Neural cells produced by epigenetic cell reprogramming approach as cellular therapeutics for neurological disorders

Recent advances in cell reprogramming technologies open up new possibilities for generation of stem cell lines and specific differentiated cell types from patient own somatic cells that can be used for disease modeling, toxicity screening and drug discovery and metabolism studies. These groundbreaking discoveries compelled researchers to think in bold ways about new approaches to research disease mechanisms, drug development, and cell-based treatments for a range of diseases and gave rise to countless applications in regenerative medicine. Over the last decade, several cell reprogramming methods such as nuclear transfer, cell fusion and transfection or transduction with pluripotent factors have been developed. However, the majority of these technologies require the exposure of cell nuclei to large reprogramming molecules via transfection, transduction, cell fusion, or nuclear transfer. These methods raise several technical, safety, and ethical issues. Recent several studies, including ours, showed that somatic cell reprogramming can be also achieved by the combination of small molecules that include modulators of chromatin structure and function combined with the modulators of specific cell signaling pathways (1-3). These data suggest that with appropriate epigenetic modifications cells can become responsive to the factors that promote multi- or pluripotency or induce cell lineage conversions.

By using this cell reprogramming approach we have been able to turn human mesenchymal stem cells (hMSCs) directly into neuronal progenitors that have the potential to generate different neuronal subtypes, such as dopaminergic, cholinergic, and GABAergic cells when further grown in appropriate neuronal differentiation media (3, 4) (Fig.1). The therapeutic effect of these specialized neural cells demonstrated in several animal models of neurological disorders such as spinal cord injury (5), Parkinson's and Alzheimer's.

Biography

Alexanian Arshak is currently the Chief Scientific Officer at Cell Reprogramming & Therapeutics LLC and an Adjunct Associate Professor in the Department of Medicine at the Medical College of Wisconsin (MCW). Previously, he held faculty positions in the Departments of Neurosurgery at MCW (2000-2013) and in the Departments of Anatomy and Neurobiology, as well as in Biochemistry and Molecular Biology, at Colorado State University (1997-2000). He has received training at universities and centers worldwide, including the Pasteur Institute and University of Montpelier in France, University of Saarland in Germany, Institute of Biochemistry in China and Russia, and Colorado State University. His research funded by the governmental grants such as NIH and Veterans Affairs, as well as other organizations such as Spinal Cord Society, Quadracci, Bryon Riesch Paralysis Foundation, AOSpine North America and International, Hansjorg Wyss and others. The areas of interest of his research are the epigenetic regulation of cell fate commitment and differentiation, development of cell reprogramming technologies to produce different neuronal and glial cell types, and elucidation of the therapeutic effect of these specialized cell types in several neurological disorders.

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