Flash talk Abstract

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Deciphering Causal Pathways That Mediate Genetic Effects on Multiomic Molecular Profiles

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Unraveling molecular processes that lead from genotype to phenotype is critical to treat genetic diseases and maintain health, as well as understand how biological pathways evolve. Until recently, however, few studies have considered how genetic variation affects processes across biological scales.

Our study aims to identify the impact of genetic variation within and between biological scales by integrating multiple omic measurements in a genetically tractable yeast population.

We have profiled the transcriptome, proteome, and metabolome for 50 genetically diverse yeast segregants. We measured variation in transcript levels, 3´ transcript isoform usage, protein levels, and the dynamics of more than 30 metabolites at four time points during exponential growth. Our dataset provides unprecedented detail about how genetic variation leads to differences in molecular profiles. We are integrating these data using machine learning techniques and prior knowledge to identify causal genetic loci and interpret how they function in the context of biochemical networks.

The findings from our study will have implications for the design and analysis of clinical omics studies aimed at discovering personalized targets for molecular intervention. We anticipate that combining measurements across multiple molecular profiles will increase our ability to detect genetic loci and understand how they lead to disease.