THE UNIVERSITY OF CHICAGO

Department of Statistics

STATISTICS COLLOQUIUM

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# Probabilistic Models of Transcriptomic Dysregulation in Human Disease

WEDNESDAY, May 2, 2018 at 4:30 PM

Eckhart 133, 5734 S. University Avenue

*Refreshments before the seminar at 4:00PM in Jones 111*

## ABSTRACT


Transcription, the fundamental cellular process by which DNA is copied to RNA, is tightly regulated in healthy human development but frequently dysregulated in disease. During or shortly after transcription, junk regions ("introns") are spliced out of the RNA to produce mature "messenger" RNA (mRNA). Massively parallel sequencing of RNA (RNA-seq) has become a ubiquitous technology to assay the "transcriptome": the collection of mRNA molecules expressed in a given tissue. However, significant computational and statistical challenges remain to translate the resulting noisy, confounded RNA-seq data into understanding of the biological system or disease state under consideration. I will describe how probabilistic models have helped us address these challenges in the context of a specific use case: uncovering the genetic basis of anthracycline-chemotherapeutic induced cardiotoxicity (ACT) using a panel of iPSC-derived cardiomyocytes from 45 individuals. We show that inter-individual variation in transcriptional response is predictive of in vitro cell damage, which in turn is associated with in vivo ACT risk. Using an efficient linear mixed model approach we detect 447 response-expression quantitative trait loci (QTLs) and 42 response-splicing QTLs, which are enriched in lower ACT Genome-Wide Association Study p-values, further supporting the in vivo relevance of our map of genetic regulation of cellular response to anthracyclines.


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