Identification of abnormal microRNA gene regulation in mesial temporal sclerosis

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INTRODUCTION: MicroRNAs are a new class of small RNA molecules (21-24nt) that negatively regulate gene expression either by translational repression or target mRNA degradation. It is believed that about 30% of all human genes are regulated by these molecules. MiRNAs are involved in many important biological processes including cell differentiation and central nervous system development. The main purpose of this study was to investigate the existence of differences in microRNA expression in mesial temporal sclerosis (MTS) and to identify the regulated target-genes.

MATERIAL and METHODS: Total RNA was isolated from hippocampal tissue of 4 patients who underwent selective resection of the mesial temporal structures for the treatment of clinically refractory seizures and we used control samples from autopsy (n=4). RNA samples were used in real-time PCR reactions with TaqMan™ microRNA assays to quantify 157 different miRNAs.

RESULTS and DISCUSSION: Bioinformatics analyzes identified three miRNAs, which were differently expressed in patients as compared to controls: let-7d and miR-29b - over expressed in patients; and, miR-30d - down-regulated in patients. A possible target gene for let-7d is Nme6 which we also found to be down-regulated in patients. In addition, Mcl-1, the putative target gene of miR-29b was also down-regulated in patients. Mcl-1 is an anti-apoptotic protein of the Bcl-2 family and its tight regulation of protein levels is necessary, because insufficient Mcl-1 can result in inappropriate cell death. Nme6 belongs to NME gene family in humans and act as inhibitor of p53-induced apoptosis.

CONCLUSIONS: We have identified three different miRNA species differently expressed in MTS and their target genes: let-7d - NME6, miR-30d - SON and miR29b - Mcl-1. Biologic functions related to the possible miRNA gene-targets are mainly neurogenesis, and apoptosis. Our results point to interesting potential molecular targets which should be explored further in additional studies of MTS.

Keywords: mesial temporal sclerosis, microRNA expression

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