ADCYAP1/PACAP and its potential regulatory long non-coding RNA may be implicated in the neurodegenerative process of MS patients

Lad et al.

Saloni Lad[1], Aaron Perles[2], Ajai Tripathi[2], Ranjan Dutta[1,2]

1. Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH
2. Department of Neurosciences, Cleveland Clinic Lerner Research Institute, Cleveland, OH

Background

Multiple Sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system (CNS). MS patients typically suffer from memory deficits, which can be attributed to significant demyelination in the hippocampus and decreased expression of neuronal proteins involved in axonal transport, synaptic plasticity, and memory/learning. Changes in gene expression following demyelination is controlled by regulatory mechanisms like microRNAs and DNA methylation.

Objective

The current project aims to determine whether long non-coding RNAs (lncRNAs) are altered following hippocampal demyelination in MS brains. The results of this study would provide additional information for therapeutic approaches to preserve and potentially restore memory function and myelin loss in MS patients.

Methods

RNA isolated from frozen myelinated and demyelinated MS hippocampi were sent for global expression profiling of lncRNAs and protein-coding mRNA transcripts. Resultant data was mined for expression of lncRNAs and their target genes. Fixed MS human brains were stained for myelin proteolipid protein (PLP) to determine extent of demyelination, Hu antigen R (HuR) for neuronal status, and identified genes for cellular localization in MS brain tissues.

Results

From the microarray, thousands of lncRNAs and protein-coding mRNAs were found to be both up-regulated and down-regulated. From these, ADCYAP1/PACAP was chosen based on its relationship with a lncRNA, G036307, its localization, and its neuroprotective function.

Conclusion

This study has identified ADCYAP1/ PACAP and its potential regulatory lncRNA, G036307 as a potential pathway implicated in the demyelination process of MS. Further studies will focus on determining a direct regulatory relationship between G036307 and ADCYAP1 and will characterize the role PACAP plays in the neurodegenerative process in MS patients.