Project description
February 7, 2019

Project title

Regulatory Roles of Long Non-coding RNAs during Blood Brain Barrier development under normal and disease condition

Research area:

Vascular biology

Brief description

In this project, we will analyze differential expression of long non-coding RNAs in endothelial cells between different regions of mouse brain, during blood brain barrier maturation and under normal or disease condition.

Aim

The aim of the projects is to charaterize lncRNAs that are involved in BBB maturation and identify lncRNAs that are associated with cerebral cavernous malformation.

Background

Long non-coding RNAs (lncRNAs) are defined as transcripts longer than 200 nucleotides that are not translated into proteins. They can be spliced and also polyadenylated. Similar to protein coding genes, lncRNAs are also expressed in a cell-type-specific manner during development and under disease conditions. The lncRNAs function as gene expression regulators at both transcriptional and post-transcriptional levels. They are known to play critical roles in many biological processes. In endothelial cells, only a handful of lncRNAs have been discovered to participate in angiogenesis and respond to vascular diseases. The lncRNAs that are associated with blood brain barrier (BBB) development are largely remained unknown. Thus, it would be important to identify lncRNAs that are involved in BBB maturation through analysis of differentially expressed lncRNAs between different developmental stage, and between disease and healthy conditions. This information would be extremely useful for the discovery of potential diagnostic lncRNA biomarkers for diseases like cerebral cavernous malformation (CCM). CCM is an abnormally formed cluster of enlarged blood vessels that can occur in the brain and spinal cord. CCM can occur in a sporadic manner (1 in 200) or a familial manner (1 in 10,000). The familial version of CCM is caused by a loss of-function mutation in one of the three genes CCM1(Krit1), CCM2 (MGfC4607, OSM, Malcavernin) or CCM3 (PDCD10, TFAR15).

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Project plan

In the project we will perform analysis of bulk RNA-seq data (have already been generated) to:
1) characterize lncRNA expression patterns in mouse cerebellum and cerebrum endothelial cells during postnatal BBB maturation at different ages of maturation.
2) compare the lncRNA expression changes between cerebellum and cerebrum, between normal and CCM conditions. If potential lncRNA candidates are identified, we will proceed and design experiments to further investigate the mechanism of these lncRNAs in gene regulation.

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