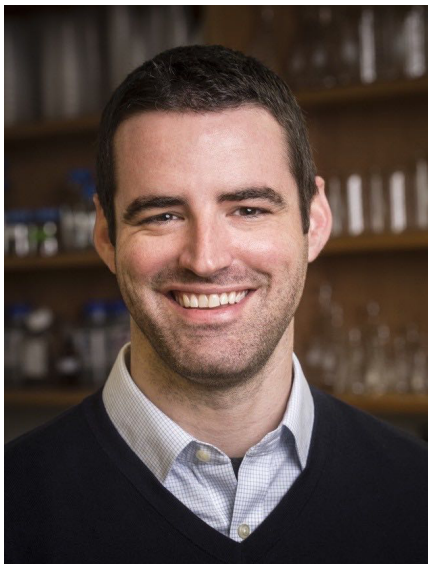
Genomic Enhancers in Brain Function and Disease

Dr. Jeremy Day

Dr. Day is an Assistant Professor in the Department of Neurobiology at UAB. Dr. Day received his Ph.D. from the University of North Carolina, conducted postdoctoral training at UAB, and joined the faculty at UAB in 2014. His lab explores the relationship between epigenetic states and neuronal function, with an emphasis on the brain circuits that regulate motivated behavior.



Abstract

Enhancers are non-coding DNA elements that function in cis to regulate transcription. Through direct interactions with gene promoters, enhancers give rise to spatially and temporally precise gene expression profiles . In the brain, the accurate regulation of these intricate expression programs across different neuronal classes gives rise to an incredible cellular and functional diversity. Furthermore, identification of disease-linked genetic variation in enhancer regions has highlighted the potential influence of enhancers in brain health and disease. This presentation will outline our efforts to characterize the mechanistic contributions of enhancers to transcriptional regulation. Enhancers undergo bidirectional transcription to generate non-coding enhancer RNAs (eRNAs), and in neurons transcribed enhancers exhibit elevated sequence conservation, enriched localization near genes involved in neuronal or synaptic function, and correlated activity-dependent regulation of putative eRNA-mRNA pairs. CRISPR-based induction of eRNA synthesis from multiple enhancers produces corresponding increases in mRNA at linked genes, functionally validating enhancer-gene predictions. Focusing on eRNAs arising from enhancers at the Fos gene locus, we find that eRNA and mRNA correlate on a single-cell level, that CRISPR-targeted eRNA delivery drives mRNA induction, and that eRNA knockdown decreases mRNA and alters neuronal physiology.
These results highlight the unique role of enhancer RNAs in activity-dependent gene regulation and neuronal function.

Date:
03/19/2019

Time: **4:00**pm

Location: SE1 270K

Host:
Dr. Ramen Saha

Molecular Cell Biology Seminar Series