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Human model system for studying the neurodegenerative disorders

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The present study provided novel molecular insights into how human neural stem cell fate determination is decided by small non-coding microRNA-137. Cell fate determination refers to a process in which a cell a can multiply and differentiate into different cell types.

Children who suffer from neurodevelopmental disorders such as Autism (ASD) show timid and repetitive behavior, and their brain does not develop properly. Another such neurodevelopmental disorder is Intellectual Disability (ID) renders the person incapable to learn, reason, make decisions and solve problems.

Both ASD and ID represent huge socio-economic burden on a global scale. Details of disturbed biological functions and the development of novel treatment strategies for such disorders have remained unmet primarily due to lack of human based models. Now scientists at NBRC have designed a human based model system to study the biological functions associated with neurodegenerative disorders like autism and ID at molecular level.

The microRNAs are small non-coding ribonucleic acids present in the cell and control gene regulation and subsequent protein formation in the cells. Although miRNAs are abundantly expressed in NSC but their role in determining the NSC fate is not fully understood.

At NBRC, team of scientists led by Dr. Yogita K. Adlakha have studied the role of a brain enriched miRNA-137 in determining the fate of human induced pluripotent stem cells (iPSCs)-derived neural stem cells (hiNSCs). IPSC derived NSCs represent an ideal model to study neurodevelopmental disorders. It was possible that the iPSCs can easily be derived from patient's blood and can easily be induced to NSC.

Research team have successfully provided first evidence in human NSCs that miR-137 inhibits their proliferation but improves their neuronal differentiation and migration. The miR-137 also down-regulates transcriptional factor MEF2A which regulates peroxisome proliferator-activated

receptor-gamma coactivator (PGC1α) transcription. This in turn decreases the levels of PGC1α which impacts mitochondrial dynamics.

Mitochondria are considered as power house of the cell, and it was observed that miR-137 increases fusion and fission of mitochondria. The process results in increased content of mitochondria, activation of oxidative phosphorylation and oxygen consumption rate in NSC.

The level of miR-137 is decreased in ASD and ID disorders and it was found that NSCs decrease with advancing age, therefore, leads to compromised regenerative capacity of the brain. The research work has been recently accepted for publication in high impact journal *Stem Cells.*

Study proposes that NSC differentiation induced by miR-137 might make a treatment regime possible for ASD and ID as well as for aging related neurodegenerative diseases.