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IN FOCUS with Dr. Brigitte Thériault

Chasing Dreams from East to West: A Postdoc's Journey to Success

By Dr. Ghada Kurban

Dr. Brigitte Thériault, a postdoctoral fellow in Dr. Brenda Gallie's research group and a rising star in ovarian cancer research, was recently awarded the *Scientific Scholar Award* from the Marsha Rivkin Center for Ovarian Cancer Research. Dr. Thériault is the first Canadian trainee to ever receive this award. "The award offers partial salary and research funds for one year and is transferrable so that young investigators can transition from a Postdoctoral Fellowship to a Principal Investigator position while maintaining monetary support," says Dr. Thériault. This funding will allow her to continue her work on KIF14, a gene involved in ovarian cancer—a disease with dismal prognosis and ineffective therapies.

A native of New Brunswick, Dr. Thériault grew up on a farm near Moncton surrounded by nature, which ignited her scientific curiosity. Discipline was instilled in her at a very young age. She tended to the daily chores that govern farm life and excelled in school, setting an example for her three younger siblings. Her desire to understand how things work, coupled with the loss of her grandmother after a long and painful struggle with breast cancer, led her to pursue a diploma in Health Sciences at the Université de Moncton. She then moved to Halifax, where she completed a BSc in Microbiology and Immunology at Dalhousie University. After graduation, Dr. Thériault worked as a Research Technician for the Canadian Food Inspection Agency, then as a Research Associate at a medical biotechnology company, and finally as a Laboratory Manager at an academic research lab at Dalhousie University. "Reimmersion in an academic

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May 2012

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University Health Network

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research environment made me realize how much I missed the thrill of scientific discovery and this prompted me to pursue my graduate studies," says Dr. Thériault. In 2003 she enrolled as a PhD candidate in Dr. Mark Nachtigal's group at Dalhousie, in the field of ovarian cancer research.


Dr. Brigitte Thériault

During this time Dr. Thériault met Dr. Brenda Gallie, a world-renowned expert in retinoblastoma. Gallie was invited to give a seminar as part of a distinguished lecture series at Dalhousie Medical School. Her group had just identified KIF14 as a gene that is not only altered in retinoblastoma, but also in other cancers, like ovarian cancer. "Brigitte was a brilliant student who stood out at a group lunch and was highly motivated to find out about KIF14 in ovarian cancer," says Gallie. After a formal interview Dr. Thériault joined Gallie's group in 2008, excited to pioneer a new translational research project in ovarian cancer.

In 2009, Dr. Thériault received a three-year grant from the US Department of Defense to continue her timely research on KIF14 and has since developed an extensive ovarian cancer research program in Dr. Gallie's lab. "She is quick to make connections between scientific concepts and synthesize logical hypotheses to drive a project. She is also a great person to work with," says Nadia Prigoda who works closely with Dr. Thériault.

Dr. Thériault's work has demonstrated the clinical utility of KIF14 as an independent prognostic indicator and potential therapeutic target in ovarian cancer. She hopes to pursue translational research in ovarian cancer as an independent principal investigator. The *Scientific Scholar Award* will allow her to study the cancer-specific epigenetic regulation of KIF14 expression in ovarian cancer. Dr. Gallie commends Dr. Thériault's independent thinking, humbleness and dedication to saving the lives of women with ovarian cancer. "She doesn't spend her time looking over her shoulder to see what others are doing—she doesn't jump on bandwagons. She does strong science, well thought-out science," adds Dr. Gallie. Dr. Thériault's work will provide the basis for future investigations into the fundamental pathways of KIF14-induced tumourigenesis and set the stage for anti-KIF14 therapy to improve the prognosis, outcome and cure rate in ovarian cancer.

About the author: Dr. Ghada Kurban is a Postdoctoral Fellow in Dr. Brenda Gallie's Laboratory at the Ontario Cancer Institute (OCI). Contact Info: gkurban@uhnres.utoronto.ca

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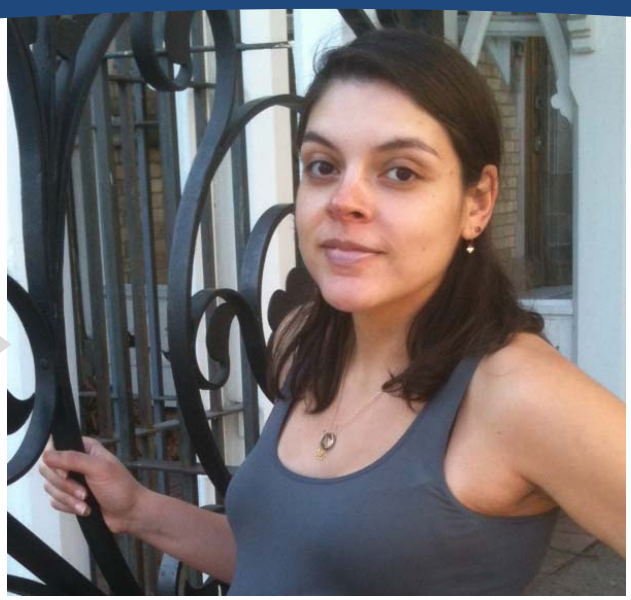
recent awardees

CIHR SHOPP Fellowship in Gastroenterolgy Research

Congratulations to Dr. Carmen Dominguez-Brauer on receiving the 2012 CIHR Small Health Organization Partnership Program (SHOPP) Fellowship in Gastroenterology Research!

In summary of her research, Dr. Dominguez-Brauer explains: “The Mule gene is overexpressed in half of all colon cancers. E3 ubiquitin ligases function to maintain a balance between oncogenes and tumor suppressors. The loss of this equilibrium usually results in cancer. These studies will allow us to understand the effects of Mule overexpression in cancer, and whether this results in tipping the scale from cell death towards cell growth.”



Postdoctoral Fellow: Dr. Carmen Dominguez-Brauer

Supervisor: Dr. Tak W. Mak
Ontario Cancer Institute
The Campbell Family Institute for Breast Cancer Research

Postdoctoral Fellow: Dr. Robin Cash

Supervisor: Dr. Robert Chen
Toronto Western Research Institute (TWRI)

CIHR SHOPP Fellowship in Dystonia Research

The 2012 CIHR Small Health Organization Partnership Program (SHOPP) Fellowship in Dystonia Research goes to Dr. Robin Cash!

Dr. Cash completed his PhD in Australia and have since completed postdoctoral projects in Germany and the USA before landing a position in Dr. Robert Chen’s Laboratory at TWRI as a Postdoctoral Fellow. His research program is entitled: “A novel brain stimulation intervention to investigate the pathophysiology and modulate plasticity in dystonia.”

Dr. Cash provides his thoughts about his award:
“It is thought that excessive excitability and plasticity in motor areas of the brain contributes to dystonia, a neurological disorder characterized by uncontrollable muscle contractions. We have recently developed a novel intervention using Transcranial Magnetic Stimulation (TMS), which is able to modulate brain activity. In this project we will investigate the efficacy of this protocol in reducing motor symptoms and further investigate the pathophysiology of dystonia. “

success

ORT travel awardees

ORT Conference Travel Awardees
Conference Report

This exciting section of *The ORT Times* will now include highlights of recent ORT Conference Travel Awardees. In this issue, learn about the latest discoveries in all fields of cancer research at the AACR annual meeting. Discover what recent advances in translational research in radiation oncology at the ICTR-PHE conference.

Dr. Shrivani Sriskathadevan is a Postdoctoral Fellow in Dr. Aaron Schimmer's laboratory. Recently, she was able to present her research at the American Association for Cancer Research (AACR) entitled, "AML cells have low reserve capacity in their respiratory chain complexes leading to increased sensitivity to palmitate induced cell death."

Click here to read about what she finds intriguing about the latest advances in Cancer Research.

Ms. Azusa Maeda, a MSc student in Drs. Ralph DaCosta and Brian Wilson's laboratory, was able to present her abstracts entitled, "*In vivo* optical imaging of tumor and microvascular response to ionizing radiation" and "Photoacoustic imaging for monitoring vascular oxygen saturation in response to ionizing radiation" at the International Conference on Translational Research in Radio-Oncology and Physics for Health in Europe (ICTR-PHE) held in Geneva, Switzerland.

Click here to read about key developments in biomedical imaging and proton therapy.

Dr. Ziqiang Yang is a Postdoctoral Fellow in Dr. Benjamin Neel's laboratory who He recently attended the AACR Annual Meeting in Chicago. He presented an abstract entitled, "Gab1 regulates epithelial cell polarity and scattering by acting as a platform for PAR proteins."

Click here to read about the latest discoveries in necrosis regulation.

Seventeen-gene signature from enriched Her2/Neu mammary tumor-initiating cells predicts clinical outcome for human HER2$^+$:ERα$^-$ breast cancer

Liu JC, Voisin V, Bader GD, Deng T, Pusztai L, Symmans WF, Esteva FJ, Egan SE, Zacksenhaus E.
Proceedings of the National Academy of Sciences (PNAS), 2012: 109(15):5832-7.
Toronto General Research Institute (TGRI)

Breast cancer is thought to represent a group of several breast tumour subtypes differing in molecular etiology, effective treatment options and patient prognosis. Breast tumours exhibiting overexpression or amplification of Human Epidermal Growth Factor Receptor 2 (HER2$^+$) are often the most aggressive, but have the option of treatment with anti-HER2 targeted therapeutics like trastuzumab. Until recently, it has been challenging to accurately identify a subset of high-risk HER2$^+$ breast tumours that lack expression of estrogen receptor alpha (ERα$^-$), and to predict whether these tumours will respond to anti-HER2 therapy.

Dr. Jeff Liu, a Postdoctoral Fellow in the laboratory of Dr. Eldad Zacksenhaus at TGRI, has begun addressing these challenges with his colleagues in the April issue of *PNAS*. The group first used a mouse model of HER2$^+$:ERα$^-$ breast cancer to identify genes whose expression correlated with enrichment of tumour initiating cells (TICs)—cells that have the capacity to sustain the growth of a tumour—in tumour samples. Expression levels of these genes were then queried in primary breast tumour datasets to derive a TIC-associated signature predictive of prognosis. Expression of this gene signature in HER2$^+$:ERα$^-$ tumours was associated with poor patient outcome and poor response to chemotherapy alone, but also with a promising response to trastuzumab.

Click here to read the full article.

We contacted Drs. Zacksenhaus and Liu to discuss the implications of this work.

ORT: How might this work lead to changes in patient care, and what will be required for its translation to the clinic?
EZ/JL: The new signature identifies high-risk patients that may be prioritized for chemo-/trastuzumab therapy. This may be particularly relevant to low-income countries where trastuzumab therapy, which cost over $40,000 per patient, is not publicly available. In contrast, the effect of trastuzumab on patients whose tumours were negative for the TIC signature was not statistically significant. However, the results do not justify at this stage withholding trastuzumab therapy from these patients. A prospective analysis of large cohorts is now needed to assess small benefits, if any, of trastuzumab in this group. The analysis has so far been performed on microarray data from RNA derived from fresh tumour biopsies. Using NanoString technology, we are now in the process of developing an assay that can be applied on formalin fixed, paraffin-embedded breast tumour tissues, which is the form in which tumours are archived in clinical centers around the globe. The application of this technology to large prospective cohorts of HER2$^+$:ERα$^-$ patients will allow translation of this prognostic signature to the clinic. A patent on this signature has also been filed.

ORT: What result did you find most intriguing in this project?
EZ/JL: The findings are important both conceptually and clinically. Conceptually they show that a signature derived from enriched TICs from a mouse model of a specific breast cancer subtype can predict clinical outcome for the human disease. These results should pave the way to the development of highly predictive signatures for other breast cancer subtypes (e.g., the multiple different “triple negative” breast cancer subtypes) as well as for other forms of cancers using enriched TICs from subtype-specific mouse models. Clinically, our findings are interesting because they identify previously unrecognized heterogeneity in human HER2$^+$:ERα$^-$ breast cancer patients that would impact future prognosis and treatment of this disease. In addition, our signature can improve the assessment of various therapeutic regimens on HER2$^+$:ERα$^-$ breast cancer patients by focusing on the signature-positive/poor prognosis subgroup.

UPCOMING EVENTS CALENDAR:

05/12 **Science Rendezvous.**
This is an annual festival celebrating Canadian science. Visit their site for more info.

05/14 **TWRI Seminar Speaker Series.**
Dr. Philipp Kaldis from the Institute of Molecular and Cell Biology (IMCB) will present "Functions of cyclin-dependent kinases (Cdks) in development and cancer." Location: TWH, WW 2-401.

05/16 **TWRI Research Day.**
This is a day to celebrate TWRI's achievements in basic and clinical research. Visit their site for more info. Location: Chestnut Residence, 89 Chestnut.

05/18 **AOMF Comprehensive Course.**
Deadline to register for the AOMF Comprehensive Course on Fluorescence Microscopy. Visit AOMF for details.

05/24 **IMS Career Seminar Series.**
"A career in Medicine and Research."
To register, email: imssacareers@gmail.com

Visit www.uhntrainees.ca for more information.

QUESTIONS?

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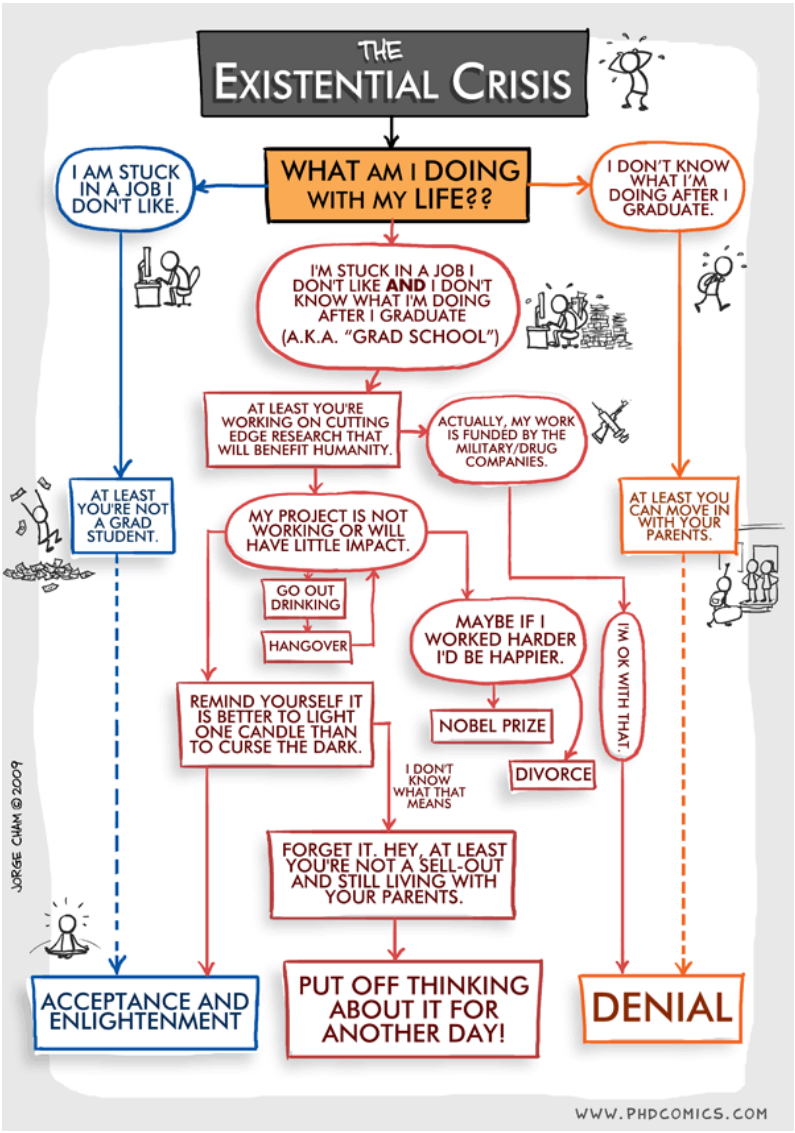
The ORT encourages trainees and scientists to send us pictures of the lab, departmental events, or eye-catching scientific images. Your submission may appear in *The ORT Times*' next issue.

(Photo: Courtesy of C. Bros, Penn Lab, OCI/PMH)



"Piled Higher and Deeper" by Jorge Cham
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