Cell type-specific Deconvolution of Heterogeneous Tumor Samples with Immunal Infiltration using Expression Data

Tumor tissue samples are comprised of a mixture of cancerous and surrounding stromal cells. Understanding tumor heterogeneity is crucial to analyzing gene signatures associated with cancer prognosis and treatment decisions. Compared with the experimental approach of laser micro-dissection to isolate different tissue components, in silico dissection of mixed cell samples is faster and cheaper. Numerous computational approaches previously developed all have their limitations to deconvolute heterogeneous tumor samples. We have developed a three-component deconvolution model, DeMixT, that can account for a third component such as the immune cell compartment explicitly and is able to address this challenging problem when the observed signals are assumed to come from a mixture of three cell compartments, infiltrated immune cells, tumor microenvironment and cancerous tissues, instead of two. Optimization-based algorithm for DeMixT is demonstrated to find a global optimum for our estimation problem and computationally feasible when it is needed to compute high-dimensional integrals. DeMixT therefore involves a novel two-stage method yielding accurate estimates of cell purities and compartment-specific expression profiles. Simulations and real data analyses have demonstrated the good performance of our method. Compared with other deconvolution tools, DeMixT can be applied more widely and provide deeper insight in cancer biomarker studies. It allows for a further understanding of immune infiltration in cancer and assists in the development of novel prognostic markers and therapeutic strategies.

Thursday, April 27, 2017
3:30 pm - 4:30 pm
Blue Cross Blue Shield Auditorium