The Potential Role of Let-7d in Pericyte Differentiation: Determining a Pathway to Target Pluripotent Stem Cells of the CNS to Differentiate to Provide a New Method for the Alleviation of Neurodegenerative Disorders and CNS Cancers

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The pericyte is a regulatory cell that rests on blood vessels throughout the body. It has multiple roles and is thought to be an endogenous source of adult stem cells. In the brain, specifically, the pericyte is a source of precursors for cells of the neural lineage. Previously reported studies have shown that the pericyte self renews and differentiates in response to basic fibroblast growth factor(bFGF). In addition, exposure to moderate hypoxia augments its stem cell activity. The pathway by which this occurs has not yet been established. It is hypothesized that hypoxia induced microRNAs(miRNA) may be critically involved. Of the pericyte miRNAs that have been shown to be overexpressed following exposure to hypoxia miRNA Let-7d was focused on as it is a key regulator of cell differentiation as shown through analysis of its gene targets using the David Ontological Database. To determine if Let-7d plays a role in pericyte differentiation, Let-7d was examined by q-RT PCR in both normal and hypoxic pericytes and in bFGF-induced pericyte neurospheres. Pericyte expression of SOX-2, a protein that has that has the dual ability to suppress Let-7d and induce differentiation, was also analyzed by Western Blot Analysis and by q-RT PCR of the SOX-2 specific mRNA in normal pericytes and in pericytes undergoing differentiation. Let-7d and Sox-2 were upregulated in neurospheres and in hypoxic pericytes. Thus, it can be concluded that Let-7d and SOX-2 are critically involved in pericyte differentiation along the neuronal lineage. For the first time, a potential signaling pathway for pericyte stem cell activity is proposed. Further understanding of the pathways that regulate pericyte differentiation may lead to new therapeutic targets in the treatment of neurodegenerative diseases.

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