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Poster Submissions

Poster Title

The Role of Nuclear Organization in Liver Sexual Dimorphism

Authors and their Affiliation

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Please describe the extent of your work in this research

BJM performed the experiments and computational analysis
DJW contributed to the study design and coordinated the overall project

Abstract Submission

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Would you like your abstract to be considered for an oral presentation (students and post docs only)?

Yes

Boston University Genome Science Institute Symposium, November 2015

The Role of Nuclear Organization in Liver Sexual Dimorphism

Bryan J. Matthews and David J. Waxman, Department of Biology, Boston University

More than 1,000 genes are differentially expressed between the sexes in adult mouse liver, and are regulated by the sex-specific growth hormone (GH) secretion patterns that onset at puberty. Epigenetic marks and chromatin state analysis has shown that less than half of these sex-biased genes have similarly sex-biased chromatin marks within 10 kb of the gene body, and indicate that distal regulatory elements are a major driver of liver sexual dimorphism (Sugathan and Waxman (2013) Mol Cell Biol, PMID: 23836885). We hypothesize that sex-based differences in nuclear organization contribute to the observed sex-bias in chromatin states and transcriptomic patterns. Large insulated loop structures called Topologically Associated Domains (TADs) are reported to integrate hormonal signaling cues to coordinate gene expression. Here, we extend this model by investigating the role of TADs in partitioning the genome and integrating sex-dependent GH signaling, including dynamic intra-TAD interactions unique to one sex. We show that mouse liver TADs retain many of the properties found in other tissues and species, including insulation of repressive histone marks and orientation of CTCF binding at their boundaries. Furthermore, we demonstrate that some TADs show coordinated sex-bias, which may help explain the distal action of sex-specific enhancers. Structural reorganization of the nucleus in response to stimuli is most common at the level of gene loops. We use a method called circularized chromosome conformation capture with sequencing (4C-seq) to investigate this reorganization and discover interactions between highly sex-biased promoters or enhancers and neighboring genes. We find that an enhancer upstream of the female-biased gene *Sult3a1* contacts multiple promoters in female but not male liver, while the promoter of the male-biased gene *Cyp7b1* interacts with a downstream enhancer in male but not female liver. These findings illustrate the contribution of local chromatin conformation to sex-biased gene expression. Overall, our model allows us to study how nuclear organization and gene expression are linked and how both are responsive to hormonal environments.

Supported in part by NIH grant DK33765 (to DJW). BJM was supported by NSF Graduate Research Fellowship DGE-1247312.