Cancer Science Institute of Singapore

Seminar Announcement

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Deciphering Cancer Etiology through Data-intensive Analyses of Germline and Somatic Variation

Date: **Thursday 2 March 2017**
Time: **11am - 12pm**
Venue: **CeLS Level 1 Auditorium**
28 Medical Drive, Centre for Life Sciences, Singapore 117456
Host: **Prof. Daniel Tenen**

Abstract:
Advances in next-generation sequencing (NGS) have propelled genomics into a data-intensive science. In order to fully leverage large cancer genomics resources, scalable software is essential. We developed SwiftSeq, a highly-parallel computational workflow for fast and efficient processing of DNA sequencing data. SwiftSeq has been utilized to process over 10,000 exomes and 500 genomes from 31 cancer types. We've subsequently used this data for multiple germline and somatic analyses. Across the germline exomes, we've shown that increased pathogenic and deleterious allele burden within ClinVar cancer risk genes is associated with earlier age at diagnosis. In breast cancer, the effect of high allele burden was as strong as mutations in BRCA1/2. By combining harmful, germline alleles with somatic loss-of-heterozygousity, we identified candidate two-hit tumor suppressor genes both within and across cancer types. Lastly, we used the somatic mutation landscape in breast tumors to explore differences amongst White American, Black American, and Nigerian women. We found that Nigerian woman had an increased prevalence of driver mutations and signatures associated with homologous recombination deficiency, regardless of subtype. Overall, these analyses highlight how large-scale, integrative analyses provide opportunities to dissect cancer etiology and disparities.

Biography:
Jason J. Pitt is a Ph.D. candidate in Genetics at the University of Chicago. He was previously a post-baccalaureate fellow of the National Cancer Institute (USA) as well as a visiting researcher at the Wellcome Trust Sanger Institute (UK). His expertise spans two domains: 1) the development of scalable software to analyze large genomic datasets; and 2) the integration of germline and somatic genetics to better understand risk alleles and mutational events in cancer. His SwiftSeq workflow has been used to uniformly process over 10,000 cancer exomes and hundreds of cancer genomes. Using this data, Jason has highlighted cancer polygenicity, identified putative risk