UTHealth
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School of Biomedical Informatics

CPH Seminar in Precision Medicine

Integrative Analysis of Long Noncoding RNA and Transcription in Neural Cell Fate Determination and Spinal Cord Injury

Jiaqian Wu, PhD
Associate Professor
The Vivian L. Smith Department of Neurosurgery
University of Texas Medical School

70% to 90% of the mammalian genome is transcribed at some point during development; however, only <2% of the genome is associated with protein-coding genes. Emerging evidences suggest that long noncoding RNAs (lncRNA; >200bp) have important functions in various biological and pathological processes. My laboratory has been systematically analyzing the expression and regulation of both coding and long non-coding RNAs in the central nervous system. It is challenging to identify lncRNA comprehensively, since lncRNAs are often expressed at lower levels and are more cell type-specific than protein-coding genes. We performed ab initio transcriptome reconstruction using nine purified cell populations from mouse cortex and detected more than 5,000 lncRNAs. ENCODE DNase I digital footprint data and Mouse ENCODE promoters were utilized to infer transcription factor (TF) occupancy. By integrating TF binding and cell-type specific transcriptomic data, we constructed a novel framework useful for identifying lncRNAs that are potentially essential in brain cell fate determination, and loss-of-function experiments confirmed that lncRNA plays a functional role in Oligodendrocyte Precursor Cell (OPC) Fate Determination In addition to the brain, we were the first to comprehensively investigate alterations in the expression of both coding and long non-coding genes in the chronic stages of spinal cord injury (SCI) using RNA-Sequencing. Through pathway analysis and network construction, the functions of differentially expressed genes were analyzed systematically. Furthermore, we predicted the potential regulatory function of non-coding transcripts, revealed enriched motifs of transcription factors in the upstream regulatory regions of differentially expressed (DE) lncRNAs, and identified DE lncRNAs homologous to human genomic regions which contain single-nucleotide polymorphisms associated with diseases. These results revealed critical pathways and networks that exhibit sustained alterations at the chronic stages of SCI, highlighting the temporal regulation of pathological processes including astrogliosis. Overall, our studies provided an unprecedented resource and a new catalogue of lncRNAs in the CNS. We present our data via the interactive genome browser at our laboratory website freely accessible to the research community (http://jiaqianwulab.org/resource.htm). We anticipate that these studies will advance the knowledge of this major class of non-coding genes and their potential roles in neurological development and diseases.

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arlisa.k.ross@uth.tmc.edu
713.500.3912

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