



2018 ICCI Cancer Research Symposium

Wednesday, May 30th, 9:00am-5:00pm, Room 1714 OVC LLC



Regional Keynote Speaker (11:30): Paul Boutros, PhD

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What makes some tumours aggressive: modeling cancer lethality

Human cancers are remarkably variable in their initial presentation. They can arise in almost every organ of the body, at almost any age. Even within a single tumour type, they vary dramatically in morphological characteristics, like their size, location within an organ and cellular structure. These larger changes are reflected in, and presumably at least partially driven by, differences in the specific somatic mutational characteristics between tumours. Indeed, while individual tumours can harbour tens to hundreds of thousands of single-nucleotide mutations, in many tumour types, the median number shared by any pair of cancers is zero. These morphological and molecular heterogeneities are mirrored by a remarkable heterogeneity in clinical outcomes. Many cancers are cured by definitive local therapy – most commonly surgery or radiotherapy. Other tumours, however, are highly aggressive, likely as a result of some combination of selection of specific subclonal populations and/or their adaptation to new selective pressures. This diversity in clinical response leads to both over-treatment of tumours which are not aggressive, and under-treatment of aggressive ones. As a result, there remains an urgent need to understand which tumours are highly aggressive, and which are not, so that therapies can be tailored to individual patients. We undertook a systematic evaluation of the origins of differential tumour aggressivity. Initially using prostate cancer as a model tumour type, we evaluate the relative contributions of somatic mutational features, epigenomic features, transcriptomic features and proteomic features. Ultimately we discover that aggressivity is a complex function of all of these, and is driven not only by snapshot of mutations present at diagnosis, but also by the evolutionary trajectory upon which the tumour is embarking. Finally, we evaluate why evolutionary trajectories differ within and between a broad range of cancer types, and offer suggestions for the derivation of evolutionarily-aware biomarkers. The highly divergent outcomes of tumours when they are localized and curable remains the single most pressing clinical challenge in almost all tumour types. High-throughput molecular assays have shed significant light on this problem, and we are at the cusp of a transformation from discovery-science to validation- and implementation-science in this space.

Dr. Paul Boutros pursued his undergraduate education at the University of Waterloo in Chemistry, with co-op training ranging from water-purification to petrochemicals. But he found his true calling during a work term at Michigan State University developing computer models of drug response. His undergraduate thesis on modeling DNA damage received first place at the National Undergraduate Chemistry Conference. In 2004, he started a PhD at the Ontario Cancer Institute, where he received the CIHR/Next Generation First Prize and an Invitrogen Canada Young Investigator Silver Award. He received his PhD in 2008 and started his independent research career at the Ontario Institute for Cancer Research, where he remains today. Dr. Boutros co-leads the Canadian Prostate Cancer Genome Network and leads an international consortium optimizing algorithms for genomic data analysis. He is a Terry Fox Research Institute New Investigator, and has been named Prostate Cancer Canada Rising Star in Prostate Cancer Research.