Speaker: Melissa Gymrek

Title:
Dissecting the role of tandem repeats in complex human phenotypes

Abstract:
Tandem repeats (TRs) are one of the largest sources of genetic variation across human populations and are well known to contribute to human phenotypes. Still, large genome sequencing efforts have focused mainly on point mutations (single nucleotide polymorphisms [SNPs] or small indels), and the contribution of more complex variant types remains largely unexplored. To address this issue, we and others have developed a suite of bioinformatics methods for genotyping TRs at population scale, identifying de novo mutations, and analyzing their contribution to human phenotypes. We have leveraged these tools to characterize genome-wide properties of TR variation and mutation in human populations. Our results reveal thousands of TRs likely implicated in expression of nearby genes and complex traits including height and schizophrenia. Finally, we demonstrate an excess of de novo mutations at TRs in individuals affected by autism spectrum disorders compared to undiagnosed siblings. This burden is strongest for mutations resulting in rare TR alleles predicted to be under negative selection (RR=2.86). Overall, our results indicate a significant contribution of TR mutations to ASD and demonstrate that incorporating TRs into future genome-wide studies of ASD and other traits will greatly expand the repertoire of genetic variation considered in large sequencing efforts.