International Association of Neurorestoratology

Stem Cell Society of India

Global College of Neuroprotection & Neuroregeneration

Indian Federation of Neurorehabilitation

IANR VII & 1st SCSI With 11th GCNN & 2nd IFNR Conference

27th Feb - 1st March 2014
Mumbai, India

Scientific Program & Abstract Book

Welcome Address

Dear colleagues,

It's a pleasure and a privilege to invite all of you to participate in the International Association of Neurorestoratology VII Annual Conference, 1st Stem Cell Society of India Annual Conference, 11th Global College of Neuroprotection & Neuroregeneration Annual Conference & 2nd Indian Federation of Neurorehabilitation Annual Conference.

The last few years have seen a quantum shift in research as well as evolution of newer therapies that are increasingly restoring neurological function in patients with injuries and diseases of the nervous and musculoskeletal systems. More than ever before advances in medicine are now dependent on interdisciplinary team work and greater interaction between basic scientists and medical practitioners. The evolution of cellular transplantation and regenerative medicine has given tremendous hope to patients with incurable neurological conditions. What is unique about Neurorestoratology is that it brings together disciplines from across the medical spectrum to cover topics of Neuroprotection, Neurorecovery, Neurorestoration, Neuroregeneration, Neuromodulation, etc. and includes laboratory scientists, rehabilitation therapists, medical physicians and specialists surgeons. It is only when these get together that translation occurs from basic concepts to bedside factors.

A special aspect of this year's IANR meeting is that it is being held along with annual conferences of the Stem Cell Society of India, The Global College of Neuroprotection and Neuroregeneration and the Indian Federation of Neurorehabilitation. There is much that is common between these specialities and we hope that the joint interaction between the prominent and established leaders of Neurorestoratology, stem cell scientists and Neurorehabilitation therapists will be stimulating and contributing to all concerned.

We welcome you all invited speakers as well as delegates to Mumbai, India to participate in this exclusive and outstanding forum, the discussions of which will result in the evolution and practice of newer treatment options. Lectures, round table conference and youth forum of IANR will be organized during the 3 days of the conference and we hope that the social programs will be enjoyable and exciting.

Once again we welcome you all to IANR VII, 1st SCSI, 11th GCNM and 2nd IFNR conference.

Yours sincerely,

Chairman of the Conference
Dr. Alok Sharma

Co-Chairmen of the Organizing Committee
Ziad Al-zoubi (Jordan) /Hari Shankar Sharma (Sweden) / Dafin F. Muresanu (Romania)

Co-Chairmen of the Scientific Committee
Geoffrey Raisman (UK) /Huang Hongyun (China) / Wise Young (USA)

Co-Chairmen of the Local Organization Committee
Nirmal Surya /Venkatramana Neelam Krishna /Arun Mukherjee

Day 1 – Thursday (27/02/2014)

MORNING SESSION

Grand Ballroom

9:00-9:30 am: Opening Ceremony

Session 1: Plenary Session		
Chairpersons: Hongyun Huang, Alok Sharma		
9:30-9:50	Geoffrey Raisman	Why Olfactory Ensheathing Cells?
9:55-10:15	Hongyun Huang	Clinical progress, opportunity and challenge of cell therapy in Neurorestoratology
10:15-10:35	Alok Sharma	A New Look at the Ethics & Regulations of Stem Cell Therapy in Neurological Disorders: The 2 Sides of a Coin
10:40 – 10:50	Discussion	
10:50 – 11:10	Coffee Break	
11:10-11:30	Wise Young	The Importance of Rehabilitation for Recovery of Function after Regeneration
11:35-11:55	Ziad M AL-Zoubi	Role of Media in Promoting or Defaming Stem Cell Therapy
12:00-12:20	Hari S Sharma	Nanodrug delivery of pharmacological agents and stem cells in CNS Injury & Repair
12:20- 12:30	Discussion	
12:30-13:30	Lunch	

Hall D

Session 5: SCSI – Stem cell therapy for neurological disorders		
Chairperson – Dr. Alok Sharma, Dr. Venkatramana N K		
13:30-13:50	Dr. Prerna Badhe	Stem Cells - Neurogenesis to Neurotherapeutics
13:55-14:15	Dr. Hemangi	Stem Cell Therapy & Other Advances for Motor Neuron Disease
14:20-14:40	Dr. Avneesh Gupte	Multiple Sclerosis : A new approach with liberation surgery & stem cell treatment under one roof
14:45-15:05	Dr. Venkatramana N K	Mesenchymal stem cells in Parkinsons disease
15:10-15:30	Dr. Vishal Warkhe	Fostering Stem cell therapeutics in India: Addressing quality cost and availability issues
15:30-15:40	Discussion	
15:40-16:00	Coffee Break	

Hall D

Session 9: SCSI – Stem cell therapy for cardiac and neurological disorders		
Chairpersons – Dr. Mrinalini Chaturvedi, Dr. B. S. Rajput		
16:00-16:20	Dr. Rajiv Kumar Srivastava	Cardiac Regeneration and Stem Cell
16:25-16:45	Dr. Lissy K.Krishnan	Differentiation of circulating multipotent adult progenitor cells into neurons
16:50-17:10	Dr. Anant Bagul	Present status of Clinical trials on stem cell in neurological disorders
17:10-17:30	Dr. Mohamed Salahudeen	Update of stem cell therapy for peripheral vascular diseases

18:30 – 19:30 Executive committee Meeting of SCSI (Meeting Room 2)

19:30 – 21:00 Cultural evening and Banquet dinner

Hall D

Session 14 : SCSI - Stem cell Therapy for neuromuscular and musculoskeletal disorders		
Chairpersons: Dr. Rajiv Shrivastava, Dr. Anjoo Gupte		
13:30-13:50	Dr. Alok Sharma	Stem cell therapy in Spinal Cord Injury
13:55-14:15	Dr. B S Rajput	Role of mesenchymal stem cells in management of Duchenne Muscular Dystrophy
14:20-14:40	Dr. Manish Khanna	Importance of Stem cells in Orthopaedic practice
14:45-15:05	Dr. Pradeep V. Mahajan	Stem cell niche and stem cell therapeutics
15:10-15:30	Dr. Anjoo Gupte	Cerebral Palsy : An experience of 6 years with autologous stem cells
15:30-15:40	Discussion	
15:40-16:00	Coffee Break	

Hall D

Session 22: SCSI – Stem cell therapy		
Chairpersons: Pradeep Mahajan and Manish Khanna		
10:20-10:40	Dr. Mohan Thomas	Cosmetic applications of adipose derived stem cell – current concepts
10:45-11:05	Dr. Asis Mukhopadhyay	Stem cell transplant: an experience from eastern india
11:10-11:30	Rajashri Mokashi	Dental pulp cells
11:35-11:55	Deepak Ghaisas	Role of corporate in the development of stem cell therapy
12:00- 12:20	Dr. Ashit Shah	Role of stem cells in Trichology
12:20 -12:30	Discussion	

Day 3 – Saturday (01/03/2014)

AFTERNOON SESSION

Session 23: Workshop on Botulinum Toxin A in Spasticity
13.30 – 15.45 pm
Nirmal Surya, Abhishek Srivastava
Tea Break 15.45 – 16.00 pm

Alok Sharma (India)
Professor of Neurosurgery & Head of Department.
LTMG Hospital & LTM Medical College, Sion, Mumbai, India
Director, NeuroGen Brain & Spine Institute Pvt. Ltd., Navi Mumbai, India
Consultant Neurosurgeon, Fortis Hospital, Mulund, Mumbai, India

A New Look at the Ethics & Regulations of Stem Cell Therapy in Neurological Disorders: The 2 Sides of a Coin

Alok Sharma

In no other field of medicine have regulations so much slowed down the development of the field as in Stem Cell Therapy. The genesis of this goes back to the ban President George Bush placed on the federal funding of embryonic stem cells lines developed after 2001. Whereas regulatory bodies are right in having stringent standards to ensure patient safety, we believe there are two sides to this issues. The other side is that many patients are being deprived of treatments that could potentially save their lives or help reduce their suffering. To look at the other side we believe that regulatory bodies need to make the following distinctions in creating future guidelines. To explain this we quote from the ICST White paper published in 2011 [1] Distinction between Experimental therapies and medical innovation:- The White paper states:- "It is important to recognize the difference between clinical trials of experimental treatments and medical invocation. Medical innovation in cellular therapy may be viewed as ethical and legitimate use of non-approved cell therapy by qualified healthcare professionals in their practice of medicine . Patients not eligible for controlled clinical trials should be able to choose unproven but scientifically validated cell therapy medical innovations, if the researchers are competent and those seeking treatment are truthfully and ethically informed. There is a place for both paradigms in the cell therapy global community." [2] Distinctions Between Different types of centers doing this work:- The ICST White paper states centers doing this work should be defined and differentiated as follows:- "[a]approved/standard therapies (e.g hematopoietic stem cell transplant and other cellular therapies approved for marketing)[b] Controlled clinical trials[c] Valid compassionate use of unapproved therapies[d] Treatments not subject to independent scientific and ethical review"Regulations should be different for each of these categories. According to usthose falling in category [c] would be those who work in accordance with the Helsinki declaration of the World Medical Association which states "'In the treatment of an individual patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available. " [3] Distinction also needs to be made between the 3 broadly different types of stem cells (embryonic, umbilical cord derived , adult) and between autologous and allogenic:-

If one were to give an example from daily life then Embryonic stem cells could be compared to Alcohol, Umbilical cord stem cells to Cold drinks like Pepsi, Coke and Adult autologous stem cells to Homemade Fruit juice. Whereas alcohol is potentially dangerous and there should definitely be tight regulations so also embryonic stem cell work should be tightly regulated. Cold drinks may not be dangerous but can be harmful so there should be quality checks in place, so also for umbilical cord cells there should be quality checks in place and these types of cells should be treated like drugs / medicines and the same regulations and quality control systems should be in place for them. However there is no need for any strict regulations for home made orange juice and so autologous adult cells should be freed up from regulations and their availability in fact encouraged since they are completely safe and have shown

clinical benefits in many conditions in various published scientific papers. We also believe that the centers / practioners following the following principles should be looked upon in a more permissive manner :- [a] Those who strictly treat patients in accordance with the Helsinki Declaration. That means they do not treat patients where other more established treatment forms are available and the patients have not already taken them. [b] The medical practioners practicing this are working within the general broad specialty of their qualifications and are dealing with diseases anatomically and physiologically that concern their broad specialty and that that they have received specialized training in cell therapy or done some basic research work in their fields.[c] Whilst doing this treatment they are also making this an object of their research and evaluating its safety and efficacy.[d] They are publishing the results and outcomes of their clinical work, including their negative results and complications if any.[e] They are taking special informed consent [f] There is a honesty and transparency to their work as shown by the fact that their clinical results are in the public domain and they present their results in national and international scientific conferences.[g] They have Institutional Committees that monitor the ethical, scientific and medical aspects of the work.[h] That quality standards are maintained that is they have GMP facilities &/or other accreditations etc. With the above principles in place we shall be able to simultaneously ensure that patients with serious illnesses get the benefit of available stem cell treatments and an adequate check is kept on medical practices in this field to ensure the safety of patients.

Role of Stem cell therapy in spinal cord injury

Alok Sharma
Neurogen Brain and Spine Institute, Mumbai
LTMG Hospital & LTM Medical College, Mumbai

Spinal cord injury most often results in extensive axonal degeneration, neuronal loss, and severe functional deficit. The functional restoration is dependent on the regeneration of the damaged axons and formation of neural connections. One of the most effective treatment strategies focusing on neural repair is the intrathecal administration of autologous bone marrow mononuclear cells (BMMNCs).

Herein we present two studies with an aim to determine the functional and clinical outcome of intrathecal administration of autologous bone marrow mononuclear cells, along with its effect on the quality of life in patients with thoracolumbar and cervical SCI.

The first study is a published study with a detailed analysis of thoracolumbar SCI patients who underwent cellular therapy followed by neurorehabilitation. The study sample included 110 thoracolumbar SCI patients. The other study was conducted in a similar setting including cervical SCI patients.

The outcome was recorded at a mean follow up of 2 years ±1 month. The outcome measures used for both the studies were Functional Independence Measure (FIM) score, American Spinal Injury Association scale (ASIA) and detailed neurological assessment. Data was statistically analyzed using McNemar's Test to establish significance between the change in symptoms and the intervention.

In the published study of thoracolumbar SCI, 100 out of 110 (91%) patients showed improvements. Improvement in trunk control was observed in 95.6% cases, bladder management in 33% with respect to shift from indwelling and condom catheter to self intermittent catheterization, partial sensory recovery in 27% and reduction of spasticity in 26%. All the patients showed improvement in postural hypotension. 38% wheelchair bound patients started walking with assistance. Functionally, 27% showed improved activities of daily living (ADLs) and 53.6% showed a positive change in FIM score. 10% cases showed a shift in ASIA scale. A statistically significant association of these symptomatic improvements with the cell therapy intervention was established using McNemar's Test. On electrophysiological studies, 2 showed improvement and 1 showed change in functional MRI.

In the study conducted on cervical SCI patients, 37 out of 50 (74%) showed improvements. Sensation recovery was observed in 26% cases, improved trunk control in 22.4%, spasticity reduction in 20% and bladder sensation recovery in 14.2%. All the 50 cases had improvement in postural hypotension. 12.24% wheelchair bound patients started walking with assistance. Functionally, 20.4% patients showed improved ADLs and 48% showed a positive change in FIM score. 6% cases showed a shift in ASIA scale. A statistical analysis using McNemar's test established a significant association of these symptoms with the intervention.

No major side effects were noted in the duration of 2 years.

In both, thoracolumbar and cervical spinal cord injury, intrathecal administration of autologous bone marrow mononuclear cells along with neurorehabilitation demonstrates statistically significant outcome both clinical and functional. In our study, a better outcome was observed in thoracolumbar injury as compared to the cervical injury suggesting that the level of SCI greatly influences the recovery of the patient. Overall, it is a safe and feasible therapeutic strategy improving the quality of life of the SCI patients.

Biography

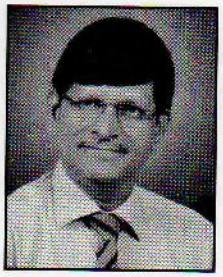
Alok Sharma is presently the Professor & Head of Department, Department of Neurosurgery LTMG Hospital & LTM Medical College, Sion, Mumbai, India and Director, NeuroGen Brain & Spine Institute,

Chembur, Mumbai and Honorary Consultant Neurosurgeon, Fortis Hospital, Mulund, Mumbai. He obtained his MBBS, M.S and M.Ch from the Seth G.S. Medical College& KEM Hospital of Mumbai University. Subsequently he trained overseas in some of the most prestigious universities of the world in Sweden, UK, Germany, USA and Japan. He has authored/edited 8 books, contributed chapters to severe textbooks, has 78 Scientific publications and has made over 125 International, National and zonal presentations. He is the Associate Editor of the Indian Journal of spinal surgery and on the editorial board of other journals. He has conducted many international and national research trials and studies, has organized numerous conferences and workshops, held many organizational positions and has been the recipient of many awards and honors in his distinguished career. He has been the pioneer in India in the field of Regenerative medicine and in particular on the use of stem cells in the treatment of incurable neurological disorders. He is the Founding President of the Stem Cell Society of India. He has set up and heads the Stem Cell-Genetic Research laboratory of the Municipal Corporation of Greater Mumbai at the LTMG Hospital & LTM Medical College. He founded the NeuroGen Brain and Spine Institute that is dedicated to stem cell therapy and neurorehabilitation. He is Chairman of the seventh annual conference of the International Association of Neurorestoratology being held in Mumbai in 2014. His other special interests include Surgery for ischemic stroke, Neurotrauma, Spinal Reconstruction, Stereotactic & Functional Neurosurgery including Psychosurgery and Neuroendoscopy.

Characterisation and Application of Human Adipose Tissue Derived Stem Cells to Regenerative Medicine

Dr. A. Anand Kumar
Head - Auto Stem Laboratories

Human adipose tissue has been shown to contain a population of cells that possesses extensive proliferative capacity and the ability to differentiate into multiple cell lineages. With the difficulties in using either embryonic stem cells (ESCs) or induced pluripotent stem cells (iPCs) in clinical situations or hematopoietic stem cells (HSCs) due to more invasive procedures associated with bone marrow aspiration, the use of adipose tissue as a viable alternative source has gained appreciation. Adipose tissue-derived stem cells (ADSCs) can be isolated from lipoaspirates or from resected adipose tissue. The large volume of tissue obtained from a liposuction procedure (average approximately 2 L) or in a resection procedure, combined with the relatively high frequency of ADSC within the digestate provides substantially more stem cells (1 × 107 adipose stromal/stem cells from 300 ml of lipoaspirate) than can be realized from bone marrow. Within the lipoaspirate or resected adipose tissue, the Stromal Vascular Fraction (SVF) from resected tissue has more percentage of CD34+ ADSCs than the SVF derived from lipoaspirate. Further, the density of stem cell reserves also varies within adipose tissue and is a function of location, type, and the process that is used to extract the stem cells. For instance, ADSC yields are greater in subcutaneous fat tissue compared with omental fat, with the highest concentrations seen in thigh fat. Similarly, compared with ADSCs from later passages, freshly isolated SVF cells and early passage ADSCs express higher levels of CD117 (c-kit), human leukocyte antigen-DR (HLA-DR), and stem cell-associated markers such as CD34, along with lower levels of stromal cell markers such as CD13, CD29 (?1 integrin), CD44, CD63, CD73, CD90, CD105, and CD166. While the consequences of the decrease in CD34 and CD105 expression in later passage ADSCs are not clear, it nevertheless implies a differential role these cells might play in the regenerative process. Furthermore, it indicates an unidentified culture induced phenotypic alterations in the stem cells that points towards epigenetic changes. Nevertheless, from a regenerative perspective, ADSCs play a major role through its paracrine supportive role than direct tissue contribution, which opens up a potential use of both autologous and allogeneic ADSCs for regenerative medicine.



Role of Mesenchymal stem cell transplantation in the management of Duchenne muscular dystrophy

Dr B.S.Rajput
Consultant orthopaedic and stem cell transplant surgeon
Visiting Consultant to;
Breach candy hospital, Mumbai
Nanavati HCG Cancer centre, Mumbai
Criticare hospital and research centre, Mumbai

DMD is a genetic disorder with no known cure as yet. As it is a fatal disorder with prevalence of 1 in 3500 male children, the researchers are working globally to come out with a definitive solution.

A lot of preclinical studies have been done but not much of concrete results have been found in clinical studies.

I would like to present the outcome of a pilot study of MSCs transplantation in DMD patients done in India for the first time, with the focus on safety and efficacy observed in last 3 years.

Cellular cancer therapy: A future conundrum or reality?

Dr. Ganapathi Bhat M.

Hon. Consultant Medical Oncologist & Stem cell transplant physician at Jaslok Hopsital
Mumbai, India

Cancer is an abnormal, uncontrolled growth in which normal homeostatic cellular control is lost and cells grow continuously, invading, crowding, and overwhelming the surrounding normal tissues. The heterogeneity of cancer cell growth may vary from multiple cumulative mutations, to failure of immune system to stop expansion or stemness of endogenous supportive niche called cancer stem cells. Scientists are elucidating this heterogeneity of cancer at the single cell level equipped with a better understanding of tumor biology and development of technologies. Identification of biomarkers to predict the risk of progression and therapeutic resistance and approaches to infer the intratumor heterogeneity, has led to novel cancer therapies like cell therapy. The current cell therapy approaches largely involve the infusion of immune cells programmed to recognize and kill tumor cells either by giving rise to a new immune system; or by activating the patient's own resident immune cells; or by directly infusing immune cells. Challenges with these cellular therapies ahead are enormous ranging from identification and selection of cells which can eliminate cancer cells without harming the neighbouring normal cells and finally translate these methodologies into clinical practice.

Hall D

Session 18: SCSI - Cellular therapy in oncology and Tissue cell banking		
Chairpersons: Dr. Avneesh Gupte, Dr. Ganapati Bhatt		
16:00-16:20	Dr. Mrinalini Chaturvedi	Perinatal Tissue Banking and Applications
16:25-16:45	Dr. A. Anand Kumar	Characterisation and Application of Human Adipose Tissue Derived Stem Cells to Regenerative Medicine
16:50-17:10	Dr. Ganapathi Bhat M	Cellular cancer therapy: A future conundrum or reality?
17:15-17:35	Jayshree Nellore	Synthesis of biogenic hydroxyapatite/ chitosan/ PVA blends loaded with proneurogenic factor: Correlation with structural and biological aspects
17:40-18:00	Dr. Smitha Bhoyar	Overview of regulatory perspective on the ethics of stem cell research and therapy
18:00-18:10	Discussion	

19:00 – 21:00 Dinner

Autologous bone marrow mononuclear cells intrathecal transplantation in Amyotrophic Lateral Sclerosis : a clinical study

Dr. Hemangi Sane, M.D (Internal Medicine, USA)
Head-Research and Development, Consultant Physician
Neurogen Brain and Spine Institute, Mumbai

Background : Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by progressive degeneration of upper motor neurons in the cerebral cortex and lower motor neurons in medulla and anterior horn of spinal cord. The etiology of the disease is poorly understood and several theories fail to determine the exact cause. The prognosis remains grim. Cellular therapy has been studied for ALS in various animal models and these advances have highlighted its therapeutic potential.

Objective: Primary objective was to study the effect of intrathecal autologous bone marrow mononuclear cells transplantation on the survival duration of the ALS patients. The secondary objective was to analyze the effect of age at onset, bulbar onset and lithium on the survival duration of the patients post cellular therapy.

Method : A retrospective controlled cohort study of total 66 ALS patients was conducted which included 46 patients in the intervention group and 20 patients in the control group. The intervention group patients underwent intrathecal autologous bone marrow mononuclear cell transplantation in addition to standard rehabilitation and Riluzole. Control group consisted of 20 patients who did not receive cell transplantation. The survival duration of these patients in both groups was compared using Kaplan-Meier survival analysis. The effect of age at onset, type of onset and lithium on survival duration in the intervention group was also analyzed.

Results : The mean survival duration of the patients who received intervention was 104 (10.9) months and those who did not was 57(5.3) months. The difference between the two was statistically significant ($p=0.043$). A clinically significant difference of 47 months in the survival duration was observed. Survival duration was significantly higher in patients with the onset of the disease below 50 years of age. Limb onset and lithium also showed improved survival duration. The higher mean survival duration of the intervention group was observed than the previously reported epidemiological studies.

Conclusion : The longer survival in the intervention group suggests that combination of intrathecal autologous bone marrow mononuclear cells transplantation with riluzole, lithium and rehabilitation may slowdown the progression of the disease. Further multicentered clinical studies are needed.

Differentiation of circulating multipotent adult progenitor cells into neurons

Lissy Krishnan & Tara S.
Thrombosis Research Unit, Biomedical Technology Wing,
Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum

Adult stem cells are being studied to develop patient-specific treatment options for many diseases. The presence of neural progenitor cell (NPCs) among heterogeneous monocyte population gives an interesting opportunity for their use as autologous source for regenerative medicine. Availability of only low numbers of NPCs in circulation demands their expansion by in vitro culture to obtain sufficient numbers for transplantation. Their multi potency implies that neural lineage commitment is essential prior to transplantation to avoid undesirable differentiation in vivo, post transplantation. The lineage committed NPCs may prove to be useful for treating spinal cord injury (SCI). Other than identification of a suitable stem cell source, challenges faced for successful transplantation are poor cell homing and survival at the injured site due to the unfavorable mileue. The hypothesis of this study is that a fibrin-based bio mimetic matrix may support in vitro selection from a mixed population, promote proliferation, and induce lineage commitment of circulating NPCs into functional neurons. The peripheral blood mononuclear cells (PBMNCs) were isolated from human and/or rat blood (Inbred Wistar strains) using Histopaque density gradient centrifugation and non- plastic adherent cells were seeded and grown on the composed matrix for 10-15 days (1,2). Cells were analyzed at specific time intervals for the expression and distribution of neural specific markers using immunocytochemistry, flow cytometry and RT-PCR. Proliferation potential of NPCs in culture was analyzed using Ki67 as marker. For testing the potency of bio mimetic matrix as cell carrier for transplantation in in vivo experiments, contusion type SCI model was created using an impactor with ~150 dyne cm-2 force. Inbred animals were used as cell donors. Lineage committed cells were mixed with fibrin matrix and transplanted. The site of injury was explanted and subjected to histological analysis.

The neurons derived from the small percentage of nestin+ progenitors in the hetergenous PBMNC was 90-95% pure by day 6 in culture. Differentiation was confirmed when MAPCs were grown in neural-specific niche in vitro; but the functional marker produced during the process of synapse formation and impulse transmission was expressed more when more KCl was added to the cultures. The current study identified peripheral blood as a potential source for deriving functional neurons. Most of the components in matrix used for influencing differentiation of NPC, such as fibrin, fibronectin, laminin, platelet-derived growth factor were obtained from human blood. Even though the number of NPC in circulation was found low, specifically selected NPC proliferate during the initial phase of differentiation. The results indicated that the composed matrix may become a suitable in vivo matrix for supporting cell homing and differentiation after transplantation at an injured neural site. Ongoing research suggests that the designed niche may also be used for differentiating adipose derived mesenchymal stem cells (ADMSC) to neuron.

Stem Cells Niche and therapeutic application of stem cells

Dr. P.V. Mahajan
Founder and Managing Director of StemRx Bioscience Solutions

Stem cell niche refers to a microenvironment where stem cells are found, which interacts with stem cells to regulate cell fate. Stem cells are considered as the building blocks of the body because of their ability to self renew and differentiate into specific tissue types. These stem cells reside in a specific niche in vivo where various microenvironmental cues form an intertwined signaling regulatory network that maintains stem cells fate and functions. Within the human body, stem cell niches maintain adult stem cells in a quiescent state, but after tissue injury, the components of the niche pass signals to these stem cells to activate them to multiply, differentiate and proliferate.

In this niche there are different regulators such as ECM molecules (Extra Cellular Matrix) molecules, biochemical cues such as soluble growth factors and cytokines and mechanical cues such as intrinsic matrix stiffness and extrinsic forces which play a major role in deciding the fate of the stem cell. Along with that cell-cell interaction, interaction between stem cells and adhesion molecules, physiochemical nature of the environment including pH, ionic strength, and oxygen tension are also important. Clustering of cell surface receptors often serves to polarize cells and in some cases it activates downstream signaling pathways. Integrins, the major class of cell surface adhesion proteins, are well known to mediate signaling through receptor clustering. These signaling pathways may be different for different types of stem cells. For example when hematopoietic stem cells are injected inside the body of the patient, homing of these stem cells depends on different signaling pathways. Several pathways have been studied in relation to hematopoesis which are SDF-1 (CXCL12)/CXCR4 signaling, BMP signaling, Mpl/Thrombopoietin (TPO) signaling, Tie2/Ang-1 signaling, hedgehog and Notch signaling, as well as Wingless (Wnt) signaling.

The microenvironment or niche can be specific to the type of the cells and accordingly niches are further classified as 'blood cell niche', 'bone cell niche', 'intestinal cell niche', 'hair follicle cell niche', 'brain cell niche' etc. Adult stem cells remain in undifferentiated state throughout adult life; however when they are cultured in vitro, they often undergo an aging process in which their morphology is changed and their proliferative capacity is decreased so it is believed that proper culturing conditions of adult stem cells needs to be improved so that adult stem cells can maintain their stemness over time. In future there is a need to engineer or optimize niche cues for differentiation towards different lineages in vitro and analyzing these homing pathways will definitely provide an understanding insight for the development of some new therapies for the treatment of even chronic diseases where stem cells may prove the only remedy. It is very important to understand how these niches can be engineered in vitro. This will help in deciding the fate of the stem cells administered in vitro. The niche must have both anatomic and functional dimensions. The niche may differ as per the type of the cell in which it has to be differentiated.

In therapeutic applications, when stem cells are administered inside the body of the receptive patient, the defined niche factors (growth factors) play an important role in giving the direction to stem cells to differentiate into required lineage. The formed lineages are then well supported by the cytokines released by immune cells inside the body of the patient which increases the proliferation and differentiation capacity of the cells and function of the damaged system is recovered. However though the process looks simple it involves lots of signaling pathways which regulates the entire process. Many a times scaffolding also play an important role in therapeutic applications.

Stem Cells - Neurogenesis to Neurotherapeutics

Dr. Prerna Badhe. MD.
Deputy Director & Consultant Neuropathologist, Neurogen Brain and Spine Institute

Neurogenesis(NG) is a complex process, with its understanding changing rapidly over the last few decades. It starts from the third week of embryonic life with the formation of neural tube and continues throughout life contradictory to earlier beliefs. Active adult NG in the mammalian brain occurs in the subventricular zone(SVZ) of the lateral ventricles, subgranular zone(SGZ) of the dentate gyrus(DG) and the SGZ of the cortex. It involves multiple orchestrated steps including self proliferation, fate specification, differentiation, maturation, neuronal migration and finally functional synaptic integration into the existing neuronal circuitry. NG is dynamically regulated by intrinsic as well as extrinsic factors like neurotransmitters, growth factors, hormones, genetic factors, stress and the highly specialized microenvironment referred to as the "neurogenic niche" or "stem cell niche" which includes the neural precursor cells, surrounding glial cells, cell to cell interaction, secreted factors and cilia. NG can be enhanced by exogenous stem cells engraftment ranging from adult neural stem cells(NSC's) to induced pleuripotent stem cells(iPSC's). These can be used in neurotherapeutics due to its ability to form dopaminergic neurons, spinal cord motor neurons, gabaminergic and cholinergic neurons, retinal precursors, oligodendrocytes and astrocytes in the treatment of neurotrauma, neurodegenerative disease, neurodevelopmental and neuropsychiatric disorders. Recent understanding of signaling mechanism including Wnt, sonic hedgehog, notch, growth and neurotrophic factors, transcription factors, bone morphogenetic proteins, neurotransmitters, and epigenetic modulators, and crosstalk between these signaling pathways in the regulation of adult NG have generated great interest in understanding the cellular and molecular mechanism underlying the functional role in adult NG, which will enable the development of targeted neurotherapeutics.

Cardiac regeneration and stem cell therapy - Advances and challenges

Dr. Rajiv Kumar Srivastava
Consultant Cardiac Surgeon

Introduction:

Significant recent developments have occurred in the field of cardiac regeneration and stem-cell therapy. Understanding the new technological advances in cell therapy will ultimate allow us to achieve a goal of cell-based cardiac repair.

Methods:

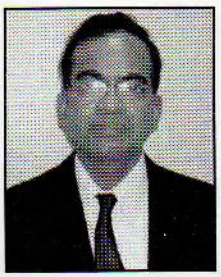
We reviewed the latest cell-based therapies (including Autologous cardiosphere-derived cells with fibroblast growth factor , endogenous c-kit+ cardiac progenitors , bone-marrow-derived stem cells), the recent clinical trials in humans.

Results :

Congestive heart failure and coronary artery disease are the leading causes of morbidity and mortality in India. Cell-based therapy has emerged as a promising approach to combat the myocyte loss and cardiac remodelling that characterize the progression of left ventricular dysfunction to heart failure. Several clinical trials have shown that a variety of autologous bone-marrow- and peripheral-blood-derived stem and progenitor cell populations can be safely administered to patients with ischaemic heart disease and yield modest improvements in cardiac function. Cell-based therapies to regenerate the damaged myocardium using endogenous cardiac progenitors have been used in the recently completed CADUCEUS and "Administration of cardiac stem cells in patients with ischemic cardiomyopathy" (SCIPIO) clinical trials.

Conclusions:

It is evident, based on the new data, that cell transplantation results in an increase in viable tissue and an improvement in functional outcome. Further optimization of methods to increase engraftment and regeneration, such as selection of cell types for treatment and growth-factor enhancement, will improve upon results. As work in the field progresses, regenerating the injured myocardium through stem cell-based therapies may become feasible as a therapeutic option for future generations.



Title: Role of Mesenchymal stem cells in Parkinson's disease

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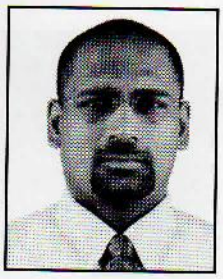
Parkinson's disease (PD) is a progressive neurodegenerative disease for which stem cell research has created hope in the last few years. Seven PD patients aged 22 to 62 years were included as prospective, uncontrolled, pilot study .The BMMSCs were transplanted into the sub ventricular zone by stereotaxic surgery. On follow up the mean baseline "off" score was 65622.06, and the mean baseline "on" score was 50.6615.85. Three of 7 patients have shown a steady improvement in their "off"/ "on" Unified Parkinson's Disease Rating Scale (UPDRS). The mean "off" score at their last follow-up was 43.3 with an improvement of 22.9% from the baseline. The mean "on" score at their last follow-up was 31.7, with an improvement of 38%. Hoehn and Yahr (H&Y) and Schwab and England (S&E) scores showed similar improvements from 2.7 and 2.5 in H&Y and 14% improvement in S&E scores, respectively. A subjective improvement in facial expression, gait, and freezing episodes; 2 patients have significantly reduced the dosages of PD medicine.

Based on this study , we again recruited 8 PD and 4 PD plus patients between 5 to 15 years after diagnosis. All patients received BM-MSCs bilaterally into the SVZ and were followed up for 12 months. PD patients had a mean improvement of 17.92% during "on" and 31.21% during "off" period on the UPDRS scoring system. Subjectively, these patients reported clarity in speech, reduction in tremors, rigidity, and freezing attacks. Those patients transplanted in the early stages of the disease (less than 5 years) showed more improvement and no further disease progression than the later stages (11-15 years). However, the PD plus patients did not show any change in their clinical status. This study demonstrates the safety of adult human BM-MSCs for transplantation and its efficacy in early-stage PD patients.



Fostering stem cell therapeutics in India: Addressing quality, cost and availability issues

CV - Dr. Vishal G Warke (brief details)
Director R & D - Cell Culture Division
HiMedia Laboratories

As the field of stem cell and primary cell research and therapeutics is poised to take off, there remain many issues that have to be addressed in order to facilitate research and therapeutics in India. HiMedia is committed to support patient treatment by making excellent quality stem cell and primary cell expansion, differentiation and cryopreservation reagents and media available to clinicians and scientists in India and globally, at very affordable prices and short delivery lead times.

Customized solutions are a need of the hour and HiMedia is supporting clinicians and hospitals by giving media and reagents in the required pack sizes and kit formulations (such as kits for cord cell banking etc), with customized media compositions as per each project requirement. These are manufactured under strict GMP compliant conditions, and are certified mycoplasma free, with endotoxins well below 0.125 EU/ml. The components used are also parenteral grade and pharmacopeia compliant, with complete traceability and documentation as per ISO 13485 and GMP norms. Thus, HiMedia can play a key role in making Stem Cell therapy affordable and accessible to one and all.

Synthesis Of Biogenic Hydroxyapatite/ Chitosan/ Pva Biocomposite Loaded With Retinoic Acid: Correlation With Structural And Biological Aspects

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The present study explores the synthesis of biogenic hydroxyapatite/ chitosan/ Polyvinyl alcohol biocomposites for delivery of proneurogenic factor, Retinoic acid for reconstruction of craniofacial deformities. In order to accomplish this aim, we started with the synthesis of hydroxyapatite using the biomolecules occluded in the kitchen wastes (CPHAp). Scanning Electron Microscopy (SEM), Fourier Transform Infrared Spectroscopy (FTIR) and X-ray Diffraction studies (XRD) studies confirmed the purity and morphology of CPHAp. Further a microenvironment for nerve cell growth was designed by synthesis of biogenic hydroxyapatite/ chitosan/ PVA blends loaded with Retinoic acid (CS-PVA-CPHAp-ATRA). The prepared biocomposites were characterized under advanced analytical instruments such as SEM, FTIR, XRD, Thermal analyses. The SEM analysis for the prepared biocomposites confirmed the formation of interconnected porous matrix. The results of FTIR confirm the biocomposite formation. The thermal stability studies demonstrated the stability of the biocomposite. From XRD the amorphous nature was confirmed, inducing suitability of the material for delivery process. Furthermore the biological properties of the biocomposite were analyzed by DPPH Radical Scavenging activity, hemocompatibility and MTT assay methods indicated that, the biocomposites are better in scaffold properties and it provides a healthier environment for cell attachment and spreading.