Proceedings ISCSG's 3rd International conference on stem cell & regenerative medicine 2019

Welcome Message from Organizing Committee of ISCSG 2019

Welcome to 3rd International conference on stem cell & regenerative medicine 2019 It's indeed a great honour and privilege for me to extend a wholehearted welcome to all the delegates for the 3rd International conference on Stem cell & Regenerative Medicine 2019 at Dr. D.Y. Patil Vidyapeeth Pimpri-Pune, Maharashtra, India. As organizing chairman of this event, I hope to bring together a good programme that stimulates both our clinical knowledge and scientific intellect. This will be through a combination of interesting lectures and engaging "hands-on" workshops that will enrich our current knowledge and clinical skills. Regenerative science holds a positive future in medical conditions which faces lot of challenges in presently available stem cell transitional research and application.

The ISCSG aims at:

To create awareness among clinicians, researchers about the regenerative science & newer development in this field. Progenitor cells application is a AN EXCITING CLINICAL CHALLENGE for all of us.

- To reuse, favour and stimulate all efforts to do Research work.
- To Create and develop international scientific relation with rest of the world.
- To elaborate, deepen and radiate the knowledge acquired in the domain and impart to those who ask for it.
- To represents this branch of medical knowledge at National & International level.
- To do all sorts of work related with the aforesaid Field.

This year we witness a great loss to stem cell industry due to unfortunate premise of Dr. Sankarnarayan in Delhi Fire Tragedy on 12th Feb 2019. In his memory we have organize Dr. Sankarnarayan oration ceremony by Dr. Ramesh Bhonde and all members of ISCSG Delegates. Our working committee member and dedicated regulatory and clinical trials advisor who paid crucial role in contacting and finalizing Government official of CDSCO, ICMR, DBT & FDA officials for conference. He had unfortunate demise while working for conference, insane Delhi fire tragedy we have organized late Mr. Santosh wale best critic paper award for young scientist under 45 years, in 3 paper competition.

Next ISCSG Conference will be conducted at AIIMS Hospital, Raipur by Alok Agrawal we wish him all the best & extend our co-operation of next upcoming ISCSG Conference.

Title: Patient-derived Induced Pluripotent Stem Cells (iPSC) Technology Towards Modelling Alzheimer's Disease.

Abstract: The last 2-3 decades have witnessed revolution in small molecules and biologics as frontiers in human medicine called the 1st and 2nd pillar of human medicine. Now in current century stem cells including other therapeutic cells are sitting on the cusp of another revolution, the third pillar of human medicine.

Our interest is in Aizheimer's disease (AD). It is a neurodegenerative disorder and represents the most common form of dementia, affecting 342, 800 Australian and 46.8 million people worldwide. With no cure so far, the projection is that this number will be double by 2030 and more than triple by 2050. Dementia is the third most leading cause of death after heart disease and stroke. Huge economic impact, in 2010, 604 billion spent worldwide. These numbers have gone up to 818 billion in 2015 and would be 2 trillion in 2030.

AD is characterized by the progressive loss of specific cholinergic neurons in the brain, which leads to gradual loss of bodily functions, long term memory loss and eventually death. The pathology of AD remains elusive due to the lack of appropriate animal and/or in vitro models, which recapitulate the human AD. The induced pluripotent stem (iPS) cells derived from patient's somatic cells and thus patient-specific iPS cells offer great potential in regenerative medicine, in drug discovery and modeling disease process in vitro. We report here the first generation of feeder-free iPS cells from Alzheimer's patient with an early onset of disease . These cells are produced by using a polycistronic lentiviral vector containing four pluripotent genes, Oct4, Sox2, Klf4 and cMyc. These iPS cells are pluripotent as demonstrated by both the in vitro and in vivo assays. These iPS cells have been analyzed by using the microarray chip and the computation of data is assisting in developing the in vitro models for this disease and for future regenerative medicine. Genome-wide microarray analysis revealed that AD-iPS cells are similar to control iPS cells and hESC lines; however, eight candidate genes differentially expressed between familial iPS cells and sporadic iPS cells. These cells exhibit disease-specific phenotype when cultured & differentiated to relevant neurons in vitro and when coaxed with specific inducers/stressors. These phenotypes could be ameliorated by using some anti inflammatory drugs. The idea indicated that it is possible to model disease in vitro and developing future therapeutics using these cells.

KULDIP SIDHU
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Title: EVALUATION IN VIVO EFFICAY OF GINGIVAL STEM CELLS FOR ALVEOLAR BONE REGENERATION

Abstract: Congenital or acquired abnormalities of the cranium and facial skeleton, including cleft defects of the palate, are of common occurrence. Reconstruction of these bony defects is important to preserve normal facial growth and function. Surgery is the mainstay for the repair of these abnormalities and in general. Correction of the defect requires extensive surgical procedures using bone graft techniques, which also require an extended healing time. Tissue engineering approaches offer promising and non-invasive alternative for palatal reconstructions, improved esthetics and better patient compliance and affordability. Our long term goal is to regenerate bone and repair these defects through tissue engineering. Autologous gingival mesenchymal stem cells (GMSCs) are an excellent source due to their ease of harvesting and minimal risk of immune-rejection. Growth factors, including bone morphogenetic protein-2 (BMP-2), a family of osteoinductive proteins, promotes the differentiation property of stem cells. Puramatrix (PM) is a novel peptide based self-assembling hydrogel scaffold that facilities GMSCs proliferation and differentiation. The combination of gingiva derived osteogenic progenitor cells and BMP2 embedded in the hydrogel and implanted in surgically created defects confirmed new bone formation in 4 weeks. The micro CT and histology results demonstrated the formation of bone in 8 weeks after implantation. The findings of the study suggest that GMCs are potential candidates for craniofacial bone regeneration.

UMA DEVI

Dr. Uma Devi Kandalam, Associate Professor, Department of Pediatric Dentistry and Director of Craniofacial Research Fellowship Program at College of Dental Medicine, Nova Southeastern University, Fort-Lauderdale, Florida, USA.

Title: Persistent DNA Damage Response Mechanisms in in Spermatogonial Stem Cells after Exposure to in vivo Genotoxic Agents in vitro.

Abstract: Spermatogonial stem cells (SSCs) are the stem cells in the testis and responsible for maintaining the integrity of their genome to help prevent reproductive failure and reduce the hereditary risk related to transmission to the offspring. Mammalian male fertility over a lifetime is maintained by an intricate balance between spermatogonial proliferation and differentiation. However, DNA damage in spermatogonia, caused by even low doses of chemotherapy, could induce germ cell apoptosis and cell cycle arrest, potentially in male infertility. SSCs therefore must have mechanisms to respond to the possibly adverse effects of DNA damage, resulting from both single (SSBs) and DNA double-strand breaks (DSBs) with DSB representing the highest risk genomic integrity. To investigate the molecular mechanisms underlying these responses, we developed an in vitro system consisting of rodent male germline stem cells. This allows the investigation of the effects of a variety of knownin vivo, phase-specific germ cell mutagens, i.e. pre-meiotic, meiotic, and post-meiotic genotoxins. These spermatogenic cell types can be separated using STAPUT unit-gravity velocity sedimentation. The Comet assay can be used to detected DNA damage and gene expression and their proteins levels can be quantified by qPCR and western blotting methods.

It was established for the first time for these compoundsin vitrothat SSCs are significantly more susceptible than spermatocytes, which are more affected than spermatids. This reflects the proportion of actively dividing cells in these cell types, suggesting a mechanism for the differential sensitivity. The approach should thus form the basis of a useful test system for reproductive and genetic toxicology in the future.

DIANA ANDERSON
(United Kingdom)

Title: Adipose Mesenchymal Stem Cell – Derived Exosomes Attenuate Retina Degeneration of Stereptozitocin induced Diabetes in Rabbits.

Abstract: Diabetic retinopathy (DR) is one of the serious complications of diabetes mellitus (DM), which lead to sever visual impairment especially in late stages of the disease. Hyperglycemia and defects in insulin signaling pathways result in many pathological process which end by the development of DR. DR involvesthe presence of microvascular defects, neuroretinal dysfunction and degeneration of the retina. Mesenchymal stem cell (MSCs) were isolated and purified from many sources, such as bone marrow, adipose tissue, fetal membrances, embryo, and cord blood and could be further utilized in tissue repair including the retina. MSCs are multipotent cells which have the possibility to transform into many types of cells involving cardiovascular, neurogenic, endothelial cells, and adipocytes. MSCs have been utilized as therapeutic agents because of their direct role in tissue regeneration and their strong anti-inflammatory properties which were discovered more recently. Moreover, MSCs have been applied in many clinical attempts for management of retinal degeneration. Exosomes are extracellular vesicles (EVs) of endosomal origin and are characterized from other vesicles derived from the cell by their origin, size, composition and shape. Accordingly, exosomes are present in supernatants of cell culture. CD81 and CD63 proteins have been utilized as specific markers of exosomes. It has been proved that exosomes may play a crucial role in transfer of mRNA, microRNAs (micRNAs) and proteins, It was found that presence of specific micRNAs, such as micRNA-17-5p, micRNA-126, micRNAs-221/222, and micRNA-296, involved in the regulation of angiogenesis. Angiogenesis, abnormal growth of retinal blood vessels, was associated with the severity of DR. MiR-221/miR-222 family sounds to negatively regulate angiogenesis by binding to the c-Kit receptor. The role of micRNA-222 in regulating the neovascularization observed in DR was detected by targeting signal transducer and activator of transcription 5A (STAT5A). Additionally, it is indicated that STAT5A is mostly regulated by micRNA-222 during inflammation-associated neoangiogenesis (20). Thus we focused on detecting the expression of micRNA-222. Recently, the functions of exosomes have been aimed to be investigated by more research. Our present study investigated the therapeutic effect of micRNA-222 containing exosomes in treatment of retinal degeneration after their injection in experimental rabbit model with DM induced by stereptozitocin (STZ).

ABDELHAKIM MOHAMED SAFWAT
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Title: Regulation of osteogenic differentiation of MSCs derived from umbilical cord and placenta.

Abstract: mesenchymal stromal cells (MSCs) offering valuable hopes for regenerative medicine due to their regenerative functions. They can be isolated from many tissues including placenta and umbilical cord. MSCs from placenta (PL-MSCs) and umbilical cord (UC-MSCs) can differentiate into osteoblast similar to that of bone marrow-derived MSCs(BM-MSCs). However, the ability is not much efficient compared to BM-MSCs. We examined the effects of BMP-2 and miRNAs on osteogenic differentiation of PL-MSCs and UC-MSCs compared to those of BM-MSCs. The osteogenic differentiation capacity after treatments was assessed by ALP staining, ALP activity assay, and osteogenic marker gene expression. The results showed that the osteogenic differentiation capacity of both PL-MSCs UC-MSCs increased after BMP-2 treatment similar to BM-MSCs. MiR-31, miR-31, miR-106a, and miR-148a were downregulated during the osteogenic differentiation . After treatment with nti miRNAs, ALP activity and osteogenic genes were increased over the time of differentiation. The data lead to the potential for using PL-MSCs and UC-MSCs as an alternative source for bone regeneration. Moreover, the information of miRNA expression and function during osteogenic differentiation may be useful for the development of new therapeutics or enhanced an in vitro culture technique required for stem cell-based therapies in the bone regeneration.

Keywords: mesenchymal stem cells,bone marrow, placenta, umbilical cord, osteoblast, microRNA,BMP-2.

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Title: Islet engineering from human postnatal stem cells for autologous transplantation in type 1 diabetes subjects.

Abstract: Type 1 Diabetes Mellitus is manifested by auto immune destruction of insulin producing beta cells in the pancreas. Currently available treatments include transplantation of isolated islets from donor pancreas to the patient. However shortage of donors and immunosupression regime limits the success of transplantation. Autologous adult stem cells are now considered for cell replacement therapy in diabetes as it has the potential to generate new islets and do not require Immunosupression. We explored the potential of human adipose tissue-derived stem cells (ASCs). and Dental pulp stem cells (DPSCs) to differentiate into pancreatic hormone expressing islet-like cell aggregates (ICAs). The mesenchymal stem cells were isolated from fat tissue obtained from plastic surgery or from extracted wisdom tooth. After confirming their stemness these ASCs/DPSCs were subjected islet differentiation cocktail using 3 stage serum free protocol. During the process of differentiation the fibroblast like adherent cell population changed into islet like cell aggregates (ICAs) which were seen floating into the culture medium. These ICAs stained positive for insulin, glucagon and somatostatin by immunoflurosence and secreted insulin in response to glucose challenge indicating their islet identity. Intra-peritoneal transplantation of these ICAs, packed in immuno-isolatory biocompatible capsules (Provided by Dr. Prabha Nair, SCTIMST Trivandrum) to STZ induced hyperglycemic diabetic mice restored normoglycemia within 3-4 weeks. Our results provide evidence that human ASCs and DPSCs could be induced to differentiate into physiologically competent functional islet like cell aggregates, which may offer alternative source for generation islets for transplantation in type 1 diabetes subjects. This open a new era for treating type 1 diabetes.

RAMESH BHONDE
Director (Research) Dr. D.Y. Patil Vidyapeeth, (DPU) Pune

Title: Clinical Needs of Regenerative Science in Orthopaedics.

Abstract: Clinical uses of Stem cells in Modern medicine specially in orthopaedics holds a positive future in treating certain conditions which faces lot of clinical challenges in presently available treatment modalities. Orthopaedics conditions like AVN head of femur, moderate stage of progressive OA, uncontrolled Rheumatoid Arthritis, DMD give enormous challenges to the treating orthopaedic surgeon. Cell therapy is the most important strategy in the management of above mentioned conditions. Defiantly autologous minimally manipulated MNCs should be ideally used. As minimal manipulation is being done so there should not be any safety concern issues. We should plan clinical trials not only from clinical perspective but also to generate sufficient evidences of cellular therapy as treatment options in such conditions. Ultimately angiogenesis and chondrogenesis are required in AVN and OA patients respectively. Hip Avascular necrosis results from interruption of normal blood flow to the femoral head which if diagnosed at earlier stage, have the option of halting the progression with stem cell therapy. Clinical grade mesenchymal stem cells with or without PRP is useful not only in OA but also in chondral lesions due to sports injury. This is the possible correct way to avoid further cartilage degeneration leading to Sec OA. MRI changes post therapy in AVN, OA must be clinically correlated.

Osteoarthritis is a common disorder in which there is not only extensive degeneration but also an aberrant attempt at repair in joints. Osteoarthritis is a leading cause of chronic disability in around 50 years and the risk of disability attributed to osteoarthritis is as great as or greater than due to any other medical condition in that age group. It even occurs in young athletes following sports related injury. The articular cartilage is especially vulnerable to damage not only in OA but also in sports injury and it has poor potential for regeneration because of the absence of vascularity of articular cartilage. Several cross sectional studies have demonstrated an age related increase in the prevalence of osteoarthritis of knee, a early control of which is best indeed.

While pain relief is the primary treatment goal of osteoarthritis medications, localized inflammation may also be relieved by using certain drugs. Managing osteoarthritis pain can involve medications, natural remedies, exercise, weight loss, joint protection, mobility aids, assisted devices and more. Stem cell therapy, using cells extracted from the same patient targets osteoarthritis specially in its early stage. Since this therapy is based on the concept of regenerating damaged cells of cartilage of knee (therapeutic chondrogenesis), it is called regenerative medicine. Autologous stem cells provide an attractive option for osteoarthritis patients and their clinicians. Platelet rich plasma (PRP) which has growth factors also coordinate repair and regeneration of intraarticular cartilage if given along with mesenchymal stem cell therapy. Autologous mesenchymal stromal/bone marrow concentrate, however, appear to be the leading candidates in treating these arthritic joints. Stem cells are receiving a great deal of scientific attention and one of the many reasons for this attention in their ability to regenerate tissues without the production of scar tissue that is generally associated with healing processes. The importance of rehabilitation for achieving expected recovery after the therapy must not be forgotten and regular follow up must be maintained to access the outcomes. Regenerative Science is thus a affective approach based on unique ability of stem cells to reproduce, repair & rejuvenate the affected damaged tissue.

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Title: USE OF DENTAL PULP CELLS IN CRITICAL LIMB ISCHEMIA.

Abstract: Critical limb ischemia is a major problem affecting the lower limb arteries resulting in amputation of toes or limbs. Diabetic patients and chronic smokers are vulnerable to this. Till today effective re-establishment of the circulation needs invasive surgeries or costly stenting procedures. Even such procedures are not successful in very distal parts of legs. Stem cells have consistently proved capacity to produce angiogenesis in the tissues where they are injected. Out of the several sources of Stem cells, the dental pulp Stem cells have demonstrated maximum angiogenic potential in several publications. How to extract, concentrate or culture the stem cells from dental pulp and use them in critical limb ischemia is explained in this talk.

DR. V.R. RAVI
MS (ORTHO), DR. S. SANKARANARAYANAN MDS, DR. D.AVINASH GANDI PH.D
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Title: Use of Nucleic Acid Tests (NAT) to Reduce the Risk of Transmission of HIV, Hep-B and Hep-C Virus from Donors of Human Cells, Tissues, and Tissue-Based Products.

Abstract: Nucleic acid testing (NAT) for HIV, HBV and HCV shortens the time between infection and detection by available testing. For donors with identified behavioral risk factors, NAT should be considered to reduce the risk of transmission and increase organ and tissue based products utilization. Informed consent balancing the risks of donor-derived infection against the risk of remaining on the waiting list should be obtained at the time of candidate listing and again at the time of organ and tissue-based products offer. We assessed the suitability of commercial NAT testing in a developing country. We have standardized and validated commercially available NAT kits with a semi automated system for detection of HBV, HCV and HIV-I. The MP-NAT(minipool) assay consists of pooling of sample, virus extraction, amplification and detection with commercially available NAT kits. An internal control (IC) is incorporated in the assay to monitor the extraction, target amplification and detection process. The sensitivity of the Altona Real Star assay at 10-MP for each viral target was evaluated, HBV showed amplification in all diluted positive samples of 100, 50, 25, 10 and 5 IU/ml. HIV and HCV infected samples showed amplification in all diluted positive of 500, 100, 50 and 30IU/ml. For HIV, out of six diluted samples of 30 IU/ml, five were amplified. In conclusion, there is sufficient evidence to recommend universal prospective screening of donors of organ and tissue-based products for HIV, HCV and HBV using current NAT platforms. The semi-automated combined system for NAT screening assays is robust, sensitive, reproducible, and this gives an additional layer of safety with affordable cost. Further study of viral screening modalities may reduce disease transmission risk without excessive donor loss.

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Title: Mesenchymal Stem cells in Diabetes therapeutics: Pre-clinical to Translation Research

Abstract: Insulin-secreting pancreatic B-cells are imperative regulators of mammalian metabolism. The deficiency of functional B-cells leads to hyperglycemia and diabetes; making patient dependent on exogenously supplied insulin. Adult Mesenchymal Stem cells (MSCs) have potential to overcome limitations of current diabetes therapy and their conditional manipulation by using potent biomolecules for islet neogenesis may open new perspectives for a radical therapeutic approach for treating both Type-I and Type-II dibetes. Hence, in the present study mouse pancreatic resident progenitors (PRP), mouse (BALB/c) and human bone marrow MSCs (mBMSCs & hBMSCs) were induced for islet neogenesis using a novel bioactive compound, Swertisin. It was observed that PRPs were already primed with key transcription factors required for islet neogenesis that allowed shortest route to islet differentiation (4 days Protocol). This is the shortest reported time for any MSC till date. Further, the same biomolecule induction on mBMSCs successfully differentiated into insulin producing cells which when transplanted back into Stretozotocine treated diabetic mice were able to ameliorate diabetes. Finally, hBMSCs were isolated, purified, characterized and differentiated into islets of Langerhans (18 Day Protocol). The neoislets produced using this method functionally characterized. These islets could sense glucose and secrete c-peptide implies maintenance of glucose homeostasis. Hence, we want to emphasize that neoislets thus generated can become an effective therapeutic tool for treating diabetes.

Prof. SARITA GUPTA

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Title: Role of Suppressor of cytokine signalling protein in neural stem cell differentiation and neuronal cell survival.

Abstract: Neuronal differentiation of Neural Stem Cells (NSCs) is a complex process that involves the interaction of many intrinsic and environmental cues. Several previous studies have focused on the regulation of extrinsic factors, but research relating to the endogenous regulation of NSCs such as intracellular structural proteins, transcription factors, etc. is less reported. Supressors of cytokine signaling (SOCS) protein family are key regulators of cellular responses to cytokinesand play an important role in the nervous system. Though various SOCS genes are expressed in the brain, till date, very few studies exist on role of SOCS in neural stem cell biology. In this study, we have examined the role of SOCS3 and SOCS6 in the differentiation of the cells of the nervous system. We isolated and cultured stem cells from different regions of rat embryonic brain. The cells of the neurospheres are at the stem cell stage and can be differentiated into different neural cell types under varied culture conditions. While exploring the expression levels of different SOCS upon neural differentiation, we identified that SOCS3 and SOCS6, were up regulated upon neural differentiation in stem cells, derived from rat as well as in neuronal cell lines. Furthermore over expression of SOCS3 in neuronal stem cells exhibited increased primary neurite number as well as neurite length and in PC12 cells, neurite outgrowth was induced under nondifferentiating conditions. We found that SOCS6 expression was more on earlier time points as compared to late days of differentiation, indicating early requirement of this SOCS molecule in the process of differentiation. This data was further confirmed by the over expression and knockdown studies.

In conclusion, the result indicated that these SOCS molecules are involved in the differentiation of neural cells, which would be potentially useful in future therapies aimed at treating neurological disease such as Glioblastoma multiforme (GBM) the most malignant among primary brain tumours due to its integral role in the regulation of neuronal differentiation on the one hand, and to increase cell survival in neurodegenerative disorders on the other hand.

DR. SAKSHI GUPTA
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Title: Exploration of pluripotent embryonic stem cells in development and therapy.

Abstract: Stem cells are considered as basic unit of development and are bestowed with self renewal and differentiation potential. Indeed, early cell fate decision machinery is multi-factorial encompassing a well-orchestrated and fine-tuned regulatory control on the temporo-spatial expression, interactions and responses of those. In this study, we have used embryonic stem cells (ESCs) possessing the pluripotent characteristics, as a model system, to discern how the event cascades fall in place in defining the niche, and the crucial influence of various key players in specifying the three germ layer derivatives during early development. Accordingly, ESCs have been successfully differentiated into ectodermal derivative such as neural progenitors, dopaminergic and serotonergic neurons as well as mesodermal derivatives such as cardiomyocytes, smooth muscle cells and hematoendothelial ones. The strategy of using live reporter based cell trapping approach, where stable ESC clones expressed fluorescent reporters under the regulatory control of tissue specific promoters, could facilitate demarcating the cells of our interest "live" among the differentiating heterogeneous cell population from ESCs and also in their further characterizations and quantifications. Moreover our study also helped demonstrating the optimum time window of action of key developmental players like Wnt and Notch during neurogenesis and cardiomyogenesis. Further, transplanting ESCs derived neural cells into the striatum of hemi-Parkinsonian rodent models reinforced their therapeutic efficacy in replenishing the damaged neurons and restoring the functional activities thereof. Overall, our study has paved way for exploring ESCs, an elegant in vitro model for development, in identifying crucial players underlying early development.

NIBEDITA LENKA
NATIONAL CENTRE FOR CELL SCIENCE, PUNE

Title: Building the Possibility of Gangrene Reversals in Clinical management of Wounds.

Abstract: Complex wounds are huge problems and associated with severe ischemia and infections leading to further tissue necrosis and development of gangrenes.

PRP as a regenerative medicine product is being studied widely for different clinical applications including of wounds, fracture impairments, tendinopathies, osteoarthritis etc.

This is based on its rich content of growth factors/cytokines which triggers, promotes tissue regeneration and further healing.

At our centre, a protocol for treatment of wounds by PRP known as Sandeep's Technique for assisted regeneration of skin (STARS therapy) have been developed and applied for treatment of different wounds including complex wounds with infections, recalcitrant ulcer, deep with exposed tendons, bones etc.

During this study, we have extended the usage to include few very challenging situations which included wounds associated with huge necrosis or limbs with impending with gangrene. They were associated with clinical signs of limb ischemia and had necrotizing skin, tendons, bones etc. exposed in the wounds. The results are very encouraging leading to the tissue regeneration in such wounds with minimum residual tissues necrotizing. Complete healing of wounds was achieved in most of them.

The PRP led regeneration and the solutions being developed are indicative of revolutionary clinical outcomes, which otherwise is not a possible through current traditional pharmaceutical/surgical based therapies. This talk is about how regenerative medicine would be game changer for wound managements.

DR. SANDEEP SHRIVASTAVA
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Title: Cancer stem cell metabolism – target for cancer therapy.

Abstract: Cancer stem cells (CSCs) are a small subpopulation of the cells in a tumor which posses two key properties; the indefinite ability to self-renewal, and the ability to give rise to different form of cancer cells. CSCs are also called as tumor-initiating cells (TICs), exhibit increased resistance to standard chemotherapy and radiation therapy. They are also thought to play a crucial role in cancer relapse and metastates as they are usually left untreated by standard form of cancer therapy. Although all ceils rely on metabolism for their energy supply , cancer stem cells have different metabolic phenotype than normal cells – that is, the way they use fuel to create energy in cancer stem cells. Cells primarily get energy through mitochondria, which depends on oxygen, and through glucose. On the contrary, SCSs have distinct and unique mechanism to derive energy; it uses both glycolysis and oxidative phosphorylation. In the quiescent state, the CSCs uses glucose; and in actively dividing state, they rely on oxygen availability. A comprehensive understanding of the underlying mechanisms will not only provide important insights into this relationship, but may also contribute to the development of novel therapeutic strategies to completely eliminate cancer. As such, the identification of effective CSC-specific therapeutics has taken main stage in the development of anti-neoplastic therapies in order to provide long-term disease-free survival in cancer patients

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