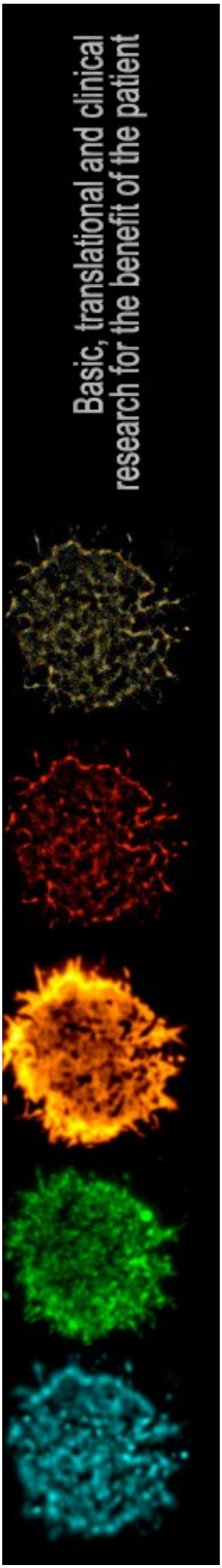


IMMUNOLOGY RESEARCH CLUSTER
MEDICAL UNIVERSITY OF VIENNA

IRC Double SEMINAR

David BRINDLEY

*(*University of Alberta, Edmonton, Canada*)*

”Coming of Age for Autotaxin and Lysophosphatidate Signaling: Clinical Applications for Preventing, Detecting and Targeting Tumor-Promoting Inflammation”

Denise HEMMINGS

*(*University of Alberta, Edmonton, Canada*)*

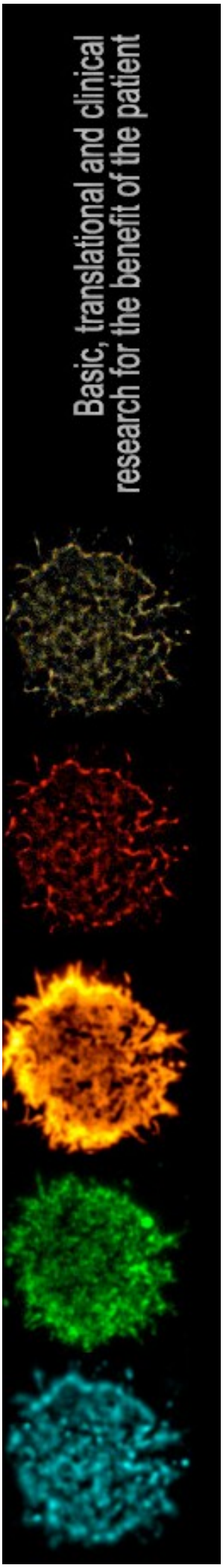
”Impact of chronic cytomegalovirus infection on breast cancer and aging”

Monday, 9th of September 2019
11 - 13 Uhr

Host: Diana Mechtcheriakova

Where: CeMM / Anna Spiegel Research Building,
Seminar Room, 3rd Floor,
Lazarettgasse 14, AKH BT 25.2, 1090 Vienna

cluster.meduniwien.ac.at/irc



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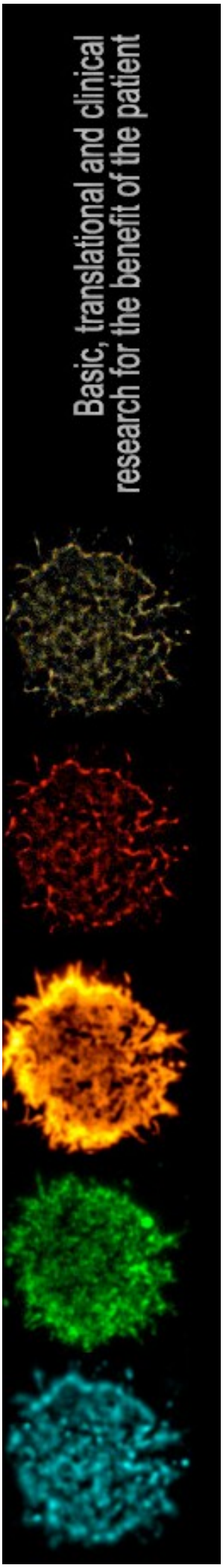
Biosketch

David Brindley studied for his PhD and his first postdoctoral fellowship in Medical Biochemistry at the University of Birmingham, England. This was under the mentorship of Dr. Georg Hübscher when he studied mechanisms for intestinal fat absorption. He spent his second postdoctoral appointment at Harvard University, Cambridge, MA, USA where he described the first bacterial multi-enzyme complex for fatty acid synthase under the direction of Dr. Konrad Bloch. He then returned to England as a faculty member in a new Biochemistry Department at Nottingham University. His main research was studying phosphatidate phosphatases (now called lipins) and their roles in regulating lipid and lipoprotein metabolism in the Metabolic Syndrome. He moved to Edmonton, Canada in 1988 to an appointment in the Biochemistry Department at the University of Alberta.

His work then led to the discovery of a second family of phosphatidate phosphatases, which are now called lipid phosphate phosphatases (LPPs). These enzymes regulate signalling by lysophosphatidic acid (LPA) and sphingosine 1-phosphate through their respective families of G-protein coupled receptors. The effects LPP1 on LPA counteract the actions of a secreted enzyme called autotaxin, which produces extracellular LPA. This knowledge changed the direction of the group because of the importance of LPA in stimulating the production of inflammatory cytokines and cyclooxygenase-2. This is part of a feedforward cycle since inflammatory cytokines increase further production of autotaxin and LPA. This inflammatory cycle is an important adaptation that facilitates wound repair. Conversely, chronic inflammation is maladaptive since it produces scarring, and immune evasion that promotes tumour growth and metastasis. The Brindley group is investigating how to use various anti-inflammatory agents to counteract the chronic activation of the autotaxin-LPA-inflammatory cycle. This knowledge can be used to overcome the loss of efficacy of chemotherapy and radiotherapy and the development of radiation-induced fibrosis.

Laboratory Homepage
https://www.ualberta.ca/biochemistry/people/faculty/david-brindley



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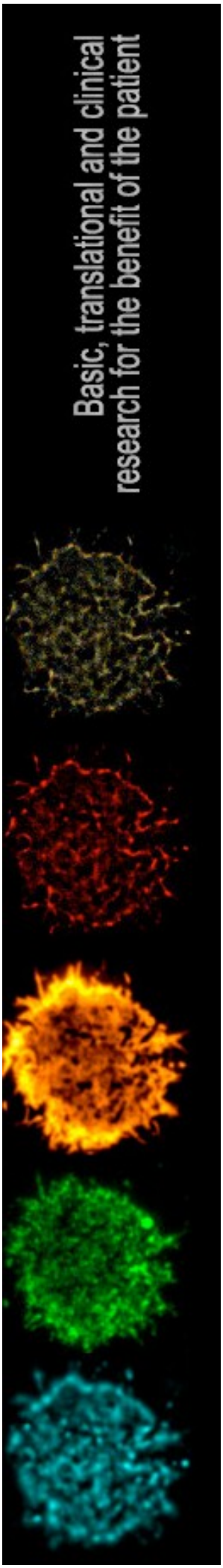
Selected recent publications

- Tumor-induced inflammation in mammary adipose tissue stimulates a vicious cycle of autotaxin expression and tumor progression. MGK Benesch, X Tang, J Dewald, W-F Dong, JR Mackey, DG Hemmings, TPW McMullen and **DN Brindley. FASEB J.** 29 (2015) 3990-4000.
- Implications for breast cancer treatment from increased autotaxin production in adipose tissue after radiotherapy. G Meng, X Tang, Z Yang, MGK Benesch, A Marshall, D Murray, DG Hemmings, F Wuest, TPW McMullen and **DN Brindley, FASEB J.** 31 (2017) 4064-4077.
- Lysophosphatidate signaling: the tumor microenvironments's new nemesis. MGK Benesch, Z Yang, X Tang, G Meng, **DN Brindley**. **Trends in Cancer,** 3 (2017) 748-752.
- Dexamethasone decreases the autotaxin-lysophosphatidate-inflammatory axis in adipose tissue: Implications for Metabolic Syndrome and breast cancer. Meng, G, Tang, X, Yang Z, Zhao YY, Curtis, JM, McMullen TPW and **Brindley DN. FASEB J.** 33 (2019) 1899-1910.

Biosketch

Denise Hemmings obtained her PhD in Medical Microbiology and Immunology (MMI) in 2001 with Dr. Larry Guilbert and did a post-doctoral fellowship with Dr. Sandra Davidge at the University of Alberta (U of A). She is an Associate Professor in Obstetrics and Gynaecology, cross-appointed in MMI at U of A, recipient of a CIHR New Investigator award in 2010 and the former Chair of Women in Scholarship, Engineering, Science and Technology (WISEST). Her lab investigates the impact of chronic infection with cytomegalovirus (CMV), a Herpesvirus, in breast cancer and also its impact on metabolic and vascular dysfunction in aging. The other major focus in Dr. Hemmings' lab is to understand the dual vascular functions of sphingosine 1-phosphate (S1P), a bioactive lipid, in pregnancy, namely permeability, vascular tone and their inter-regulation. She is interested in S1P-mediated vascular adaptations during pregnancy and the factors that disrupt these responses such as elevated proinflammatory cytokines, leading to pregnancies complicated by preeclampsia and intrauterine growth restriction. One mechanism by which S1P signalling pathways may be disrupted is maternal infection with CMV. The impact of this normally innocuous virus infection on vascular function, placental



development and immunological adaptations, particularly with respect to S1P signalling during pregnancy, form part of her research program. Dr. Hemmings is funded by operating grants from the Canadian Institutes of Health Research (CIHR), the Women and Children's Health Research Institute and the Canadian Breast Cancer Foundation. Dr. Hemmings serves on several student advisory committees and reviews for many journals and funding agencies. She has a passion for training students and since her appointment in 2005 has trained or mentored more than 60 students from the junior high school to the post-doctoral fellow level. Through her connections with WISEST, she is passionate about encouraging young women to enter, stay and advance in science, engineering and technology careers. As the Graduate Program Coordinator and the Reproductive Sciences Division Director, Dr. Hemmings also encourages students and staff in the basic sciences to step outside of their comfortable scientific boundaries to forge interdisciplinary links with clinicians and epidemiologists.

Selected publications

- Yang Z, Tang X, Meng G, Benesch MGK, Mackova M, Belon AP, Serrano-Lomelin J, Goping IS, Brindley DN, **Hemmings DG.** "Latent cytomegalovirus infection in female mice increases cancer metastasis," Cancers (Basel) Mar 29:11(4) E447, 2019
- Cao AT, Kerage D, Mackova M, Brindley DN, **Hemmings DG**. "Sexual dimorphism of metabolic and vascular dysfunction in aged mice and those lacking the sphingosine 1-phosphate receptor 3," Experimental Gerontology 99:87-97, 2017
- Kerage D, Brindley DN and **Hemmings DG**. "Novel insights into the regulation of vascular tone by sphingosine 1-phosphate," Placenta Feb 17: S86-S92, 2014
- Gombos RB, Brown JC, Teefy J, Gibeault RL, Conn KL, Schang LM, **Hemmings DG**. "Vascular dysfunction in young, mid-aged and aged mice with latent cytomegalovirus infections," Am J Physiol Heart Circ Physiol 304(2):H183-94, 2013