Tentative Outline

Special Thematic Issue for the journal Current Neuropharmacology

Title of the Thematic Issue

Stem Cell Transplantation Therapy in Neurological Disorders: Current Status and Future Directions

Guest Editor: Prof. Mohammad Amjad Kamal

[1] King Fahd Medical Research Center, King Abdulaziz University, Saudi Arabia

[2] Enzymoics, 7 Peterlee Place, Hebersham, NSW 2770

[3] Novel Global Community Educational Foundation, Australia

Co-Guest Editor: Eshak I. Bahbah and Ahmed Negida

Faculty of Medicine, Al-Azhar University, Damietta, Egypt

- **Scope of the Thematic Issue:**

Stem cells include embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs), and tissue-derived stem cells, such as bone marrow (BM), and adipose-derived stem cells. Stem cell-derived neurons have the potential to integrate into the existing neural networks of the host brain. Moreover, stem cell transplantation appears to increase acetylcholine levels to improve cognition and memory in the animal model. Further, stem cells secrete neurotrophic factors to modulate neuroplasticity and neurogenesis. Mesenchymal stem cells (MSCs) derived from BM (BMMSCs) were able to home in on the injured brain and increase the number of positive cells for choline acetyltransferase. Furthermore, BMMSCs were able to remove Aβ plaques from the hippocampus and to reduce Aβ deposits through the activation of endogenous microglia. Moreover, the transplantation of adipose-derived stem cells allowed them to differentiate into neuron-like and astrocyte-like cells around the hematoma. It accompanied by up-regulation of vascular endothelial

growth factor expression and improvement of neural function, suggesting that adipose-derived stem cells benefit neural differentiation and induce functional improvement. Despite these primary observations, stem cell transplantation is still insufficiently considered in the clinical practice, and treatment options are limited and frequently associated with large debate. Therefore, the purpose of this special issue is to present high-quality review articles on the current status and future directions of stem cell transplantation in neurological disorders.

Sub-topics:

The sub-topics to be covered within the issue should be provided:

- Stem Cell Treatment for Alzheimer's disease
- iPS cell technologies: significance and applications to Parkinson Disease
- From human embryonic stem cells to therapeutic dopaminergic neurons
- Application of iPS cell transplantation in spinal cord injury
- Stem cell therapy for Age-related neurological disorders:
    1. Huntington's disease
    2. Stroke
    3. Traumatic brain injury
    4. Amyotrophic lateral sclerosis
    5. Multiple sclerosis
    6. Multiple system atrophy

Important Dates:

Manuscript Submission deadline: 15 September 2020

Peer Review Due: 15 October 2020

Revision due: 15 November 2020

Final manuscript due: 31 December 2020

Galley proof expected date: Feb 2021

Proposed manuscript #1

Efficacy and safety of mesenchymal stem cell therapy in multiple sclerosis: A systematic review & meta-analysis

Md Asiful Islam*, Shoumik Kundu, Sadia Alam, Tareq Hossan*

Corresponding Authors: Md Asiful Islam (asiful@usm.my , ayoncx70@yahoo.com) & Tareq Hossan (thossan@juniv.edu)

Md Asiful Islam

School of Medical Sciences, Universiti Sains Malaysia

Abstract

Stem cell therapy represents a potentially useful approach to slow or prevents progressive disability in multiple sclerosis (MS). The objective of this systematic review and meta-analysis would be to assess the efficacy and safety of stem cell therapies in MS. Different databases like PubMed, Scopus, Google Scholar, would be searched systematically by using appropriate keywords. The protocol would be registered under PROSPERO. This SRMA would be followed based on the guideline of PRISMA. The primary end point would be disease progression [defined as the Expanded Disability Status Scale (EDSS)]. Any kind of cell therapy interventions would be considered, and randomised or quasi-randomised controlled studies would be judged. Mean-differences would be calculated, and a forest plot would be presented. Funnel plots would be generated for assessing the publication bias. The expected outcome would be to find out the efficacy and safety of stem cell therapies in patients with MS.

Proposed manuscript #2

Extracellular vesicles, stem cell therapy and the role of miRNAs in neurodegeneration

A.M. Belkozhayev[a], M. Al-Yozbaki[b], A. George[b,c], R. Ye Niyazova[a] and C.M. Wilson[b,d] *

[a]al-Farabi Kazakh National University, Faculty of Biology and Biotechnology, Almaty, Republic of Kazakhstan; [b]Canterbury Christ Church University, School of Human and Life Sciences, Life Sciences Industry Liaison Lab, Sandwich, UK; [c]Jubilee Centre for Medical Research, Jubilee Mission Medical College & Research Institute, Thrissur, Kerala, India; [d] Novel Global Community Educational Foundation, Australia.

C.M. Wilson *(*https://www.scopus.com/authid/detail.uri?authorId=8319597400)

Abstract

There are different modalities of intercellular communication governed by cellular homeostasis. In this review, we will explore one of these forms of communication called extracellular vesicles (EVs). These vesicles are released by all cells in the body and are heterogenous in nature. The main function of EVs is to share information through its cargo consisting of proteins, lipids and nucleic acids (mRNA, miRNA, dsDNA..) with other cells which has a direct consequence on their microenvironment. We will focus on the role of EVs of mesenchymal stem cells (MSCs) in the nervous system and how these participate in intercellular communication to maintain the physiological function and to provide neuroprotection. However, deregulation of this same communication system could play in role in a number of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, multiple sclerosis, prion disease and Huntington's disease. The release of EVs from a cell provide crucial information to

what is happening inside the cell and thus could be used in diagnostics as well as in therapy. In addition, we consider the role of trinucleotide repeats in neurodegenerative diseases with a view to focus on miRNA profiling, prediction of their binding and their potential role in diagnosis and stem cell therapy. We will discuss and explore new avenues for the clinical applications of using engineered MSC-EVs and their potential therapeutic benefit in the treatment of neurodegenerative diseases.

Proposed manuscript #3

Recent advances in synaptosomal proteomics in Alzheimer's disease

Faraz Ahmad[1]*, Shafiul Haque[2#], Mohammad Amjad Kamal[3], Ghulam Md Ashraf*[3,4]

[1] Department of Anatomy, University of Otago, Dunedin - 9016, New Zealand; [2]Research and Scientific Studies Unit, College of Nursing & Allied Health Sciences, Jazan University, Jazan - 45142, Saudi Arabia; [3]King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia; [4]Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Chemical synapses in the brain are focal hot spots for interneuronal signalling, signal transduction and its plasticity. Structurally, synapses comprise axon termini or the presynapse (vesicles filled with neurotransmitters that function as molecular signals), synaptic clefts (extracellular matrix and adhesion molecules) and postsynaptic density or PSD (with receptors for neurotransmitters that rely the chemical signalling). The proteinaceous inventory of presynapse and the PSD comprise of proteins that mediate and regulate neurotransmitter release, their receptor binding and perception and rely of chemical signals. Moreover, short- and long-

term structural and functional alterations that are necessary for the optimal higher order brain functions are also mainly dependent on the protein dynamics at the synapses. Not surprisingly, disruptions in the synaptic physiology are considered as the major pathogenic mechanisms underlying progression of a number of neurodegenerative disorders, including Alzheimer's disease. This review briefly discusses the subcellular fractionation protocols and the related biochemical approaches for isolation of synaptic compartments. In addition, it discusses the progresses made in understanding the pathological alterations in the synaptic proteome in neurodegenerative disorders, particularly focussing on Alzheimer's disease dementia.

Key words: Alzheimer's disease; neurodegenerative disorders; proteomics; synapse; synaptosome.

Proposed manuscript #5

Exploring the Association of Oxidative Stress with More Than Three Hundred (300) Neurological Disorders

Waseem Hassan[1], Hamsa Noreen[1], Shakeela Rehman[1], Joao Batista Teixeira da Rocha[*2], Mohammad Amjad Kamal[3,4,5]

[1] Institute of Chemical Sciences, University of Peshawar, Peshawar, Khyber Pakhtunkhwa, Pakistan;
[2] Departamento de Química, Centro de Ciências Naturais e Exatas, Universidade Federal de Santa Maria, Santa Maria, RS, Brazil ; [3] King Fahd Medical Research Center, King Abdulaziz University, P. O. Box 80216, Jeddah 21589, Saudi Arabia; [4] Enzymoics, 7 Peterlee Place, Hebersham, NSW 2770
[5] Novel Global Community Educational Foundation, Australia

*https://orcid.org/0000-0003-3829-0595

Tentative abstract:

Brief Description - A diverse array of endogenous and exogenous sources are involved in free radical productions, which are either the cause or consequence of more than 100 human pathologies. Mechanistically, lipid and protein oxidation, protein mutilation, DNA damage, and neuronal dysfunction are some of the reported pathways. **Major Aim -** The present work aims to review the associations of OS with Neurological Disorders. Please note that we aim to cover more than 300 Disorders as given below in the table. **Proposed Results -** The proposed results or table after browsing the approximate 300 disorder may be presented like below table (last table). **Proposed Methodology -** We will use different search terms like, "oxidative stress and neurological disorders," "free radicals and neurodegenerative disorders," "oxidative stress, free radicals, and neurological disorders," and "association of oxidative stress with the name of disorders taken from below table. The standard references of pathologies will be in conjunction with the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders and the World Health Organization's International Statistical Classification of Diseases and Related. **Main Conclusion -** We will try to cover the genetic, pharmacological, biochemical, preclinical therapeutic studies, case reports and clinical trials to explore the molecular aspects of neurodegenerative disorders which might be associated with OS.

Proposed manuscript #8

Emerging Potential of Stem Cells Therapy to Combat Alzheimer's Disease Pathogenesis

Md. Sahab Uddin[1,2,*], Md. Tanvir Kabir[3], Abdullah Al Mamun[1,2], Ghulam Md Ashraf[4,5,*]

[1]Department of Pharmacy, Southeast University, Dhaka, Bangladesh

[2]Pharmakon Neuroscience Research Network, Dhaka, Bangladesh

[3]Department of Pharmacy, BRAC University, Dhaka, Bangladesh

[4]King Fahd Medical Research Center, King Abdulaziz University, Jeddah, Saudi Arabia

[5]Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia

***Corresponding authors:**

Md. Sahab Uddin: msu-neuropharma@hotmail.com, msu_neuropharma@hotmail.com

Ghulam Md Ashraf: ashraf.gm@gmail.com, gashraf@kau.edu.sa

Abstract

Alzheimer's disease (AD) is a progressive neurological disorder, and the characteristics of this disorder include difficulty in performing daily tasks, confusion, and memory loss. Several new therapeutic agents have failed in clinical studies since these agents cannot halt or stimulate the regeneration of neural cells which are already damaged. Furthermore, these agents provide symptomatic relief only. Thus, a more comprehensive understanding regarding the mechanism of stem cell therapy might lead to the development of novel and effective treatments for this devastating disorder. In this article, we will review several stem cell studies in terms of both clinical and preclinical techniques used to combat AD treatment. We will also focus on the current approaches of experimental stem cell therapies and their drawbacks as well as their future use in clinical studies.

Proposed manuscript #14

Mysteries of Claustrum of Insula (Secrets of the Brain Fence): Implication in the context of Stem Cell Transplantation Therapy in Neurological Disorders

Nikolenko V.N.[1,2], Kudryashova V.A.[1], Rizaeva N.A.1[1], Oganesyan M.V.[1], Dubovets A.A.[3], Borminskaya I.D.[3] ….. *and Aliev* G.*

[1]FSAEI HE I.M. Sechenov First MSMU MOH Russia (Sechenov University) 8 Trubetskaya St., building 2, Moscow 119991, Russia 2 Lomonosov Moscow State University Leninskie Gory, Moscow 119991, Russia

[2]Lomonosov Moscow State University Leninskie Gory, Moscow 119991, Russia

[3]Faculty international school "Medicine of the future" of Sechenov First Moscow State Medical University (Sechenov University), St. Trubetskaya, 8, bld. 2, Moscow, 119991, Russia.

[4]"GALLY" International Research Institute, San Antonio, TX, USA.

*Correspondence: Prof. Gjumrakch Aliev, MD & PhD, Professor & President "GALLY" International Research Institute, San Antonio, TX, USA. Phone: +1(440) 263-7461; +7-964-493-1515. [aliev03@gmail.com, cobalt55@gallyinternational.com]

Abstract. All mammals in the brain have a poorly studied formation of grey matter called claustrum (fence), which translates as *"hidden, secret"*. The fence has extensive connections with various areas of the cerebral cortex and subcortical nuclei. Opened more than two hundred years ago, this structure is still in the focus of attention of anatomists and clinicians. However, information on the origin, structure and functions of the fence, available today, remains quite controversial. Few are wondering why we need this mysterious structure. In this paper, we decided to determine to understand the secrets of the fence and understand how this small part of the brain affects in human neurological disorders and possible implication of this knowledge in the context of stem cells transplantation in neurological disorders such as Alzheimer, Parkinson and other incurables diseases.

Goal. To analyze the known data on the brain fence, describe its anatomy, cytoarchitectonics and development during the progress of the ontogenesis process. Investigate exact nature of the structures the fence is connected with and understand why these connections are necessary. Find out what role the fence plays in the functioning of the brain that most likely can be used for the stem cells transplantation.

Materials and methods. We used the materials of scientific literature obtained from Google. Scholar, Elsevier, NCBI MedLine, Scopus, and analyzed the data found their generalization and systematization.

Results. Although the advent of the latest methods made it possible to investigate the fence at the molecular, physiological, and behavioral levels, the functions of this structure are currently not fully understood. The anatomical position, relatively homogeneous cytoarchitectonics and an extensive network of connections allow us to conclude that the fence participates in the integration and processing of incoming information and, accordingly, in the formation of a holistic picture of perception. In addition, there are studies that prove that there is a change in the structure and volume of the fence in PD, AD, autism, schizophrenia and depressive disorders.

Conclusion. These studies take into account the structure, ontogeny and function of the fence, to better understand the global role of this structure that able to open a new direction for the treatment of neurological disorders.

Keywords: fence, claustrum, fence functions, fence ontogenesis, fence blood supply, information processing, fence neurons and communications, neurological disorders, stem cell transplantation