hospital, University of British Columbia

KAREN LAM, PhD, Strategic Development Officer, PROOF Centre

7 years
The PROOF Centre brings research findings into real-world practical use
The Centre of Excellence for the Prevention of Organ Failure (PROOF Centre), is an independent, not-for-profit organization funded initially by the NCE CECR program in 2008, that develops high-value, biomarker-based multi-marker blood tests to enhance the assessment of risk, presence, progression and response to therapy for heart, lung and kidney failure patients. The cross-disciplinary team at PROOF Centre harnesses the power of clinical, molecular and computational sciences to advance a complex agenda of bringing innovation to the clinical laboratory. The Centre is closely affiliated with and supported by the University of British Columbia and Providence Health Care.

PROOF Centre’s core strengths, which evolved for several years before the Centre was formally inaugurated, relate to critical guidance by expert clinicians regarding unmet needs in clinical management that could be addressed by modern sensitive and specific blood tests, molecular science of human biology and its systems, layered data analytics, and the magnetism of the challenge in its Mission to bring together teams across all disciplines, sectors and geographies. Together this team draws on all perspectives necessary to mature and implement new blood tests. Such tests are driven by the desire to prevent disease or catch it early in an accurate fashion, and to enable physicians and their teams whether in primary or quaternary care settings. Such a thrust is also influenced greatly by patient needs and comforts. Tools to accelerate and make more efficient drug discovery programs of the pharmaceutical industry are also front and centre.

Since PROOF Centre’s formal beginning in 2008, the team has developed blood test content for more than 15 indications in acute and chronic heart failure, chronic obstructive lung disease, asthma, chronic kidney disease, and heart and kidney transplantation. As alluded to, the Centre begins biomarker discovery studies based on assessment of clinical and market needs and using samples from carefully phenotyped patients. The team follows rigorous computationally - and SOP - driven processes for receiving biomarker data from high-throughput technology platforms (e.g., microarray-based or RNAseq-based RNA expression and epigenetic profiling, and mass spectrometry-based proteomics and metabolomics), and analyzes the information using a computational pipeline (Fig. 1) that has now been widely published.

**FIGURE 1. PROOF CENTRE BIOMARKER DEVELOPMENT PIPELINE**

Each biomarker program begins with understanding patients’ and clinical needs. Blood tests are tailored to maximize patient benefit while reducing healthcare costs. Working at the interface between data, technologies, human biology and end-users, the PROOF Centre brings research findings into real-world practical use.
Chronic Kidney Disease (CKD)

Based on successful discovery work, the PROOF Centre recently began a partnership with AstraZeneca and The Canadian Study of Prediction of Death Dialysis and Interim Cardiovascular Events (CanPREDDICT) to identify biomarkers of chronic kidney disease progression. The discriminative power of the markers identified would allow for development of new tools to help physicians and pharmaceutical companies to identify patients with rapidly progressing CKD, facilitating more individualized treatment and supporting the development of new CKD therapies.

Heart Failure

In addition to transplant rejection, the PROOF Centre team has been working with investigators at St. Paul’s Hospital and Alberta HEART on biomarker solutions along the life cycle of heart failure. We have found molecular biomarkers that significantly improve upon current markers of heart failure (e.g., B-type natriuretic peptide) in correctly identifying patients as having or not having chronic heart failure. We have also developed tests to identify subtypes of chronic heart failure and to monitor patients for recovery of heart function from drug therapy. For acute heart failure patients, we have identified biomarkers that predict outcomes such as survival and response to mechanical circulatory assist device therapy. These tools are expected to lead to better patient care through more appropriately targeted therapies.

Transplantation

Our biomarker development experience in the translational setting began 10 years ago with the Biomarkers in Transplantation (BiT) program (originally funded competitively by Genome Canada, with major partners IBM and Novartis). Together with our partners and collaborators, we accrued a large, international cohort of heart and kidney transplant patients and identified gene-expression and protein biomarkers of acute allograft rejection. Our most advanced biomarker test, used for monitoring acute rejection in heart transplant patients, is currently in late development stages and is expected to be implemented at the St. Paul’s Hospital clinical laboratory for validation and real-time studies in 2015. Once validated, the test could save up to two-thirds of heart transplant recipients from having invasive heart biopsies in the first 12 months post-transplant. The BiT program has since served as a model for other PROOF Centre biomarker initiatives. A closely related program of work has uncovered a signature to discriminate patients with and without chronic heart rejection (expressed pathobiologically as cardiac allograft vasculopathy). This marker set is soon to be evaluated in an international cohort of heart transplant patients.

Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) is another major focus at the PROOF Centre and its many collaborators. Our COPD program began in 2009 with partners such as GlaxoSmithKline (GSK) and Genome BC, and is currently funded by Genome Canada in a program of work led by Drs. Don Sin and Raymond Ng. The goal of this particular program is to improve COPD patient care by developing new blood tests that will help identify patients who are at high risk of acute exacerbations (lung attacks) of COPD (AECOPD), as well as those who are in the early stages of an AECOPD. Our team has already identified promising blood-based protein, gene expression, and epigenetic signatures that can predict or diagnose AECOPD. We are now replicating these signals in different patient cohorts and will develop the most promising markers as clinical assays for implementation in clinical laboratories in Vancouver and Montreal. The impact and value of our blood tests on patients, doctors and healthcare systems will be studied by our team through health economic modeling and cost/utility analyses.

Chronic Kidney Disease (CKD)

Based on successful discovery work, the PROOF Centre recently began a partnership with AstraZeneca and The Canadian Study of Prediction of Death Dialysis and Interim Cardiovascular Events (CanPREDDICT) to identify biomarkers of chronic kidney disease progression. The discriminative power of the markers identified would allow for development of new tools to help physicians and pharmaceutical companies to identify patients with rapidly progressing CKD, facilitating more individualized treatment and supporting the development of new CKD therapies.
A Framework for Collaboration and Innovation

We work effectively across disciplines, sectors, organizations and geography, and use our computationally-driven biomarker discovery and development process to support organizations and research groups looking to augment their programs with molecular solutions (Fig. 2). Major ongoing collaborations at the PROOF Centre include biomarker projects related to muscular dystrophy (The Jain Foundation), spinal cord injury (Dr. Brian Kwon), allergic rhinitis and asthma (AllerGen NCE, Adiga Life Sciences), stroke assessment (Dr. Andrew Penn), diabetes (Personalized Medicine Initiative), cystic fibrosis (Dr. Brad Quon), and comprehensive health appraisal (Molecular You). Working at the interface between data, technologies, human biology and end-users, the PROOF Centre of Excellence is truly able to implement research findings into real-world practical use as an end-to-end, patient-focused engine for transformative biomarker solutions.

- Biomarker discovery and development
- Transcriptomics, proteomics, metabolomics, integrated omics
- Computational and systems science analysis
- Clinical expertise: cardiac, renal, pulmonary, clinical chemistry
- Clinical patient recruitment and management
- Companion diagnostics
- Assay development and validity testing
- Biomarker scientific consultation
- Biomarker intellectual property management
- In-licensing and out-licensing blood test content
- Collaborative partnership to access competitive funding

FIGURE 2. PROOF CENTRE STRENGTHS AND SERVICES

Exemplary Recent Publications 2013-2015


Introduction
The renewed UBC Medical Undergraduate Program (MDUP) curriculum launches in August, 2015. With UBC Senate’s approval of the renewed curriculum proposal, the undergraduate program can now admit the Class of 2019 students into a renewed program. The following is a brief overview of curriculum design, assessment structures, and implementation considerations. Please visit our curriculum renewal website for up-to-date detailed information and current status.

Curriculum Structure
All the courses in the renewed curriculum have been designed with consideration of the principles detailed in the Dean’s Task Force on MD Undergraduate Curriculum Renewal Final Report. To this end, we have been mindful to take an integrated, developmental, competency-based approach to the design. For example, we have created transitional courses to support students at critical developmental periods in their education, as well as built course structures that provide bigger building blocks for integration.

The renewed course structure starts with a 3-week Transition into Medical Education (MEDD 410) course, which introduces the medical school experience, foundational science content, and clinical science content. It also introduces students to the case-based learning and clinical experiences formats, which may be new to some students. This first course also introduces the overall assessment framework that will be used to evaluate student performance in meeting objectives, course learning outcomes, year-level milestones, and ultimately the program’s exit competencies. Following the Transition into Medical Education course, the remainder of Years 1 and 2 is organized into four integrated foundational courses and two Flexible Enhanced Learning courses.

The four integrated courses are Foundations of Medical Practice I, II, and III (MEDD 411, 412, and 421), which represent the first three terms in Years 1 and 2, as well as the Transition into Clinical Education (MEDD 422) course, which is the last term of Year 2. In these four courses, each week will draw upon content from body systems, themes, and...
clinical experiences. Based on the week’s clinical presentation, content from these areas will be integrated and delivered in a variety of educational activities, including lectures, small group sessions, case-based learning, labs, online modules, and clinical office visits.

The clinical presentations are ordered developmentally to provide an integrated curriculum that builds from basic to complex. Later topics intentionally revisit, or spiral [http://cr.med.ubc.ca/what-is-a-spiral-curriculum/] back to, earlier ones to reinforce important topics, and integrate material across years. This developmental approach culminates with the Transition into the Clinical Education course (MEDD 422), which has a similar organizing structure as the preceding courses, but also has a heavier focus on preparing students for their clerkship experiences in Years 3 and 4. The Flexible Enhanced Learning I and II courses (MEDD 419 and 429) also run throughout Years 1 and 2. These courses offer a unique opportunity for medical students to pursue a variety of learning experiences and scholarly activities within a flexible learning space. They emphasize the importance of a broad understanding of scholarship, engagement, and social accountability by allowing students to undertake individualized directed studies options through various learning streams and activities. MEDD 419 in first year will also prepare students for scholarly work through a Foundations of Scholarship component. The goals of these courses are to foster innovation, creativity, and critical thinking in the context of social responsibility and accountability, and to prepare graduates for roles as scholars, lifelong learners, and leaders throughout their medical careers. In Year 3 there are two courses, Clerkship (MEDD 431) and Flexible Enhanced Learning III (MEDD 439). As in the current program, the year-long Clerkship course provides students with core experiences across the breadth of medicine through both clinical and academic learning opportunities. Students will interact with patients under the supervision of faculty members in order to develop a solid foundation of knowledge, skills, and abilities required for medical practice. In the renewed structure, disciplines that previously had dedicated courses are combined with related disciplines in three 16-week blocks within the year-long clerkship course. This new structure allows for increased integration among disciplines. In addition Year 3 has the third Flexible Enhanced Learning course which is a 4-week block (MEDD 439) at the end of the clerkship experience for students to complete additional activities.

Year 4 consists of clinical electives followed by the final transition course entitled, Transition into Postgraduate Education and Practice (MEDD 448). The aim of this course is to consolidate previous learning, and to support students’ transition into residency and into a career of medical practice. Students will work through a series of cases, some of which will be multifaceted and representative of the complex patients they will work with in residency, while other cases will be more focused and often tied to a specific medical discipline. ▶
Programmatic Assessment

The renewed assessment framework is a system of integrated components built upon the collective strength of each assessment modality. Each assessment modality is well suited to assessing certain types of content and competencies. When these modalities are combined within each course, a programmatic assessment framework is achieved that ensures learners are developing and meeting the competencies for graduation.

Within the renewed assessment framework the four assessment modalities are: written examinations (including traditional MCQ and progress tests), portfolio assessments, workplace-based assessments, and objective structured clinical examinations (OSCEs). Portfolios and progress testing are being introduced as new assessment modalities for the undergraduate program. Workplace-based assessment, OSCE, and traditional written examination modalities are currently used in the program, but will be enhanced and effectively integrated into the overall renewed assessment framework.

[http://cr.med.ubc.ca/cr-assessment-development/osce/]

RENewed COURSe STRUCTURE

<table>
<thead>
<tr>
<th>Year</th>
<th>Course</th>
<th>Duration</th>
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<tbody>
<tr>
<td>1</td>
<td>MEDD 410</td>
<td>3 weeks</td>
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<tr>
<td></td>
<td>MEDD 411</td>
<td>14 weeks</td>
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<tr>
<td></td>
<td>10 MEDD 419 half-days (1 wk)</td>
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<td></td>
<td>MEDD 412</td>
<td>14 weeks</td>
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<tr>
<td></td>
<td>10 MEDD 419 half-days (1 wk)</td>
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<tr>
<td>2</td>
<td>MEDD 421</td>
<td>14 weeks</td>
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<tr>
<td></td>
<td>10 MEDD 429 half-days (1 wk)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>MEDD 431 - Block A</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>MEDD 431 - Block B</td>
<td>16 weeks</td>
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<tr>
<td></td>
<td>MEDD 431 - Block C</td>
<td>16 weeks</td>
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<tr>
<td></td>
<td>MEDD 439</td>
<td>3 weeks</td>
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<tr>
<td>4</td>
<td>MEDD 441</td>
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<td>MEDD 442</td>
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<td>MEDD 445</td>
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<td></td>
<td>MEDD 446</td>
<td>4 weeks</td>
</tr>
<tr>
<td></td>
<td>MEDD 448 part 1</td>
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<td></td>
<td>CarMS</td>
<td>3 weeks</td>
</tr>
<tr>
<td></td>
<td>MEDD 448 - part 2</td>
<td>13 weeks</td>
</tr>
</tbody>
</table>

The renewed assessment framework is a system of integrated components built upon the collective strength of each assessment modality. Each assessment modality is well suited to assessing certain types of content and competencies. When these modalities are combined within each course, a programmatic assessment framework is achieved that ensures learners are developing and meeting the competencies for graduation.
Implementation Considerations

The renewed course structure and assessment framework have implementation considerations for all functions that enable delivery of the undergraduate program, including Administration, Faculty Development, Technology, Facilities and Room Booking, Educational Assessment Unit, Curriculum Management Unit, and Library Operations. We are working closely with representatives from all of these functions across all undergraduate program sites to ensure that the renewed program is feasible and effectively implemented.

In addition, the Evaluation Studies Unit is evaluating targeted areas of the Curriculum Renewal project to provide just-in-time feedback that guides planning and implementation.

**Conclusion**

Current detailed development and implementation planning is continuing for the MD undergraduate program to be ready to launch the renewed curriculum in August, 2015. Please visit the Curriculum Renewal website (http://cr.med.ubc.ca/) for more information. There is a Q&A forum (http://cr.med.ubc.ca/resources/faqs/) if you have further questions.

If you would like to get involved, please email us at mdcurric.renew@ubc.ca. We are always interested in maximizing engagement across the Faculty of Medicine.
LOOKING BACKWARDS – LOOKING FORWARDS

The Graduate Program in Pathology and Laboratory Medicine was started in 1970 and has graduated 410 students up to 2014. At the time of writing, we are one of the larger programs at UBC, and within the Faculty of Medicine, with 76 registered students (45 PhD students, 29 MSc students and 2 MD/PhD). Of these, 20 are international students. Over the past 5 years, the total number of students has decreased slightly despite increasing enrollment. This is desirable and is due to an increase in the number of students completing their degrees within desired timelines. All students received funding from their host laboratory, but many receive competitive awards; both internal and external to UBC. Notably, 6 students have won Vanier Scholarships over the past 5 years.

We believe the Graduate Program in the Department has become established as a “program of choice” by faculty and students since we have developed a reputation of professional, comprehensive and supportive mentoring. Our Program being awarded the 2014 Peter Larkin Award from UBC for contributions to student development from amongst all programs at UBC supports this notion. The core of this award comes from student engagement in the program and their vocal support for the program, its leadership, and the administrative staff.

Elements of the program that we believe “fuels” our success are:

Rolling application/acceptance process
This ensures rapid turnaround and response to students about proposed supervisors. Early interactions between the Program Director and prospective students starts to establish the value of strong relationships between students and the program’s administration.

Rigorous attention to the formation and operation of the students’ supervisory committees
There are no exceptions to the “12 month rule” for formal meetings.

Confidential meetings between the Program Director and each student
These meetings take place 1 to 2 times per year and enable communication for the program’s expectations to the students (e.g., committee meetings, comprehensive exams, thesis completion etc.).

Exit interviews with graduating students
These meetings confirm that the “students first” approach by the Program Director and the Program Assistant has high value to the students throughout their time in the program.

The size of our program is “just right”
The program is small enough such that the administrative staff know each student and supervisor well and it is easy for all to access personalized support. By contrast, it is large enough that there is a great deal of internal wisdom regarding past and acceptable practices. Students and supervisors learn the processes, policies, and procedures from each other through shared experiences.
Historically, the Graduate Program has been led and managed by a Graduate Advisor/Director and Program Assistant:

2003-2009

These were Dr. David Walker (2003-2009) and Penny Woo (1992-2009), respectively.

2009-2014

From 2009 to 2014, these roles were taken over by Dr. Haydn Pritchard (2009-present) and Farrah Rooney (2009-2011)/ Aleya Abdulla (2011-2014) and Heather Cheadle (2014-present).

Sept 2014-present

Although Haydn Pritchard retired from UBC in September 2014, he will stay on as Program Director in a part-time capacity. His duties will include the overall leadership of the program but he will be supported by a group of committed faculty who will champion each of the sectors of the Graduate Program. We have developed a “working council” model whereby each member of the Graduate Studies Committee takes on a role as Associate Program Director with specific roles and responsibilities. Currently, these individuals conduct the day-to-day management of their portfolios in consultation and mentorship of the Program Director.
Hi everyone, I’m a first year Master’s student working in Dr. Helene Cote’s lab. Our lab focuses on studying the effects of HIV and antiretroviral treatment drugs on mitochondrial DNA and cellular markers of aging. My particular area of research is identifying potential neurocognitive and neurodegenerative consequences for children exposed to HIV and antiretrovirals during pregnancy. I graduated in 2012 from Mount Royal University in Calgary with a degree in Psychology, although I also spent several years before that studying biochemistry and theoretical physics at the University of Calgary. I worked for several years in a provincial laboratory picking up knowledge about pathology, tissue typing, and forensics, which is how I came to be interested in studying laboratory medicine. When I’m not in the lab I enjoy snowboarding, hockey (coaching, watching, and playing), and jogging in my spare time. I chose to come to UBC because I had heard many great things about their science program, but getting away from the cold and snow in the wintertime was certainly appealing as well! Working in Dr. Cote’s lab also presented a great opportunity to bridge my interests in lab medicine and brain disease.

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Yulia Merkulova MSc
Supervisor: David Granville

I am studying the roles of serine proteases called granzymes in tissue injury and wound healing. I graduated with a BSc in Microbiology and Immunology from UBC. I am passionate about arts and design as much as I am about science. I chose UBC because it harbors a great scientific community with diverse research interests and is located in a beautiful city.

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Nicha Boonpattrawong MSc
Supervisor: Angela Devlin

I’m currently working at Dr. Devlin’s lab at the Child and Family Research Institute. My research is on developmental programming and cardiovascular disease. I’m interested in studying the effect of maternal obesity, during gestation, on the offspring vascular health. I will also be looking at the mechanism underlying developmental programming, which is hypothesized to be due to epigenetic. I recently graduated from University of Toronto with an Honours Bachelor of Science degree. After completing my undergraduate studies, I decided to trade the cold, snowy winter of Toronto for rainy – but still beautiful – Vancouver. I fell in love with the city and the campus when I first came to Vancouver for vacation. I was set on coming to UBC once I’ve heard about the Pathology program and found a great supervisor. The department is also comprised of experts in diverse field of research; I hope to be able to learn not only in my research field but interdisciplinarily. As for my personal interests, I love travelling, photography, movies, and hiking.

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Abigail Baticados MSc
Supervisor: Christian Steidl

I have a degree in veterinary medicine from the University of the Philippines, where I did clinical instruction in animal pathology, disease diagnostics principally in farm animals and was a veterinarian of military trained K9 bomb sniffer dogs. Beyond science, I volunteered in community outreach programs to increase public health awareness on anthropozoonotic diseases, belonged to a chorale society and participated in Rodeo sporting events. My research focus is to fundamentally understand the immunoregulatory processes that are involved in the lymphoma tumor microenvironment during TMEM30A inactivation and to determine whether these mutations identify a potential predictive biomarker in a DLBCL cohort treated homogeneously with R-CHOP. The study of lymphoma is fascinating due to these tumors being found within the very organs in which immune responses are initiated and yet no apparent response is elicited. It becomes even more interesting because it comprises an immensely heterogeneous group with different etiologies and histological subtypes. Studying in UBC has given me the unique opportunity to be mentored by Dr. Christian Steidl who is a known game-changer in the field of lymphoma research. It is remarkable to be in this laboratory and have the freedom and cutting edge resources to explore and challenge existing paradigms and possibly by biological discovery add to the existing armamentarium against lymphoma.
Jack Calder MSc
Supervisor: Will Lockwood

My research area is looking at Lung Cancer, focusing on non-small cell lung cancer, with my research focusing on finding and verifying the target of a compound found to kill a broad range of lung cancer cell lines but which doesn’t kill normal cells. I did my undergraduate degree at the University of Victoria, graduating with a Bachelors of Science with a major in Microbiology and a minor in Environmental Studies.

I enjoy playing many different sports including tennis, squash, soccer, volleyball, and ultimate Frisbee. Professionally I am still unsure exactly what I would like to do, though I am contemplating continuing to do my PhD or undertaking a genetics technologist course. The reason I choose UBC was because I really wanted to work at BC Cancer as I had heard for several people that it was one of the best if not the best opportunities in Canada to work in the cancer field. It is also located on the West Coast which is an added benefit as it is my favourite part of Canada that I have visited.

Amanda Henderson MSc
Supervisor: Angela Devlin

Hello! My name is Amanda and I’m excited to join the Department of Pathology & Laboratory Medicine as a new graduate student. I am working in Dr. Angela Devlin’s lab at CFRI. My research here will investigate maternal folate/ vitamin B12 imbalances during pregnancy and the effects on offspring health, particularly in terms of obesity and diabetes. I’ve always had an interest in health science and had originally planned to become a physiotherapist. I’m from Calgary, but completed my undergraduate studies at a small private school in the suburbs of Chicago, IL. During my time as an undergrad, I quickly fell in love with genetics and molecular biology, and redirected my career path towards research. Outside the lab, my life revolves around soccer. I’ve been playing competitively since I was 5 years old, with no plans to stop in the near future. I also enjoy snowboarding, running, binge-watching TV shows, and eating delicious food. I chose UBC because of the high academic standards, reputation of world-class research, and interest in my supervisor’s work. The location doesn’t hurt either!

Emily Button PhD
Supervisor: Cheryl Wellington

I am working with Dr. Cheryl Wellington to investigate the role of HDL (high density lipoproteins), or “good cholesterol”, in Alzheimer’s disease. The main lipoprotein in the brain, apoE, is found in multiple isoforms in humans including apoE4 which is one of the greatest risk factors for Alzheimer’s disease. During my undergraduate degree at the University of Waterloo, I studied human physiology and nutrition and got involved with research in the lipid field. My interest in lipids as well as my time spent working with dementia patients made Dr. Wellington’s lab a great fit for me. These experiences combined with the beautiful campus and city lead me to UBC. Outside of research related activities I enjoy running and biking around Vancouver and exploring all of the great places to eat!

Farhia Kabeer PhD
Supervisor: Sam Aparicio

I graduated in medicine and for many years worked as a clinician in Pakistan. I got the opportunity to come to Canada to do my Masters in Experimental Medicine from McGill University where I was at the breast cancer biology unit at IRCM in Montreal. My PhD is also focused on breast cancer research by studying patient-derived xenografts.

Usama Abbasi MSc
Supervisor: Jay Kizhakkedathu

Hi! My name is Usama Abbasi. I am very passionate about sports, outdoors, boardgames and loads of tv shows. A fun fact about me; I was born and raised in Hong Kong, I came down to UBC for my undergraduate studies in the Bachelor of Medical Laboratory Sciences. Now I am a new graduate student pursuing a Master’s degree.
Troy Pereira MSc
Supervisor: Aly Karsan

I am interested in the processing of prohormones in beta cells within diabetic and prediabetic environments. More generally, I am interested in the stress response of islet cells in both type 1 and type 2 diabetes. I completed a Bachelor of Science in Biochemistry at UBC in 2014, during which time I competed for the university on the varsity Alpine Ski Team, winning a collegiate National Championship in 2012, and achieving 2nd Team All-American status twice during my four years with the team. Upon graduation I was interested in pursuing health sciences research while maintaining my passion for skiing and the outdoors. It was then an easy choice to continue my studies at UBC in Pathology and Laboratory Medicine as it provides excellent research facilities and field-leading faculty members, along with some of the world’s best outdoors for backcountry skiing and climbing.

Samantha Burugu PhD
Supervisor: Torsten Nielsen

I am a PhD student in Dr. Torsten Nielsen’s lab, part of the Genetic Pathology Evaluation Centre located in the Jack Bell Research Centre. The lab is interested in biomarker development in breast cancer and my thesis is on the clinical utility of immune biomarkers in breast cancer. Our objective is to help/guide clinical practice in breast cancer. I hope to work in diagnostic development after my PhD. I have a bachelor's degree in Biopharmaceutical Science from the University of Ottawa and a Master's degree in Microbiology and Immunology from McGill University. My research background varies from analytical chemistry to HIV immunology and I think it illustrates well a part of my personality as someone who is always looking for something new to learn/try etc… I chose UBC for its excellent oncology research facilities and the fact that it is conveniently located in a great city!

Austin Taylor MSc
Supervisor: Bruce Verchere

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Sohyeong Kang MSc
Supervisor: John Priatel

I am studying the role of several intronic micro-RNAs and their host gene that are up-regulated in poor-outcome acute myeloid leukemia patients. I received my B.Sc in Microbiology and M.Sc in Pharmacology and Therapeutics from the University of Manitoba. My M.Sc work was focused on gestational diabetes and the metabolic health outcomes of offspring. When I am outside of the lab I enjoy staying active and lifting weights as well as playing the guitar. I chose UBC and the department of Pathology and Laboratory Medicine because of its great reputation and the great reputation of my principal investigators lab in general. It will provide me with the necessary tools to learn a completely new area of research while giving me the opportunity to branch out, collaborate and showcase my work to a broad audience.

Sohyeong Kang MSc
Supervisor: John Priatel

My name is Sohyeong Kang, a new graduate student starting January, 2015. My research project has not been decided yet, however, I am interested in studying MALT1 function in human CD8 and CD4 T cells. I graduated with honors of Bachelor of Science at the University of Toronto, majoring in human biology and animal physiology. During my undergraduate years, I studied various fields of science, which allowed for building a wide range of supportive background knowledge. Also, I had a chance to volunteer as a summer student at Dr. Li Zhang's laboratory and my project was to help characterize the anti-leukemic properties of human double-negative T (DNT) cells. I enjoyed the laboratory experience and my research interests grew which motivated me to work on the same project as a fourth-year thesis student. This valuable research experience influenced me in making the decision to enter graduate school and pursue a career in science.

I chose UBC to achieve my goal as a Master student because of the strong personal and facility supports. The graduate studies program in the Department of Pathology and Laboratory Medicine is very organized and well directed. Also, there are great faculty members available to support me throughout the graduate program.

Troy Pereira MSc
Supervisor: Aly Karsan

I am studying the role of several intronic micro-RNAs and their host gene that are up-regulated in poor-outcome acute myeloid leukemia patients. I received my B.Sc in Microbiology and M.Sc in Pharmacology and Therapeutics from the University of Manitoba. My M.Sc work was focused on gestational diabetes and the metabolic health outcomes of offspring. When I am outside of the lab I enjoy staying active and lifting weights as well as playing the guitar. I chose UBC and the department of Pathology and Laboratory Medicine because of its great reputation and the great reputation of my principal investigators lab in general. It will provide me with the necessary tools to learn a completely new area of research while giving me the opportunity to branch out, collaborate and showcase my work to a broad audience.
Gunjan Kumar MSc  
Supervisor: Peter Black

I am currently looking at the molecular mechanisms underlying resistance to chemotherapy in bladder cancer with a focus on cisplatin and gemcitabine based treatments. An insight into this problem which has been at the forefront of cancer therapy would then allow us to counter the resistance and improve patient prognosis. I completed my undergraduate degree at the University of Toronto with a BSc (Hons) in Biochemistry and Human Biology after which I joined Dr. Fabio Rossi’s lab at the Biomedical Research Centre at UBC as a research volunteer for 4 months, followed by a research student position with Dr. Peter Stirling at the BC Cancer Research Centre. This finally led me to my current position as an MSc student with Drs. Peter Black and Mads Daugaard at the Vancouver Prostate Centre. Most of my spare time outside the lab is spent outdoors, hiking trails which have been relatively unexplored and taking in the sights around this beautiful city. I also enjoy brewing beer and cooking which are hobbies that help me unwind after a long day at work.

Karen Simmons MSc  
Supervisor: Soren Gantt

I completed my Bachelor of Science in Microbiology and Immunology at UBC. During my degree I completed 12 months of my Co-op education in Agassiz, BC at the federal Pacific Agricultural Research Center, where I discovered my love of scientific research. I’m interested in infectious diseases and the arms race between the infectious agent and the immune system. In particular I have a keen interest in viral infections, which brought me to Dr. Marc Horwitz’ lab for my undergraduate thesis project, and ultimately to the department of Pathology at UBC. I am now working in Dr. Soren Gantt’s lab at the Child and Family Research Institute where I am investigating the early events during primary acquisition of herpesviruses. I aim to develop a successful career in research as an investigator and communicator of science.

Brennan Wadsworth MSc  
Supervisor: Kevin Bennewith

I am studying how to resolve the poor vasculature and low oxygen levels often found within tumours. I believe this to be an important field of work because these characteristics have been shown to promote aggressive and therapy resistant forms of cancer. My interest in this project stems from my undergraduate background and research experience in cardiovascular function and cellular biology from my BSc in Kinesiology at the University of Waterloo in Ontario. I chose to come from Ontario to UBC because of the high number of quality researchers here in Vancouver. Joining UBC also gives me the opportunity to enjoy the amazing west coast of Canada. All in all I spend my non-study time hiking in the area, biking, relaxing at the beach, reading, playing hockey, and watching tv.

Adam Yu MSc  
Supervisor: Jacqueline Quandt

Hi my name is Adam Yu and I am a graduate student at Dr. Jacqueline Quandt’s laboratory. Our main area of research is in the study of neuroprotective proteins and immunology and their role in multiple sclerosis. I did my undergraduate degree in the Bachelor of Medical Laboratory Sciences at the University of British Columbia, which is where I first started to gain significant exposure to research. Through this program and several other research lab positions, I have developed a significant interest in immunopathology. I chose to study at UBC because of its commitment to the field of research and how the pathology program represents a large multidisciplinary field providing several different opportunities and experiences that will allow me to grow as a researcher.

Anja Mottok MSc  
Supervisor: Christian Steidl

My research focus is on lymphoma biology and molecular genetics with the goal to elucidate tumor-microenvironment interactions in B cell malignancies, especially Hodgkin lymphoma and primary mediastinal large B cell lymphoma. I am holding an MD degree from the University of Frankfurt/Main (Germany) and before joining the Steidl lab I was working at the Institute for Pathology, University of Wuerzburg. In 2013 I received board certification in surgical pathology. I have a broad expertise and special interest in hematopathology and conducted research in the field of Hodgkin’s lymphoma and JAK-STAT signalling. If I am not in the lab or the class room I enjoy watching sports and reading books.
William Lockwood, PhD
Scientist, Integrative Oncology
British Columbia Cancer Agency
Assistant Professor, Pathology & Laboratory Medicine
University of British Columbia
Dr. Lockwood was born and raised in Kamloops, British Columbia and received a BSc in Microbiology and Immunology from the University of British Columbia (UBC) in 2004. After summer studentships focused on cancer genetics and neuroscience, he completed his PhD in Pathology and Laboratory Medicine at UBC in 2009 where he studied the genetic events driving the development of different lung cancer subtypes. He then moved to Memorial Sloan-Kettering and the National Institutes of Health for post-doctoral training with National Cancer Institute Director Dr. Harold Varmus where he expanded his efforts in lung cancer research to include mouse models and drug screening.

Dr. Lockwood joined the BC Cancer Agency as a Scientist in mid-2014 with an Assistant Professor appointment in Pathology and Laboratory Medicine at UBC following later that year. Dr. Lockwood’s research focuses on determining the critical events in lung cancer initiation, progression and response to therapy. His previous work has identified new mutations and disrupted signalling pathways in lung cancer as well as novel small molecules that inhibit lung cancer cells. He has also defined biomarkers for early cancer detection and targets to tailor subtype specific therapeutic strategies. Dr. Lockwood’s lab utilizes an integrative strategy to understand lung cancer biology that incorporates the genomic analysis of human tumour samples and functional screens in genetically engineered mouse models of lung cancer with high-throughput screening of chemical compounds across lung cancer cells. The aim is to identify the key genes that are altered during lung cancer development while simultaneously characterizing novel inhibitors of these identified genes and their corresponding pathways that show promise for use as targeted therapies. Dr. Lockwood’s research team currently consists of five outstanding lab members, including three current and former Pathology and Laboratory Medicine students, and he is always looking to add additional members to this growing team.

In addition to his research program at the BC Cancer Agency, Dr. Lockwood is also a course co-coordinator for PATH 535/635 that focuses on scientific communication. He is the recipient of many major awards including the CIHR Jean-Francois St. Denis Fellowship in Cancer Research, the BCCA Betty Rice Award for Lung Cancer Research, the International Association for the Study of Lung Cancer Young Investigator Award and recently, a Michael Smith Foundation for Health Research Scholar Award.

Dr. Lockwood currently lives in Coquitlam with his wife Amber and their three kids, Liam (6 years old), Isla (4 years old) and Gunnar (1 month old). He plays lacrosse and watches football in his spare time and enjoys getting outdoors to hunt, fish, hike and camp whenever possible.
Little known facts about Dr. Lockwood:

- Had a pony named Dusty when he was a kid
- Was pursuing graduate studies in microbiology until switching to cancer research at the last minute
- His favorite hockey team is the Edmonton Oilers and he has a deep-seated hatred for the Canucks, which makes life in Vancouver difficult
- Took a year off after high school to play lacrosse in Ontario and won a National Championship
- Became interested in science and human health by reading his mom’s nursing school text books when he was a kid
- Was featured in newspapers and radio interviews across Canada for his research – on hockey statistics
- Won “British Columbia Lacrosse Player of the Year” a very long time ago
- Lost a grandfather to lung cancer which is one of the reasons for his field of research
- First date with his future wife was watching a hockey game – featuring their brothers on either side of a heated Kamloops-Kelowna rivalry
- Has been confused with Conan O’Brien on multiple occasions despite being almost a foot shorter than the comedian

.. JUST FOR FUN

- WHERE WERE YOU BORN?
  W.L.: The Loops. Kamloops, B.C.
- WHAT WAS YOUR FIRST JOB?
  W.L.: Bagging groceries and stocking shelves at Coopers Foods.
- WHAT MOTIVATES YOU TO WORK HARD?
  W.L.: Stories, mostly personal, about those affected by cancer.
- WHAT IS YOUR FAVORITE THING ABOUT YOUR CAREER?
  W.L.: Interacting with bright, energetic people on a daily basis and investigating interesting questions with no current answers.
- WHAT WOULD YOU SING AT KARAOKE NIGHT?
  W.L.: Led Zeppelin
- IS THERE SOMETHING YOU CONSTANTLY LOSE AT YOUR HOUSE OR ANYWHERE?
- WHO IS YOUR FAVORITE AUTHOR?
  W.L.: Orwell. I like to think of UBC as Big Brother.
- WHAT ARE YOUR HOBBIES?
  W.L.: Lacrosse, hunting, camping, hiking.
- IS THERE ANYTHING YOU WISHED WOULD COME BACK INTO FASHION?
  W.L.: Grunge. I have a lot of flannel plaid shirts.
- FOR WHAT IN YOUR LIFE DO YOU FEEL MOST GRATEFUL?
  W.L.: My beautiful wife and kids.
- WHAT DO YOU USUALLY DO WHEN YOU HAVE LEISURE TIME ON YOUR HANDS?
  W.L.: See above. I have three kids. What’s leisure time?
- WHERE IS THE FARDEST YOU HAVE EVER TRAVELED?
  W.L.: Japan.
- WHAT IS USUALLY YOUR FIRST THOUGHT WHEN YOU WAKE UP?
  W.L.: Get to the lab.
Dr. Hardwick started as the Head of Pediatric Microlab at VGH in 1965, and then became the Head of Pathology at BC Children’s Hospital in 1970. He continues to be a part of the Anatomical Pathology Department. One of Dr. Hardwick’s most memorable experiences was developing the perinatal screening program with the approval of parents and practitioners. Looking back on his time here, creating C&W where he was chair for 17 years, was a huge task from 1964-1982 when it opened! Working with colleagues, notably Sydney Israels, Phil Ashmore, and other department heads to do this was one of his most rewarding memories.

Emeritus Alumni News:

Dr. Hardwick has concluded an 8 year term as Secretary of the International Academy of Pathology - the world’s oldest and largest academic pathology organization. During this period the IAP has been excited to provide pathology education to under-served areas of the world through reactivated and expanded country Divisions and Assemblies of nations - Asia Pacific Assembly, Latin American Assembly, African Assembly and European Assembly - a foundation for future successes.

Dr. Hardwick and Leslie Marsh’s book published by Palgrave Macmillan ‘Propriety and Prosperity - New Studies on the Philosophy of Adam Smith’ contains contributions by 15 global leaders in economics and philosophy.

LONG SERVICE AWARD
Thanks for the memories
Creative Science is an initiative conceived by Dr. Niamh Kelly, Associate Professor in the Department of Pathology and Laboratory Medicine. It began in 2010, as a response to a need for improved science education. It is a program directed at high school students, which incorporates creativity into the science learning process.

The conversation about science education centers around a need for improved scientific literacy for all citizens and improved access to science as a career choice, particularly for women and minorities. The goal of the Creative Science program is for high school students to come to view science as a skill for life, and a subject that is worthwhile studying throughout their schooling.

For many years, Dr. Kelly has been an active proponent of bringing scientific knowledge from the academic university setting into the community. The Creative Science program sprung from a collaboration between Dr. Kelly and Dr. Carol-Ann Courneya, who was managing an initiative to challenge UBC medical students to create artistic pieces inspired by their emerging knowledge of the cardiovascular system. Dr. Kelly expanded on that theme to engage high school students (grade 8-12) in science through arts. Students are introduced to the program during a field-trip to UBC; at various educational sites including our own William Boyd Museum of Pathology.

During the subsequent months, as they work through their science curriculum, they are challenged to represent their understanding of key scientific concepts through the creation of an artistic piece in a medium, or genre, of their choice. The program has been running in several Vancouver secondary schools since 2010, and has also expanded into the Surrey school district this year.

Creations presented to date range from visual art to photography; from culinary art to fabric art; from short stories, novellas and plays to comic books; and, from board games to YouTube videos, some of which can be viewed on our website, www.explorecuriocity.org/community/actionprojects/CreativeScience/FeaturedProjects.aspx (follow link, then select "Creative Science" and then "Featured Projects").

A vital component of the success of this program is that university students from the arts and the sciences, including several Pathology graduate students, are recruited as mentors. High school students are placed in interdisciplinary groups with the mentors, who connect with the students online, answering their questions and offering formative feedback at regular intervals.

The project has successfully engaged several other UBC students in various voluntary roles, including web
development and mentorship coordination. Mentors have given feedback that they enjoyed gaining teaching experience and skills in science communication through their mentoring roles. High school students have gained new perspectives on their capabilities in both the arts and the sciences, and have benefited from exposure to student role models from UBC and Emily Carr University of Art and Design. Teachers we have worked with say that the program has opened up many possibilities for students in self-directed and creative learning methods.

The project is now in its fifth year, and has been awarded NSERC PromoScience funding to allow for its ongoing expansion and to facilitate research into outcomes associated with this ‘creative’ approach to science learning. Dr. Jane O’Hara has been hired as Creative Science Project Director thanks to this funding. With an interest in shifting students' attitude toward science, we have developed “Attitudes and Beliefs about Science” surveys which are being completed by students engaged in the project this year. Also this year, we have partnered with the Great Northern Way campus to host an exhibition of students’ creative Art/Science pieces. We are interested in making this an annual event. If you would like to become involved with this outreach venture, or would like to know more, please email Jane at: johara@brc.ubc.ca.

UBC Neuroscience graduate student making an assessment of a triptych (a three-panelled artwork) representing the processes of DNA replication, transcription and translation, created by a grade 12 student.

Mentors were invited to assess creative works produced by students; in 2012, 75 projects were brought to the Pathology Education Centre, and assessed by over 50 UBC student mentors, including several Pathology graduate students. This photo shows three students (on the left is Pathology PhD student, Sara Saberi) making an assessment of a comic book representation of DNA synthesis made by a grade 12 student.
Competition

AUTHOR: MICHELLE DITTRICK, RESEARCH PROGRAM MANAGER
PATHOLOGY & LABORATORY MEDICINE
CHILDREN’S & WOMEN’S HEALTH CENTRE OF BC

Congratulations to Dr. Jeff Terry and Dr. Suzanne Vercauteren!! Two Children’s & Women’s clinical research teams each receive a pair of small project grants.

Dr. Jeff Terry is off to a very successful start of his career at C&W. Jeff joined the site as a pediatric & perinatal pathologist in August 2014. From the onset of his appointment he expressed a keen interest in research, with a focus on examining genetic expression using archival placenta specimens. A collaboration was soon formed between Dr. Terry and Dr. Wendy Robinson’s team at the Child & Family Research Institute to study potential markers of amniotic fluid infection (a complication of pregnancy where the placenta, membranes, and fluid surrounding the baby in the uterus becomes infected). Already, the team has received two small project grants which nicely complement one another. A CFRI Clinical Translational Seed Grant was jointly awarded to Dr. Jeff Terry & Dr. Irina Manokhina, post doctoral fellow in Dr. Wendy Robinson’s lab, for their project entitled MicroRNA Profiling in Acute Chorioamnionitis Using Archival Placental Tissue. This study represents the initial phase of development of a blood test for amniotic fluid infection (AFI) and involves identifying changes in placenta that occur in response to AFI. To achieve this, miRNA profiling will be used to examine widespread genetic changes in placentas affected by AFI will be compared to normal placentas, as infected placental tissue shows a genetic response to the infection. The results of this comparison will identify specific genetic markers in placenta that change when AFI occurs. These markers will then be investigated further in subsequent studies with the goal of developing a blood test that can detect AFI before development of complications, such as preterm labor. Such a test could have a significant positive impact on both short and long term outcomes for children, mothers, and families affected by AFI.

Secondly, a BC Children’s Hospital Pathology & Lab Medicine Microgrant was awarded to Jeff for a project entitled The Optimization of a Chromogenic in situ Hybridization Protocol to Detect miRNA in Archival Placental Tissue. An important supplement to the aforementioned study, this project aims to confirm localization of miRNAs to placenta and to confirm changes of miRNA expression detected by qRT-PCR using a second, unrelated method.

Visualization of miRNAs by in situ hybridization has been developed and employed successfully for FFPE tissue, however, these applications have been in the research setting and the use of these approaches on standard archival FFPE tissue from pathological specimens has not been described. The objective of this research proposal is to optimize a miRNA chromogenic in situ hybridization (CISH) protocol for standard archival placental specimens and to apply it to detection of miR-210, which has been identified in our preliminary qRT-PCR studies as decreasing in response to AFI, and miRNA-141, which is very highly expressed in placenta and detectable in maternal serum, to demonstrate the applicability of this approach.

Dr. Suzanne Vercauteren, in collaboration with Dr. Gregor Reid’s Lab at CFRI and with Dr. Patrice Eydoux, has also received funding from both the CFRI Clinical Translational Seed Grant and the BCCH Pathology & Lab Medicine Microgrant. Their research program Prospective generation of pediatric leukemia relapse by xenotransplantation has a long term goal of improving personalized treatment of childhood leukemia. Children with leukemia who have detectable disease after their initial chemotherapy are at significantly greater risk of relapse than children in whom the leukemia is no longer detectable. However, at present there is no way of predicting the sensitivity of the future relapse to different chemo- or targeted therapies. The research team will approach this problem using two complimentary studies. First, they will attempt to expand leukemia cells in mice using leukemia-positive samples obtained from children on therapy and will compare the cells that grow in the mouse to those that progressed in the patient. Secondly, they will perform cytogenetic microarrays on mouse-derived samples and patient relapse samples. Microarrays performed for clinical purposes at diagnosis will be reviewed and used as comparators. This will allow the team to evaluate whether similar clones were selectively expanded in the two environments. If successful, this program may provide the basis for a reliable method to evaluate potential relapse leukemia cells before they become apparent in the patient. This would allow therapy regimens to be optimized prior to onset of the clinical emergencies.
Summary:
Viruses are everywhere; they are found in all living species, including farm animals. However, as long as the animals are healthy, their defense systems (immune system) keep them under control. About 10,000 years ago, humans learned to domesticate certain docile animal species, and to breed them for food and clothing. These farming practices worked reasonably well, except for the occasional outbreak of viral diseases such as foot and mouth disease, cattle plague (rinderpest), African swine fever, avian influenza, and salmon rhabdoviruses. However, since the advent of intensive industrial farming practices after World War Two, these and other animal virus diseases have become much more frequent, as a consequence of the stressful existence of the animals. In these conditions the animal defenses can no longer control the viruses, which then multiply and disseminate freely. Sophisticated gene sequencing techniques have shown that, each time one of these viruses multiplies, they mutate to produce new strains. Sometimes these new virus strains are more pathogenic (disease inducing) than their predecessors, and can spread to new species, including wildlife. The international global trade in animals helps this process.

Professor Hudson attempts to explain all this in language suitable for the general reader, with help from accompanying light-hearted anecdotes and illustrations. He also encourages us, faced with the prospect of ever increasing industrial farms, to reconsider how we really want to produce our food.
Nickolas Myles, MD, PhD, FRCPC
Anatomical Pathologist, St. Paul’s Hospital
Clinical Assistant Professor
Department of Pathology and Laboratory Medicine
University of British Columbia

Life-long learning: pathologist learning evidence-based medicine

Looking back, less than one year after completing MSc Evidence Based Medicine at the University of Oxford, UK: A retrospective view from Dr. Nick Myles (Nikita Makretsov), Clinical Assistant Professor of Pathology, St. Paul’s Hospital Vancouver, Canada
WHAT PROMPTED ME TO STUDY FOR AN MSC IN EVIDENCE-BASED HEALTH CARE?

N.M.: The decision to start work on another degree (having completed a PhD in Oncology in 1995, an MD 1993, and two residencies in pathology in 1996 and 2004) was not an easy one. Part time study for a full time pathologist means effectively no holidays or weekends for several years. As an anatomical pathologist, a lot of our work is still largely based on expert opinions and assumptions that everything pathologists do is of benefit for the patients. I was inspired to learn that the main objective of evidence-based medicine is to develop sustainable health care for REAL benefits for our patients, based on scientific proof. The University of Oxford Center of Evidence Based Medicine was the best place to learn the nuts and bolts of evidence-based medicine, directly from the world leaders in the field. Luckily, as I quickly realized, Oxford offered an excellent culture immersion by mixing intense and demanding study time with lovely socials and brainstorms during mid week pub-crawls.

HAS THE OXFORD MSC HAD AN IMPACT ON MY PROFESSIONAL LIFE?

N.M.: During my dissertation (thanks to support from Dr. Blake Gilks, co-director of CIQC – Canadian immunohistochemistry quality control program and John Garatt, CIQC program leader), we prospectively collected and analysed 5-year longitudinal data provided by about 80 Canadian pathology laboratories on the diagnostic accuracy of estrogen and progesterone tests in breast cancer. The ER and PR tests are critical decision making points for medical oncologists, as they are used to predict benefit from hormonal therapy in breast cancer, which has been convincingly shown to reduce long-term mortality. As with any cancer drugs, they have significant side effects and therefore a personalized approach is necessary, and this requires accurate test results. To make testing reliable and comparable, good quality control procedures are necessary. My goal was to develop a practical methodology for quality control, to account for the inevitable test errors (due to the sensitivity and specificity of the reagents) and to use statistical modelling techniques to reliably identify the outliers and drifters while avoiding false alarms.

Under the guidance of Dr. Sue Mallett from Oxford and with help of Dr. Teresa Peres, a senior statistician from Madrid, we developed this methodology from learning about diagnostic accuracy. We were able to visualize a large amount of test data as forest plots of test sensitivity and specificity. Their 95% confidence intervals showed the range of uncertainty in quality control assessments. We also explored several methods of modelling to compare the diagnostic accuracy among different laboratories. We observed unique patterns of statistical distribution in the data, and interpreted this for quality control in pathology. This is the first time that this has been done, to my knowledge. I am very pleased that this methodology is under consideration for implementation by Canadian Immunohistochemistry Quality Control. I expect that statistically robust and evidence-based quality control will have a profound effect on oncology practice. Although it is indirect, patients will benefit in different regions of Canada and around the world, as reliable and reproducible laboratory breast cancer testing will have a potential to maximize the treatment benefit while avoiding unnecessary exposure to cancer therapy in a more personalized and targeted way.

Having Oxford credentials is an extremely valuable addition to my academic background as a breast cancer pathologist and clinical researcher. I co-ordinated the business meeting of the European Society of Pathology in London this past September. The organizing committee agreed to include an evidence-based agenda for the first time in the history of this society. I am proud to be among the invited speakers at this meeting. Also, recently the Royal College of Physicians and Surgeons of Canada has supported my application for further professional development through a grant in EBM. I am excited that I was able to take an additional module “Teaching Evidence-based practice” in Oxford past fall and re-join EBM learning community!

HOW DO I SHARE MY LEARNING WITH MY COLLEAGUES?

N.M.: With support of my colleagues at St. Paul’s we’ve initiated a transformation of our departmental journal club into critical appraisal pathology sessions. The feedback has been overwhelmingly positive. I have submitted several abstracts to European and Canadian pathology meetings based on the results of my research. I am also thinking about my MSc dissertation publication in a format of a small book.

WHAT IS MY NEXT CHALLENGE?

N.M.: My immediate challenge is the implementation of evidence-based practice into pathology and laboratory medicine. One of the common misconceptions about EBM is that it is all about medical interventions and clinical trials and is not applicable to laboratory diagnostic testing. My goal is to remove this misconception and spread the word about modern EBM in the pathology community through critical appraisal and teaching of evidence-based practice (and perhaps future participation in biomarker-driven genomics clinical trials) as hugely applicable to the area of modern diagnostic testing.
BC Cancer Agency scientists make an internationally significant discovery, mapping the evolution of breast cancer ‘avatars’

A just-published paper in the prestigious journal *Nature* highlights how researchers at the BC Cancer Agency are using human breast cancer ‘avatars’ — models of human breast cancers — to measure how complex cancers develop and change over time.

The research is unprecedented because it uses single cancer cells to expose how breast cancers evolve, and how to identify the cell populations that expand and dominate over time.

“We can now look at cancer as a kind of cellular superbug, with the ability to change over time and in response to treatments,” said Dr. Samuel Aparicio, head of the BC Cancer Agency Department of Molecular Oncology, Nan and Lorraine Robertson Chair of Breast Cancer, Professor, University of British Columbia, and senior author of the paper. “Because of this research we have a way to identify the cancer ‘super-cells’ and stay one step ahead of disease progression.”

The study is the most comprehensive lab model of analysis of cancer evolution. It uses a combination of genomic sequencing and a novel computational model—PyClone — developed by BC Cancer Agency scientist. Dr. Shah is the co-senior author of the study and the Canada Research Chair in Computational Cancer Genomics. The team, including authors Dr. Peter Eirew, Adi Steif and Jaswinder Khattra, has set a gold standard for the measurement of breast cancers’ evolution over time —resulting in a critical standard for future pre-clinical drug testing. The published findings provide the global cancer community with an invaluable method to track the cell populations and mutations that dominate and emerge as the driving force of a person’s cancer.

“We now have the ability to determine which individual cancer cells are the ‘resilient’ ones, which, if left untreated, will have the most impact on patient survival,” said Dr. Shah, scientist, BC Cancer Agency, and Associate Professor, University of British Columbia, Departments of Pathology and Laboratory Medicine and Computer Science.

The research, vital to future drug studies, proves that treating cancers is akin to shooting at a moving target. Different cell groups within a complex cancer have varying abilities to survive and grow, and this causes the composition of the cancer to change over time and in response to drug therapies. Until now, the evolution of a patient’s cancer has been largely overlooked from a treatment perspective without a way to accurately analyze and measure the changing cell populations. With the power of genomic sequencing being integrated into patient trials at the BC Cancer Agency, this major advance comes at a critical time, providing a model to determine a cancer’s growth trajectory.

“Today, we are light-years ahead in the understanding of cancer, thanks to the work of Dr. Aparicio and Dr. Shah and their research colleagues, who have the support of BC Cancer Foundation donors in their ability to influence the next wave of targeted cancer care,” said Douglas Nelson, President & CEO, BC Cancer Foundation.
Quick Facts

- Research was conducted in lab models using patient-donated human breast cancer tissue samples, so-called “avatars” of human cancer.

- The team’s novel approach combines technologies to sequence mutations in individual cancer cells with powerful statistical models (PyClone) to determine how different cell populations evolve over time.

- The research was carried out by lab scientists and “bioinformaticians” at the BC Cancer Agency and University of British Columbia, in collaboration with the University of Cambridge.

- Human cancers, including breast cancers, are comprised of many clones (cell populations) which have differing mutations and evolve dynamically in space and time. The study shows a level of predictability in the evolution patterns even in complex cancer cases.

- Understanding how different cell populations evolve is key to understanding how cancers become resistant to drugs, and may lead to the development of new combination drug approaches targeting different cell populations at the same time.

- The study shows that evolution is more extensive in cancer avatars than had been previously thought. This is vital information for scientists conducting lab-model based drug testing.

- Genomic mutations identified at the time of diagnosis are important factors in determining how the cellular make-up of a cancer may change over time.

- Research points to the importance of studying the clonal dynamics (cell populations) in future investigations of drug response and tumour biology.

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“We now have the ability to determine which individual cancer cells are the ‘resilient’ ones, which, if left untreated, will have the most impact on patient survival.”

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The BC Cancer Agency, an agency of the Provincial Health Services Authority, is committed to reducing the incidence of cancer, reducing the mortality from cancer, and improving the quality of life of those living with cancer. It provides a comprehensive cancer control program for the people of British Columbia by working with community partners to deliver a range of oncology services, including prevention, early detection, diagnosis and treatment, research, education, supportive care, rehabilitation and palliative care. For more information, visit www.bccancer.bc.ca.

The BC Cancer Foundation is the bridge that connects philanthropic support and research breakthroughs in cancer knowledge. As the fundraising partner of the BC Cancer Agency and the largest funder of cancer research in this province, we enable donors to make contributions to leading-edge research that has a direct impact on improvements to cancer care for patients in British Columbia. We fund with the goal of finding solutions.

Finding genetic clues to intellectual disabilities

Sophisticated new DNA analyses are offering families invaluable information that will help in the care of new syndromes

For most people with intellectual disabilities (ID), and their families, knowing the genetic cause of a disability would be of great value, offering new understanding and possibilities for improved care.

Standard chromosome analysis methods help diagnose some disabilities, such as Down syndrome, but causes of many other forms of intellectual disability that affect millions of children can’t be found this way. Not knowing what caused an ID and what health issues lie ahead is a hardship for many parents.

University of British Columbia researcher Dr. Evica Rajcan-Separovic has taken on the challenge of finding genetic causes for IDs that currently defy detection, leading eventually to improved care.

With co-investigator Dr. Suzanne Lewis, a UBC clinical professor in Medical Genetics, support from BC’s Children’s Hospital, Child and Family Research Institute and many genetic centers countrywide, Dr. Rajcan-Separovic assembled a study population of 1,000 children. Most of the children were from BC and were identified as having an ID with no known cause.

“Previously, children with developmental delay would only have chromosome testing,” said Dr. Rajcan-Separovic. “But microscope analysis is low resolution and an abnormality of a small segment of DNA can be easily missed.”

To get a better look at chromosomes the team initially went beyond microscopic analysis to the intricate process of chromosome microarray analysis.
A patient’s DNA is compared segment by segment to normal DNA. Mutations such as deleted or duplicate genes are highlighted by a computer analysis.

Using microarray analysis, the team found that 150 of the 1,000 ID’s tested did indeed have genetic defects, which could be the cause of the children’s developmental delays.

Strikingly, two of the children had hidden genetic abnormalities that became key elements to Dr. Rajcan-Separovic’s breakthrough research.

The pair, an unrelated girl and boy from BC, had the same genetic defect. In the long thread-like structure of a single chromosome, the microarray revealed that a single, almost identical, segment of genetic material was missing from both children. The pair shared abnormalities of facial features, had visual impairment, behavioural issues and a range of other common physical abnormalities and health issues.

“The geneticists who saw the two children commented that they resembled each other as if they were siblings,” said Dr. Rajcan-Separovic.

The children’s matching genomic and clinical data, led to the description of a new microdeletion syndrome of ID. After the research was published, geneticists around the world identified 20 new identical cases, creating a new source of shared information for the families. “If you know there is a possibility of early onset of health issues, for example impaired vision or kidney problems, in a child with a syndromic ID, measures can be taken to possibly avert or minimize those adverse outcomes,” says Dr. Rajcan-Separovic.

The next step for the UBC team is unravelling the ID mystery for the remaining 850 children in their group. No cause, genetic or otherwise has been found for their disabilities. The researchers are stepping up their investigative technology to use next generation genetic sequencing. This approach will detect abnormalities at a nucleotide level, the smallest component of a single DNA molecule.

Dr. Rajcan-Separovic is an Associate Professor in the Department of Pathology, UBC, Clinical Cytogeneticist in the Department of Pathology in Children’s and Women’s Hospital; and Scientist at Child and Family Research Institute.
This is an unprecedented time for those involved with pathology and laboratory medicine in our province; however, the Minister of Health has promised to move thoughtfully through this process. A new entity will take time to put in place and the current lab service delivery model will remain status quo for the next few years.

The Lab Reform Act, passed in April 2014, enables the government to organize pathology and laboratory medicine services under a single legislative structure for BC. Taking this provincial approach to laboratory management is seen to have several benefits, including an opportunity to improve quality and patient safety through province-wide standardization and implementation of best practices. Provincial governance could also result in optimization of lab services and implementation of a standard test menu for the province. One menu would improve the process of adding new tests and remove tests that are redundant or are no longer clinically relevant. The greatest opportunity expected from a move to a provincial structure will be the ability to reinvest savings (gained from improvements and efficiencies) directly back into the lab system.

Since passing the Lab Reform Act, the Ministry of Health has been consulting with health authorities and doctors of BC, on provincial lab governance and structure, as well as what regulations need to be in place to commence the Act. At the recent BC Association of Laboratory Physicians (BCALP) meeting, the Deputy Minister of Health shared that the Ministry is considering a provincial lab entity outside of the existing health authorities, although at this time no firm decision has been made. The proposed provincial lab agency would operate within a new provincial body, reporting to a separate Board of Directors.

The initial role of a provincial lab agency would be to set provincial pathology and laboratory standards and to oversee the overall budget for laboratory medicine, which could include service contracts with private providers and service level agreements with public providers.

Patient care and service to health care providers remain a priority. The Minister of Health has committed to the creation of a lab advisory committee, reporting to him, to advise on key lab agency and service issues. It is also likely that the new Board, to which the lab agency would report, would include a minimum of two lab physicians. In 2016, up to $10 million has been committed to address outstanding clinical workload needs and to implement the academic framework for laboratory physicians. BCALP and
the Ministry of Health are expected to begin work on those areas shortly.

The actual legislation for the Lab Reform Act is expected to commence in the fall. By that time, it is anticipated that the Minister will have appointed a Board of Directors and begun the initial steps to construct a provincial lab organization. Once the legislation is enacted and the provincial lab agency is up and running, negotiations with the health authorities and planning of future lab services will begin.

This is an unprecedented time for those involved with pathology and laboratory medicine in our province; however, the Minister of Health has promised to move thoughtfully through this process. A new entity will take time to put in place and the current lab service delivery model will remain status quo for the next few years.

A provincial system will offer even more opportunities to share best practices and to improve quality, safety and service. I know that we will all be an integral part of shaping this provincial pathology and laboratory medical system.
Our Department would like to extend a formal welcome to an outstanding group of faculty members who arrived in Fall/Winter 2014/15

CHEN WANG, PHD, MSC
Visiting Scientist

My name is Chen Wang. I graduated with a doctor degree from China in September 2012 and now I’m working here as a visiting scientist with Prof. Honglin Luo. We’re going to identify the role of autophagy in the pathogenesis of dilated cardiomyopathy. Besides doing research, I enjoy doing sports like climbing, hiking, swimming and playing badminton. I’m so happy to be here and looking forward to working with everyone.

BO RAFN, PHD, MSC
Post Doctoral Fellow in the lab of Dr. Sorensen

I have a background as a biological and chemical research technician, working for two years at the Danish diabetes health care company Novo Nordisk A/S. During this work I became inspired to do independent research and started studying Biochemistry. I obtained both my MSc and PhD at the Danish Cancer Society Research Center and University of Copenhagen, Denmark. Thus far my research focus has been on aberrant receptor tyrosine kinase (RTK) signaling with a special emphasis on invasive ErbB2 signaling transduction pathways in breast and ovarian cancers. In April 2014 I joined Dr. Poul Sorensen’s group in Molecular Oncology at BCCRC on a project based on the hypothesis that reactive oxygen species (ROS) is instrumental for transformation by oncogenic RTKs, and that the RTK-driven ROS generation is tightly regulated through specific signaling events. Beside my work here I enjoy to spend time with my wife and little daughter. I often listen to music and do physical exercise like hiking, running and playing different kinds of racket sports.

NAOYA TANABE, MD, PHD
Post Doctoral Fellow in the lab of Dr. Hogg

Hello everyone. My name is Naoya Tanabe. I came from Japan. I am a pulmonary physician and researcher. Several months have passed since starting my work in Vancouver, and I would really like to thank all the members for helping me to adjust to my new environment. In my PhD course in Japan, I studied the mechanism of the development and progression of COPD, especially emphysema, by using CT images in human and histology in animal models. Now I am working on micro CT, histology and gene expression analysis to reveal the structural and molecular features of different emphysema subtypes and COPD phenotype.

I have two lovely daughters, and playing with them in my free time is a great pleasure. I greatly look forward to meeting you.

ANILKUMAR PARAMBATH, PHD
Post Doctoral Fellow in the lab of Dr. Kizhakkedathu

I am a chemist working on the development of novel materials for applications in biology and medicine. I studied Chemistry at University of Calicut, Kerala, India for my Bachelors and Masters Degrees. I researched on the development of supramolecular templates for fine tuning nanostructures of electrically conducting polymers in the laboratory of Prof. M. Jayakannan at National Institute for Interdisciplinary Science and Technology (NIIST), Trivandrum, Kerala, India for my PhD in 2010. Subsequently, I moved to the laboratory of Prof. Y.-P. Sun at Clemson University, USA to study the chemistry of carbon nanostructures. After spending two years at Clemson, I joined the research group of Dr. E. Doris at Institute of Biology and Technology, Commissariat à l’ Energie Atomique (CEA), Saclay, France and worked on the development of therapeutic nanomicelles. Recently, I joined the laboratory of Prof. J.N. Kizhakkedathu at Department of Pathology and Lab Medicine. At UBC my work involves the development of new polymer systems for applications in proteomics and smart catheters development. My research interests are in the areas of polymer chemistry, materials chemistry and nanoscience. From my previous research activities I have published 26 research papers and one book chapter.

In my spare time I enjoy watching movies, listening to music and...
BING WANG, MD, PHD, FRCPC, DABMM
Clinical Instructor, Kelowna General Hospital

I am excited to join the Department of Pathology and Laboratory Medicine as a medical microbiologist. I received my MD and PhD from Sichuan University, China, and completed my residency at the University of Ottawa, Ontario. I am currently working in the Interior Health microbiology service and Infection Control based at Kelowna General Hospital. My research interests include utilization of advanced technology to improve the quality of microbiology service and yeast susceptibility. I am involved in teaching medical students and supervising student research projects. I look forward to working with my colleagues in the Department of Pathology and Laboratory Medicine.

Outside of work, I enjoy spending time with my family and hiking in beautiful BC. I like to read my favorite novels in my backyard with Okanagan Lake and the Kelowna Mountain in the background.

STEVEN YUE SHEN, MD, PHD
Post Doctoral Fellow in the lab of Dr. Granville

I completed my medical training at Shanghai Medical College Fudan University in 2004 and worked as a physician at Shanghai Center for Disease Control and Prevention for 3 years. In 2007 I moved to Sweden and completed my PhD in medical science at Umea University. During my PhD training, I learned microsurgery techniques and became one of the few in Europe who can perform myringotomy and tympanoplasty on mice. In February 2014, I joined Dr. David Granville's laboratory at Centre of Heart Lung Innovation, St. Paul's hospital, UBC. I am now working on research projects related to cardiac fibrosis, radiation-induced dermatitis and diabetic wound healing.

In my spare time I enjoy watching movies and playing with my daughter.
PATHOLOGY MOSAIC

Each of us a mosaic
composed of tiles;
Symphonies of experience,
places and beings.

Some tiles background noise
Others so bright we are
seemingly blinded.

Years pass, patterns
become more intricate;
awe-inspiring.

Time shared here
adding tiles altering
self-perception to
Enhance brilliance.

Beyond the symphonic intensity
The eternal glow of
Your tile nestles inside
Like Autumn colours,
Warmly comforting.

AUTHOR: J. XENAKIS