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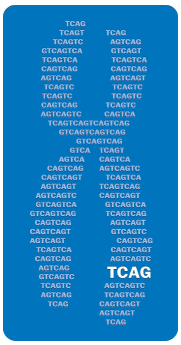

"Mutation discovery in cancer using next generation sequencing and probabilistic models"

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Tuesday, November 3, 2009, 12:00pm
Yip / Friesen Red Seminar Room, Donnelly CCBR (160 College St.)

Abstract: **The advent of next generation sequencing (NGS) has propelled the field of cancer genomics forward such that it is now cost-effective to interrogate entire genomes or transcriptomes of clinical tumor samples for the presence of somatic mutations – often the key driver genomic alterations in tumorigenesis. NGS generates a massive number of short sequence reads which once aligned to a reference human genome can reveal positions containing single nucleotide variants (SNVs). These are positions in a genome/transcriptome for which at least one allele differs from the reference human genome and can be either germline polymorphisms or somatic mutations. The challenge in SNV detection is that the alleles are represented by a stochastic distribution of allelic counts in the aligned reads. To model this distribution and infer the presence of SNVs, we developed a probabilistic method called SNVMix. SNVMix is based on an extended Binomial mixture model. We used an expectation maximization (EM) method to fit the model to data which allows the model parameters for cancer datasets to deviate from distributions assumed in normal genomes (and used by other methods). A novel feature of the model is that it probabilistically weights the contribution of each read and base to the inference of an SNV by leveraging alignment and base quality scores. I will show how these advances confer increased accuracy over competing methods when evaluated against a ground truth data set. Moreover, I will describe results of applying this model in two recent studies in ovarian and breast cancer: namely the discovery of a novel recurrent and defining mutation in the FOXL2 gene in granulosa cell tumours of the ovary and the first description of mutational evolution of a breast cancer seen at nucleotide resolution.**

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