Mapping tissue-specific circuits to reveal pathways 
disrupted in complex diseases

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Mapping perturbed molecular circuits that underlie complex diseases remains a great challenge. I will give an overview of our work on (1) mapping tissue-specific transcriptional regulatory circuits and (2) identifying disease pathways within these circuits and other molecular networks. We recently developed a comprehensive resource of 394 cell type- and tissue-specific gene regulatory networks for human, each specifying the genome-wide connectivity among transcription factors, enhancers, promoters and genes (http://regulatorycircuits.org). We analyzed regulatory architecture across lineages and found that disease-associated genetic variants often disrupt regulatory networks in tissues that drive pathophysiological processes. The study shows that tissue-specific regulatory circuits might be key to reveal pathways underlying complex disorders. To this end, we now launched the Disease Module Identification DREAM Challenge, an open community challenge to systematically assess module identification methods across diverse types of gene and protein networks (http://synapse.org/modulechallenge).

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