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Recent advances in the integrative molecular epidemiology of breast cancer

Friday
Sept 30, 2016
12:00 – 1:00 pm

LOCATION:
**Peter Gilgan Centre for Research
and Learning**
Room 11.9701, 11th Floor
686 Bay Street

Abstract:

Genome-wide association studies (GWAS) have identified over 94 loci associated with breast cancer (BrCa). However, these explain only 16% of the familial relative risk for BrCa, and the causal mechanisms at these loci remain largely unknown. To identify additional BrCa loci and identify likely causal genes at known loci, an international consortium recently conducted a GWAS meta-analysis of 119,000 cases and 110,000 controls, including 62,000 cases and 46,000 controls genotyped as part of the OncoArray network (<http://epi.grants.cancer.gov/oncoarray/>). I will present the results of this expanded GWAS, with an emphasis on integrative analyses that combine GWAS summary statistics with ancillary data, including eQTL information, experimental DNA-sequence annotation, and summary statistics from GWAS of other cancers and cancer-related traits. For example: (1) We leveraged eQTL data across 45 tissues to conduct a Transcriptome-Wide Association Study (TWAS) of BrCa—testing the association between predicted gene expression levels and risk of BrCa. This TWAS identified twenty-nine novel BrCa loci and highlighted candidate genes at known loci. (2) Using summary statistics from GWAS of other cancers, we showed that common variants contribute to shared heritability between BrCa and ovarian, colorectal, lung and prostate cancers. (3) We identified genomic features enriched for BrCa-associated markers and used this information to choose candidate markers for follow-up experiments. I will close with a discussion of open statistical problems in integrative molecular epidemiology.

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