Directing the Fate of Mesenchymal Stem Cells towards Neuronal Lineage for their Potential Use in Cellular Therapeutics

Aisha Ishaque[1], Irfan Khan[1], Asmat Salim[1,*], Rida-e-Maria Qazi[1], Tuba ShakilMalick[1], Durriyyah Sharifah Hasan Adli[2]

[1]Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan

[2]University of Malaya, 50603 Kuala Lumpur, Malaysia

ABSTRACT

Introduction: Neurodegenerative disorders are strongly associated with loss of neuronal function and are often fatal. The regeneration potential of neuronal cells is not enough to cope with the damage caused by the degeneration. One approach is to use regenerative medicine whereby stem cells can be exploited to regenerate the cells of the multiple lineage. Regenerative medicine is concerned with the maintenance of structural and functional integrity of an organ or tissue that suffers from chronic situation as a result of an injury. Stem cells are unique cells as they possess remarkable property of being differentiated into a variety of other cells types. By exploiting stem cell therapy, various diseases can be targeted e.g. congenital defects and diseases that are the result of older age.Stem cells are of various types but mesenchymal stem cells are of great interest for the researchers because of their therapeutic potential to treat degenerated tissues.MSCs have been shown to differentiate into lineages other than mesoderm under the influence of their microenvironment i.e. MSCs differentiate to keratinocytes of ectodermal lineage and hepatocytes of endodermal lineage. Apart from this, MSCs also possess the potential to differentiate into neuronal lineage.

Objectives: The current study is focused on the differentiation of rat bone marrow derived mesenchymal stem cells (MSCs) into neuronal lineage by two bioactive constituents*;* alpha pinene (AP), and thymoquinone (TQ).

Methods: Concentrations of both these compounds (20 µM for AP, and 12 µM for TQ) were used for the treatment of MSCs, as optimized by MTT assay. Cells were divided into 4 groups, (1) normal MSCs having no treatment, (2) MSCs treated with 20 µM of AP, (3) MSCs treated with 12 µM of TQ, and (4) MSCs treated with a combination of both the compounds, 20 µM of AP + 12 µM of TQ to observe their synergistic effect.

Results and Conclusion: Both compounds, alone and in combination, were able to induce neuronal differentiation with significant expression of neuron specific markers *NSE, Nestin, MAP2, Nefl* and *Tau*. Astroglia with significant expression of *GFAP* was also observed in each treated group. Germ layer specific markers were also analyzed in each group; AP treated group showed significant upregulation of endodermal (*AFP, Sox17,* and *MixL1*) and mesodermal markers (*Mesp1*, *Tbx20*, and *T Brachyury*) showing the transition of ectoderm to other two germ layers. Current study concludes that alpha pinene and thymoquinone have the potential for efficient differentiation of rat bone marrow derived MSCs to neuronal as well as astroglial cells. However alpha pinene treatment also induced endoderm and mesoderm specific gene expression. These differentiated neurons can be a potential source for treating neurodegenerative disorders thereby can be the promising candidates for their use in cellular therapeutics to cope up with neurodegenerative ailments.

Keywords: artificial intelligence; convolutional neural network; coronavirus 2019; chest Xray; deep learning models; clinical informatics.