



MD/PhD Program Newsletter



Dr. Carol P. Herbert

Dean

Greetings from the Dean

Congratulations on the first issue of the Schulich MD/PhD Newsletter.

I take great pride in this program which responds to the need for career clinician-scientists that has been identified as a leading program not only locally, but also worldwide. Over the past few years, our MD/PhD program has grown significantly, as we work to build a cadre of Canadian research leaders who have committed to becoming clinician-scientists by taking this educational path. We are very proud of the excellent training that our MD/PhD students receive in the laboratories of their supervisors and mentors, and of their concurrent outstanding undergraduate medical education. Through the dedication of the leaders of our program, we have been able to provide personal attention to the needs and desires of our students. Our graduates are positioned for success, and I look forward to celebrating their achievements in the future, and welcoming many graduates back as faculty members at Schulich Medicine & Dentistry.

I hope you enjoy getting to know something about our students and program through the newsletter.



Welcome from Dr. Jim Lewis, Program Director

Although our MD/PhD program is in its early stages of growth, we have accomplished an enormous amount over the last few years. This newsletter is an opportunity to give our program a higher profile and generate excitement about our accomplishments.

As a clinician-scientist myself (Respirologist at St. Joseph's Health Care London and Principal Investigator at the Lawson Health Research Institute), I realize the complexity but importance of translating basic scientific discovery to the patient's bedside. Our program is structured to facilitate training of individuals who will ultimately be able to "bridge the gap" between the laboratory and clinical medicine. Currently we have 15 outstanding students in the MD/PhD program. Over the next few years, we will keep you up-to-date on their individual accomplishments both professionally and personally. We are very proud of the MD/PhD Program here at the Schulich School of Medicine & Dentistry, and I feel we are clearly defined by the quality and character of our students. I am honoured to be involved and am grateful for the support of Dean Herbert, as well as outstanding administrative and personal guidance from our program administrator, Vicki Vanstrien.

As always we welcome any comments and/or suggestions for improvement and hope you find this newsletter informative.

Details of our program, with descriptions and pictures of our students can be found on our website at www.med.uwo.ca/medicine/md_phd

Program overview:

The MD/PhD Program at Western, which officially began in 1995, aims to select a few exceptional students with a passion for research to combine this with undergraduate medical training. The MD/PhD Program fosters training with a leading scientist and the integration of laboratory work and medical school, and as well compresses the time to obtain both degrees to just seven years.

Recently, the program has grown in both visibility and numbers, now boasting 15 students. We believe that we are still small enough to know and mentor our students...but we are certainly big enough to be on the map of elite clinician scientist training in Canada.

Our MD/PhD candidates represent a broad range of scientific research, genetics, kinesiology, and medical imaging, as some examples, in outstanding world-class laboratories. You will read about some of their successes in the next few pages.

Publications from our students:



Tom Appleton

1. Attur, M, Palmer, G, Al-Mussawir, H, Dave, M, Klar, A, Teixeira, C, Rifkin, D, **Appleton, CT**, Beier, F and Abramson, S (2008). F-spondin, a neuroregulatory protein, is upregulated in Osteoarthritis and regulates cartilage metabolism via TGF-beta activation. *FASEB J* In Press.
2. **Appleton, CT**, Usmani, SE, Bernier, SM and Beier, F (2007). Transforming growth factor alpha suppresses the chondrocyte phenotype and Sox9 expression in osteoarthritis. *Arthritis Rheum* 56(11):3693-3705.
3. McErlain, DD, **Appleton, CT**, Litchfield, RB, Pitelka, V, Henry, JL, Beier, F and Holdsworth, DW (2007). Longitudinal subchondral bone adaptations in a rodent surgical model of OA using in vivo micro-Computed Tomography. *Osteoarthritis Cartilage* 16:458-469.
4. **Appleton, CT**, Pitelka, V, Henry, JL, and Beier, F (2007). Global analyses of gene expression in early experimental osteoarthritis. *Arthritis Rheum* 56(6):1854-1868.
5. **Appleton, CT**, McErlain, DD, Pitelka, V, Schwartz, N, Bernier, SM, Henry, JL, Holdsworth, DW and Beier, F (2007). Forced mobilization accelerates pathogenesis: characterization of a preclinical surgical model of osteoarthritis. *Arthritis Res Ther* 9(1): R13. **BMC Highly Accessed Designation*



Mike Berger:

1. **Berger, MJ** and TJ, Doherty. The role of the neuromuscular system in the development, progression and rehabilitation of osteoarthritis of the knee. *Critical Reviews in Physical Rehabilitation Medicine*. 19(3), 2007 p. 227-249



Matt Cecchini:

1. Morley S, **Cecchini M**, Zhang W, Virgulti A, Noy N, Atkinson J, and Manor D (2008) Mechanisms of ligand transfer by the hepatic tocopherol transfer protein, *J Biol Chem* 283, 17797-17804.
2. Seifried LA, Talluri S, **Cecchini M**, Julian LM, Mymryk JS, and Dick FA (2008) pRB-E2F1 Complexes are Resistant to Adenovirus E1A-Mediated Disruption, *J Virol* 82, 4511-4520.



Derek Cool:

1. Bax J, **Cool D**, Gardi L, Knight K, Montreuil J, Sherebrin S, Romagnoli C, Fenster A. *Mechanically Assisted 3D Ultrasound Guided Prostate Biopsy System*. *Medical Physics* 35(12), Dec 2008.
2. **Cool D**, Sherebrin S, Izawa J, Chin J, Fenster A. *Design and Evaluation of a 3D Transrectal Ultrasound Prostate Biopsy System*. *Medical Physics* 35(10), Oct 2008.



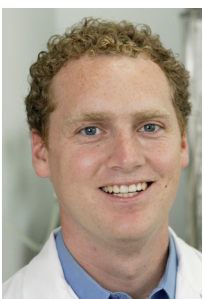
Mark Kirchof:

1. Tao Dong*, **Mark G. Kirchof***, Herb E. Schellhorn, RpoS regulation of exponential phase-specific genes in Escherichia coli K-12. *Molecular Genetics and Genomics*, 2008.
*these authors share first authorship
2. **Mark G. Kirchof**, Luan A. Chau, Caitlin D. Lemke, Santosh Vardhana, Peter J. Darlington, Maria E. Marquez, Roy Taylor, Kamilia Rizkalla, Isaac Blanca, Michael L. Dustin, and Joaquin Madrenas. *Modulation of T Cell Activation by Stomatin-like Protein 2*. *Journal of Immunology*, 2008.



Piya Lahiry:

1. **Lahiry P**, Al-Attar SA, Hegele RA. Beta-Thalassemia with focus on the Indian Subcontinent and the Middle East. *The Open Hematology Journal* 2008, pp.5-13 (9).
2. Joy T, **Lahiry P**, Pollex RL, Hegele RA. Genetics of Metabolic Syndrome. *Current Diabetes Report*. 2008, 8(2):141-148. PMID: 18445357.
3. **Lahiry P**, Pollex RL, Hegele RA.. Uncloaking the Genetic Determinants of Metabolic Syndrome. *J. of Nutrigenetics and Nutrigenomics*. 2008, 1:118-125.



Matthew Lanktree:

1. **Lanktree M**, Hegele RA (2008) Copy number variation in metabolic phenotypes. *Genomic Cytogenetic Res* Accepted.
2. **Lanktree M**, Oh J, Hegele RA (2008) Genetic testing for atherosclerosis risk: inevitability or pipedream? *Can J Cardiol* Accepted.
3. **Lanktree M**, Cao H, Rabkin SW, Hanna A, Hegele RA (2007) Novel LMNA mutations seen in patients with familial partial lipodystrophy subtype 2 (FPLD2; MIM 151660). *Clin Genet* 71:2:183-6.



Shirine Usmani:

1. Appleton CT, **Usmani SE**, Bernier SM, Aigner T, Beier F. Transforming growth factor alpha suppression of articular chondrocyte phenotype and Sox9 expression in a rat model of osteoarthritis. *Arthritis Rheumatology* 2007 Nov;56(11):3693-705.

Update on the Clinician Investigator Trainee Association of Canada:

By Tom Appleton

Clinician Investigator (CI) training in Canada has become a forerunning issue in recent years. To represent the interests of trainees with respect to CI training, the Clinician Investigator Trainee Association of Canada (CITAC) was officially launched in 2006. At the inaugural meeting (conjoined with the Canadian Society for Clinical Investigation (CSCI) meeting in Ottawa), several priorities were identified including a need to strengthen trainee networking in Canada and to collect and distribute data regarding current program structures, trainee satisfaction and long-term program outcomes.

CITAC's first year was spent organizing the association by defining and building a network of institutional representatives (2006 Western representative was Tom Appleton) and executives, formalizing short- and long-term goals and, in September 2007, the first annual general meeting (AGM) was held. The meeting was a great success, culminating in a formalized relationship with the CSCI, an established partnership with the American Physician Scientists Association (APSA) and feedback on future goals. Also at the meeting, Tom Appleton (MD/PhD 2011) was elected Vice President, External and Mike Berger (MD/PhD 2012) was elected Western institutional representative.

The subsequent year was extremely busy for the CITAC executive. First and foremost, CITAC representatives across the country worked with the CSCI to fundraise and plan for the annual Young Investigator Forum (YIF) which was held September 24-25 in Toronto, in partnership with Friends of the CIHR (FCIHR). The YIF was held in conjunction with the CITAC AGM where five new committees were struck, each with its own mandate. A strong contingent of Western MD/PhD students were involved in this year's AGM and into the coming year: Tom Appleton was re-elected Vice President, External, Mike Berger was elected Mentorship Committee Chair, Shirine Usmani (MD/PhD 2014) was elected Membership Committee Chair and Piya Lahiry (MD/PhD 2013) was elected Annual Meeting Committee Chair. A new Western institutional representative for CITAC has yet to be appointed. Tom Appleton also won the Best Poster Award in the poster competition at the Young Investigator's Forum.

In the past year, CITAC has also built important relationships with several Canadian and international associations. These include the CSCI, the Canadian Federation of Medical Students (CFMS), the American Physician Scientists' Association (APSA), the Swiss MD/PhD Association, the Association of Faculties of Medicine of Canada (AFMC) and several others.

Through several focus groups and surveys it was determined that mentorship is the most important aspect of training that is lacking in current Canadian CI training programs. Accordingly, CITAC has also developed a national Mentorship Program, through which all members of CITAC (all Canadian CI trainees) now have access to established clinician investigators with a wide array of clinical and research interests for career advice and guidance. There are currently over 60 mentors across Canada registered through the CITAC Mentorship Program. The CITAC Mentorship Program was officially launched at the 2008 AGM in Toronto and is accessible to members via the CITAC website. If clinician investigators have an interest in getting involved in mentoring through the CITAC program they are encouraged to contact the Mentorship Committee Chair, Mike Berger (MD/PhD 2012) via the CITAC website at: www.citac-accfc.org.

Meet our New Students

Western MD/PhD welcomed three new students this fall: Rohann Correa, Christopher Johansen and Pencilla Lang.

Pencilla enters her second year of medicine, and Rohann and Chris are beginning with their PhD Research. Rohann has offered his thoughts about his research project on the next page. Thanks Rohann!



Christopher



Pencilla



As one of the newest members of the Schulich MD/PhD program, I feel very fortunate to begin my studies with intriguing research that I'm truly passionate about. Initiating my PhD research in the Translational Ovarian Cancer Research Program has so far proven to be the perfect fit for an MD/PhD student. Under the direction of Drs. Gabe DiMattia and Trevor Shepherd, I'm looking forward to learning a great deal about molecular and cell biology, as well as developing the ability to formulate sound scientific questions and the right experiments to answer them. As an added bonus, the clinical connections our lab has established with gynecologic oncology surgeons allows me to participate in such things as disease site team meetings and interactive observerships in the OR, among others. Importantly, these are unique and fantastic opportunities to truly deepen my understanding and familiarity with the disease on which my research is focused.

Without a doubt, I find the work I will be doing in the next few years to be highly motivating. As I have learned, ovarian cancer is the most lethal of the gynaecologic malignancies. If caught early, ~90% of patients are cured, but unfortunately most cases are often detected at an advanced stage of disease when prognosis is dire. A key objective of our research program is to better understand the molecular signaling events that bring about and sustain peritoneal metastasis and subsequent hemorrhagic ascites accumulation, both hallmarks of advanced ovarian cancer. To this end, collaboration with gynecologic oncology surgeons at the London Regional Cancer Program has allowed our lab to acquire and bank primary epithelial ovarian cancer (EOC) cells derived from patient ascites. These cells are grown in a novel 3D suspension culture that accurately simulates patient ascites fluid and results in the formation of multicellular 'spheroids.' Very similar spheroids occur naturally in fresh ascites samples, and significantly, we have documented re-attachment and aggressive disaggregation of these in vivo spheroids – a process likely contributing to EOC peritoneal spread in the patient.

My project will focus on a few key proteins that are likely instrumental to spheroid (i) formation and maintenance, (ii) re-attachment to the patient's peritoneum, and (iii) disaggregation and establishment of a secondary nodule. Using our patient sample cells in 3D culture, as well as a novel ex vivo avian embryo model, I will analyze these proteins in the context of relevant signaling pathways (for example, pathways involved in the epithelial-to-mesenchymal transition or in the aberrant production of vascular endothelial growth factor). Subsequently, I will modulate activity/expression of these proteins using new and established targeted inhibitors as well as adenovirus/retrovirus-delivered over-expression and shRNA constructs. Through these experiments, I hope to build a better understanding of the significant signaling proteins important in advanced ovarian cancer, particularly in peritoneal dissemination of the disease. This could in turn lead to targeted therapies to manage and combat advanced stage disease, thereby reducing the heavy toll this malignancy takes on women in Canada and around the world.

Personal Student Updates/Congratulations to:

- **Derek (MD/PhD 2009)** and Erin Debicki on the birth of their daughter, Sydney Claire, a little sister for Noah. Sydney was born on June 19 and tipped the scales at 7 lbs, 13 oz.
- **Tom Appleton (MD/PhD 2011)** and Sonja Gustafson were married in London on Saturday, August 9.
- **Matthew Lanktree (MD/PhD 2011)** and Laura VanderBeek were married in Zurich on September 13.
- **Brenna Market (MD/PhD 2014)** and Vikram Velker were married in Windsor on August 3.
- **Piya Lahiry (MD/PhD 2013)** received the Canadian Institutes of Health Research, Institute of Genetics (IG) and the Canadian Gene Cure Foundation MD/PhD Studentship Award (2008-2013). Way to go Piya!
- **Brenna Market-Velker (MD/PhD 2014)** won first place for Best Graduate Student Presentation at the 2008 Paul Harding Research Day for the Department of Obstetrics and Gynaecology in May.