Focus on Faculty #61
Alexandre Orthwein

Dr. Alexandre Orthwein joined the Gerald Bronfman Department of Oncology as an Assistant Professor in January 2016. He is a Principal Investigator at the Lady Davis Institute-Segal Cancer Centre. He currently holds a Canada Research Chair Tier 2 in Genome Stability and Hematological Malignancies.

Dr. Orthwein is a native from Alsace, France and his last name means (in improper German) "the wine of the place"; as such, he would never refuse a glass (or two) of a good local Gewürztraminer. He completed all his undergraduate studies at the Université Louis Pasteur in Strasbourg, France before moving to Montreal to complete his graduate studies at Université de Montréal in the laboratory of Dr. Javier Di Noia, where he studied the importance of the HSP90 molecular chaperoning pathway in B-cells during antibody diversification. Subsequently, he completed a postdoctoral fellowship in DNA repair/genome stability in the laboratory of Dr. Daniel Durocher at the Lunenfeld-Tannenbaum Research Institute (Toronto).

Since his appointment as an Assistant Professor, Dr. Orthwein developed a research program focused on understanding how DNA repair pathways are controlled in different *in vitro* and *in vivo* models, with a particular focus on B-cells and their associated malignancies. In particular, his team has completed several *in vitro* genome-wide CRISPR-based screens to define the landscape of genes involved in chemo-response, with the ultimate goal of providing clinicians with better diagnosis and predictive tools as well as novel therapeutic targets for relapsed/refractory patients. His group has also been interested in characterizing variants of

unknown significance identified in different cohorts of patients affected with breast and/or ovarian cancer, in collaboration with Drs. Foulkes and Rivera.

"Mens sana in corpore sano" – Research does not always run smoothly as experiments may not work out and it can take several rounds of reviews to finally get a paper published. Dr. Orthwein has found that an effective way of relieving frustration and keeping a certain level of sanity is by maintaining a healthy body by going frequently to the gym.

Dr. Orthwein greatly enjoys his role as mentor and student advisor; he also dearly values the collaborative work that he participated in over the past couple of years. Here are some of the articles that he is particularly proud to have partaken in:

Sherill-Rofe D, Rahat D, Findlay S, Mellul A, Guberman I, Braun M, Bloch I, Lalezri A, Samiei A, Sadreyev R, Goldberg M, **Orthwein A,** Zick A, Tabach Y. Mapping global and local co-evolution across 600 species to identify novel homologous recombination repair genes. Genome Res. (2019) doi: 10.1101gr241414.118

Findlay S*****, Heath J*****, Luo VM, Malina A, Morin T, Djerir B, Li Z, Samiei A, Simo-Cheyou E, Karam M, Bagci H, Rahat D, Grapton D, Lavoie EG, Dove C, Khaled H, Kuasne H, Mann KK, Oros Klein K Greenwood CM, Tabach Y, Park M, Côté JF, Maréchal A, **Orthwein A.** SHLD2/FAM35A co-operates with REV7 to coordinate DNA double-strand break repair pathway choice. EMBO J. (2018) doi: 10.15252/embj.2018100158. (* co-first authors)

Rivera B, Di Iorio M, Frankum J, Nadaf J, Fahiminiya S, Arcand S, Burk D, Grapton D, Tomiak E, Hastings V, Hamel N, Aleynikova O, Giroux S, Hamdan F, Dionne-Laporte A, Zogopoulos G, Rousseau F, Berghuis A, Provencher D, Rouleau G, Michaud J, Mes-Masson AM, Majewski J, Bens S, Siebert R, Narod S, Akbari M, Lord C, Tonin P**, Orthwein A,** Foulkes W. A Functionally Null RAD51D Missense Mutation is Strongly Associated with Ovarian Carcinoma. Cancer Res. (2017) 77(16):4517-4529

Hilmi K, Jangal M, Marques M, Zhao T, Saad A, Zhang C, Luo V, Syme A, Rejon C, Yu Z, Krum, A, Fabian MR, Richard S, Alaoui-Jamali M, **Orthwein A**, McCaffrey L, Witcher M. CTCF facilitates DNA double-strand break repair by enhancing homologous recombination repair. Sci Adv. (2017) 3(5):e1601898

Orthwein A*, Noordermeer S*, Wilson MD, Landry S, Enchev RI, Sherker A, Munro M, Pinder J, Salsman J, Dellaire G, Xia B, Peter M, Durocher D. A mechanism for suppression of homologous recombination in G1 cells. Nature (2015) 528(7582):422-6 (* co-first authors)