GENETICS, BIOINFORMATICS, & SYSTEMS BIOLOGY COLLOQUIUM

Thursday November 18th 12:00PM PST on Zoom!

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Password: Genetics

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DOE JOINT GENOME INSTITUTE, GENOMIC TECHNOLOGIES LAWRENCE BERKELEY NATIONAL LABORATORY

In Vivo Studies of Human Genome Function

Transcriptional enhancers are a predominant class of non-coding DNA function. The fundamental importance of enhancers is increasingly evident as human genetic studies link growing lists of enhancer variants to disease. However, substantial challenges remain in resolving pathogenic from benign enhancer sequence changes. To begin to fill this void, we developed a site-directed CRISPR-enabled mouse enhancer-reporter assay that allows the rapid and robust assessment of the impact of enhancer variants on spatiotemporal activity in vivo. We applied this high throughput method to understand enhancer mutations connected to neurological, cardiovascular, and developmental disorders. To date, we have tested thousands of variants using this approach and will present on the spectrum of mutations that contribute to functional changes in vivo. To further validate these results, we used genome editing to introduce select human mutations into the orthologous mouse enhancer and assessed their impact on whole organism function. Our work illustrates the power of large-scale CRISPR-enabled transgenesis to understand enhancer function and to comprehensively interrogate how non-coding variants affect human biology.

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