Thursday december 15
12:00 PM PST
VIRTUAL

Zoom Info:

Link: https://uchealth.zoom.us/j/81222723480?pwd=ZVhJV0liT2hnaEZFK1htZStNVTJ5Zz09

Password: Genome

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GBSBC PRESENTS:

JESSICA TOLLKUHN, PHD

COLD SPRING HARBOR LABORATORY

REGULATION OF BRAIN SEX DIFFERENCES BY STEROID HORMONE RECEPTORS

Gonadal steroid hormones are the principal drivers of sex-variable biology. In the brain, estrogen (17β-estradiol) establishes neural sex differences in many vertebrates and modulates mood, behavior, and energy balance in adulthood. To understand the diverse effects of estradiol on the brain, we profiled the genomic binding of estrogen receptor alpha (ERα), providing the first picture of the neural actions of any gonadal hormone receptor. We investigated the relationship between ERα occupancy and sex-biased gene expression in the posterior bed nucleus of the stria terminalis (BNSTp), a sexually dimorphic node in limbic circuitry that modulates sex-differential social behaviors such as aggression and parenting. In adult animals we observe that levels of ERα are predictive of the extent of sex-variable gene expression, and that these sex differences are a dynamic readout of acute hormonal state. Unexpectedly, we find that adult sex differences in chromatin accessibility are driven principally by testosterone, which both opens and closes chromatin in males. In neonates we find that transient ERα recruitment at birth leads to persistent chromatin opening and male-biased gene expression, demonstrating a true epigenetic mechanism for brain sexual differentiation. To understand the mechanistic basis of ERα target specificity, we queried our multiomic datasets to identify cluster-specific regulators of cell type identity. We identified and validated Nfix as a "terminal selector" in a male-biased cell type and demonstrated its cooperative recruitment with ERα to a subset of target genes. Collectively our data identify gene programs that underlie the effects of estradiol on brain health and disease and illustrate the potential for discovery of novel gene regulatory strategies in behaviorally relevant neuronal populations.