10th Annual Conference on

Stem Cell & Regenerative Medicine

October 08-09, 2018 | Zurich, Switzerland

Scientific Tracks & Abstracts

Day 1

Stem Cell Congress 2018

Day-1

SESSIONS

Stem Cells | Regenerative Medicine | Stem Cell Transplant | Cancer Stem Cell | Stem Cell Banking | 3D Bioprinting & Biofabrication

Chair: Joseph Choukroun, Pain Clinic, France

SESSION INTRODUCTION

Title: Extraction of blood mesenchymal stem cells with the low speed centrifugation concept: Applications in regenerative medicine
Joseph Choukroun, Pain Clinic, France

Title: Chimerism in allogenic hematopoietic stem cell transplant beyond surveillance of engraftment
Ganapathi Bhat Mugulthimoole, Jaslok Hospital and Research Centre, India

Title: Regeneration of infarcted myocardium using activated adult stem cells
Cai Dongqing, Jinan University, China

Title: Dissecting the role of EIF5A signaling in breast cancer
Marie Therese Rached, The Institute of Cancer Research, UK

Title: Application of clinical grade hUC-MSCs in the treatment of uterine scars in rats
Shuzhen Wu, Southern Medical University, China

Title: *In situ* tissue engineering concept for enhanced bone defect regeneration– functionalization of biomimetic scaffolds with an autologous growth factor mix from hypoxia-exposed hBMSC
Anastasia Gabrielyan, University Hospital Carl Gustav Carus, Germany

Joseph Choukroun, J Stem Cell Res Ther 2018, Volume 8
DOI: 10.4172/2157-7633-C4-041

Extraction of blood mesenchymal stem cells with the low speed centrifugation concept: Applications in regenerative medicine

Joseph Choukroun
Pain Clinic, France

Regenerative therapy with stem cells has gained tremendous momentum over the past decade as a modality geared towards markedly improving wound healing of various tissues by utilizing undifferentiated autologous host cells. While stem cells may be isolated from various locations in the human body, more recently it has been shown that low levels of mesenchymal stem cells also exist circulating within peripheral blood. Platelet rich fibrin (PRF) is a regenerative modality that utilizes peripheral blood + centrifugation protocols without the use of anti-coagulants to create a three-dimensional tissue engineering scaffold containing both growth factors and autologous cells. Very recently, it has been shown that modifications to centrifugation speed and time following recently developed concepts (the low-speed centrifugation concept or LSCC) resulted in a marked increase in host cells and growth factors. Within these scaffold constructs, mesenchymal stems cells were also found following collection with this relatively painless and low-cost modality. The objective of the present talk will be to present recent modifications to centrifugation speed and time to optimize stem cell quantities within PRF. Thereafter, the biological data supporting their numbers, as well as their potential for clinical applications will be presented with data coming from many fields of medicine including for the regeneration of osteoarthritic knees, dental regenerative medicine, orthopedic grafting, and for facial esthetics.

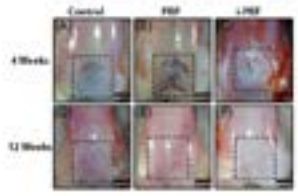

Figure 1

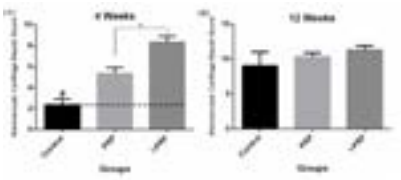

Figure 2

Recent Publications

1. J Choukroun and S Ghanaati (2018) Reduction of relative centrifugation force within injectable platelet-rich-fibrin (PRF) concentrates advances patients' own inflammatory cells, platelets and growth factors: the first introduction to the low speed centrifugation concept. European Journal of Trauma and Emergency Surgery 44(1):87-95.
2. Wang X, Zhang Y, Choukroun J, Ghanaati S and Miron R J (2018) Effects of an injectable platelet-rich fibrin on osteoblast behavior and bone tissue formation in comparison to platelet-rich plasma. Platelets 29(1):48-55.
3. El Bagdadi K, Kubesch A, Yu X, Al-Maawi S, Orlowska A, Dias A and Choukroun J (2017) Reduction of relative centrifugal forces increases growth factor release within solid platelet-rich-fibrin (PRF)-based matrices: a proof of concept of LSCC. European Journal of Trauma and Emergency Surgery 1–13.
4. Miron R J, Fujioka-Kobayashi M, Hernandez M, Kandalam U, Zhang Y, Ghanaati S and Choukroun J (2017) Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry? Clinical Oral Investigations 21(8):2619-2627.

Biography

Joseph Choukroun completed MD from University of Montpellier, France 1979 and is a Specialist in General Surgery, Anesthesiology from the same university. He is also a Specialist in Pain Management from the University of Strasbourg, France. He is the Owner of Private Pain Clinic, Nice France. He is the President of SYFAC, international symposium on growth factors. He is the Inventor of the PRF techniques: L-PRF, A-PRF and i-PRF. He is a Researcher working in Form Lab at the University of Frankfurt. He is the Author of several scientific publications and is recognized as an International Speaker.

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Ganapathi Bhat Mugulthimoole, J Stem Cell Res Ther 2018, Volume 8
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Chimerism in allogenic hematopoietic stem cell transplant beyond surveillance of engraftment

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Allogeneic hematopoietic stem cell transplantation (HSCT) is an established standard of care for various haemato-lymphoid malignancies and several other disorders. The transplant immunobiology is highly influenced by the contents of the graft and the host graft immune interactions. On one hand, the controlled and complete transfer of the donor hematopoietic and immune systems to the host is suggestive of the reliable augmentation of immune recovery. Post transplant donor cell dynamics is closely related to graft failure, graft-versus host disease and disease relapse. Therefore, surveillance after transplantation using accurate quantification of hematopoietic chimerism is useful for following up patients after HSCT. Post transplant chimerism of complete donor origin is necessary for cure of malignant disorder while coexistence of both recipients and donor will be sufficient from curative perspective though graft rejection and failures are undesired outcome irrespective of disease. Surveillance of chimerism beyond engraftment is imperative for the early finding of graft failure and for judgement of prognosis. It also directs the clinician to intervene and initiate strategies like modifying immune suppression or donor leucocytes infusion to improve chimeric status in order to conserve the graft and facilitate cure of underlying diseases. Attempts are also being made to gain a deeper understanding of additional cell subsets in chimerism analysis, which could also play a role in influencing immunological reconstitution. Close chimerism check not only gives insight to identify the early adverse outcomes of allogeneic HSCT, but also meantime guide to initiate suitable intervention to safe guard overall outcome of patient in terms of declining the morbidity and mortality.

Biography

Ganapathi Bhat Mugulthimoole is a Senior Consultant Medical Oncologist and Stem Cell Transplant Physician at Jaslok Hospital and Research Centre, since 2006. He gained specialized training in Stem Cell Transplantation as part of the ESH-EBMT (2007), La Baule, France (2011) and ICAS training program (2009) at Ulm University, Germany. He is also a Member of academic organizations namely ESMO, EHA, Asia Pacific Bone and Marrow Transplantation group and an affiliate of the American Association for Cancer Research and BITs Congress. He is also an Editorial Member of various international scientific journals.

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Cai Dongqing, J Stem Cell Res Ther 2018, Volume 8
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Regeneration of infarcted myocardium using activated adult stem cells

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Regeneration of infarcted myocardium is still a big challenge in clinic. Stem cell therapy has shed light to regenerate the infarcted myocardium. However, low survival rate of transplanted stem cells and very low terminal differentiation of transplanted stem cells limit therapeutic effects of stem cells to achieve functional and structural regeneration of infarcted myocardium. Recently our lab developed a novel activated adult stem cell therapy for infarcted myocardium. We applied bio-activated strategy to pre-activate adult endogenous cardiac stem cells and adult bone narrow stem cells and then transplanted into infarcted myocardium in rat model. We found that these novel adult stem cell therapies were able to decrease the infarct size and improve the myocardial function significantly. Importantly, the therapeutic effect of this novel therapy is more effective than non-activated stem cells. Our finding suggested that this novel strategy might be considered as novel stem cell therapy for us to further develop the novel approach to regenerate infarcted myocardium.

Biography

Cai Dongqing completed M D at Guangzhou Medical College in 1987, PhD at The Chinese University of Hong Kong in 2000, Postdoctoral Associate at Weill Medical College of Cornell University, USA in 2000-2003. He works as a Professor and Director at Key Laboratory of Regenerative Medicine, Ministry of Education, Jinan University. He is a Director at Department of Developmental and Regenerative Biology, Jinan University. His Scientific interests are Aging and microenvironment in regeneration of myocardial infarction (MI); Cardiac vascular specific targeting and therapy (stem cell and therapeutic angiogenesis) for MI; Aging and regeneration of Tissue & Organ. He published 40 SCI papers. Grant: 2003 - present: The Major Research plan of the National Natural Science Foundation of China-Key program, National Key R&D Program of China, 863, International collaboration grant of Ministry of Science & Technology, Seven NSFC-grants, etc.

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Notes:

Marie Therese Rached, J Stem Cell Res Ther 2018, Volume 8
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Dissecting the role of EIF5A signaling in breast cancer

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Triple negative breast cancer (TNBC) is a highly recurrent subtype of breast cancer with the worst prognosis, potentially attributed to the presence of cancer stem cells within these tumors. The elongation initiation factor 5A (EIF5A) is a protein with a unique amino acid, hypusine, synthesized post-translationally from the polyamine spermdine through step wise enzymatic reactions. This hypusination crucial for EIF5A activity and cell proliferation has been reported in multiple cancers; however, its function in breast cancer requires further understanding. We showed increased expression of EIF5A mRNA and protein as well as its hypusinated form in a subset of TNBC cell lines compared to non-TNBC lines using gene expression and western blot studies (n=12). To better understand how inhibition of EIF5A hypusination influences TNBC, we inactivated EIF5A pathway with inhibitors targeting the hypusine forming enzymes. We confirmed that loss of EIF5A hypusination was associated with alteration in cell cycle progression, reduced proliferation and survival in a subset of TNBC cell lines using flow cytometry and cytotoxicity assays. At the molecular level, cell cycle alteration among subtypes was associated with changes in CDK2 activity. The stem cell associated transcription factor c-MYC showed potential differential regulation following drug treatment in a subset of TNBC cell lines suggesting its potential role in EIF5A pathway activity. These studies suggest a distinct role of the polyamine/hypusine pathway during cell cycle progression and proliferation of a subset of TNBC. Targeting this pathway using anti-tumor therapeutic agents might provide means to effectively combat the aggressive TNBC subtype.

Biography

Marie Therese Rached has completed her PhD in Metabolic Signaling in 2014 at Imperial College, London. She is currently pursuing Postdoctoral training at The Institute of Cancer Research in Sutton, United Kingdom. Previously she worked as a Research Staff Associate at Columbia University, New York, where she published multiple papers on the role of the skeleton as an endocrine organ regulating energy metabolism.

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Shuzhen Wu et al., J Stem Cell Res Ther 2018, Volume 8
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Application of clinical grade hUC-MSCs in the treatment of uterine scars in rats

Shuzhen Wu and **Xin Luo**
Southern Medical University, China

Full thickness injuries of the uterus may trigger uterine scar formation after cesarean section, ultimately leading to a variety of obstetrical complications or infertility. The main mechanisms of uterine scar formation involved in acute or chronic inflammatory response, collagen deposition and muscle fiber regeneration. Now-a-days, few methods have adequately solved these problems. Human umbilical cord derived mesenchymal stem cells (hUC-MSCs) have excellent function in immune regulation, tissue regeneration and functional reconstruction and have shown great promise in clinical applications. The objective of this study was to investigate the effect of hUC-MSCs construct on inflammation regulation, collagen degradation and functional regeneration in rat uterine scars following full thickness excision of uterine walls. In our research, the clinical grade hUC-MSCs would be prepared strictly following the international standards of the International Society for Stem Cell Research (ISSCR). In order to establish a rat model of uterine scars, a 2.0 cm in length, full thickness incision of uterine walls was performed around 0.5 cm from each uterine horn. A total of 100 rats were randomly assigned to five groups, including a normal group (n = 20), eutocia group (n = 20), cesarean group (n = 20), control group (saline n = 20) and hUC-MSCs group (n = 20) to investigate the effect of clinical grade hUC-MSCs treatments on the structure and function of uterine scars. Saline or hUC-MSCs were injected surrounding each uterine scar, respectively. At days 15, 30, 60 and 90 post-transplantation, the superparamagnetic iron oxide nanoparticles (SPIONs) labeled hUC-MSCs were detected and traced in vitro by MRI. The planting, distribution and migration of hUC-MSCs in uterine scar were dynamically detected by MRI and fluorescence tracing of the living image of a small animal. Haematoxylin eosin staining, Masson's trichrome staining, immunofluorescence staining, western blot and real-time PCR for collagen, matrix metallo proteinases, inflammatory factors, chemokine, bFGF, PDGF-BB and VEGF were performed. We would like to find out the value of hUC-MSCs according to the research mechanism.

Figure 1: Effect of hUC-MSCs on inflammation regulation, collagen degradation and functional regeneration in rat uterine scars.

Recent Publications

1. Fan D, Xia Q, Wu S, Ye S, Liu L, Wang W, *et al.,* (2018) Mesenchymal stem cells in the treatment of Cesarean section skin scars: study protocol for a randomized, controlled trial. Trials 19(1):155.
2. Fan D, Wu S, Ye S, Wang W, Wang L, Fu Y, *et al.,* (2018) Random placenta margin incision for control hemorrhage during cesarean delivery complicated by complete placenta previa: a prospective cohort study. Journal of Maternal-Fetal & Neonatal Medicine DOI: 10.1080/14767058.2018.1457638.
3. Liu Y, Fan D, Fu Y, Wu S, Wang W, Ye S, *et al.,* (2018) Diagnostic accuracy of cystoscopy and ultrasonography in the prenatal diagnosis of abnormally invasive placenta. Medicine (Baltimore) 97(15):e0438.
4. Fan D, Wu S, Wang R, Huang Y, Fu Y, Ai W, *et al.,* (2017) Successfully treated congenital cystic adenomatoid malformation by open fetal surgery: A care-compliant case report of a 5-year follow-up and review of the literature. Medicine (Baltimore) 96(2):e5865.

Biography

Shuzhen Wu is currently an obstetrician in Southern Medical University Affiliated Maternal & Child Health Hospital of Foshan. She graduated with her Master's degree in Obstetric (2009-2011), and her undergraduate degree in Medicine (2004-2009) from Shantou University Medical College, China. Her academic and research interests lie in high-risk obstetric, placenta previa, fetal in utero treatment, and regenerative medicine and stem cell clinical therapy.

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Anastasia Gabrielyan et al., J Stem Cell Res Ther 2018, Volume 8
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In situ tissue engineering concept for enhanced bone defect regeneration– functionalization of biomimetic scaffolds with an autologous growth factor mix from hypoxia-exposed hBMSC

Anastasia Gabrielyan[1], Mandy Quade[1], Anja Lode[1], Michael Gelinsky[1], Seemun Ray[2], Jessica Grafe[2], Volker Alt[2] and **Angela Rösen-Wolff[1]**
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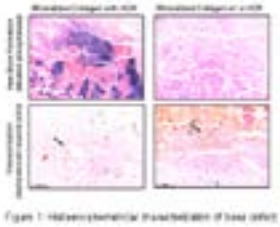
[2]Justus Liebig University, Germany

The potential for self-regeneration of bone tissue is not sufficient to regain the original function in the case of extensive lesions, osteoporosis, injury or tumor resection. Hence, the main goal of bone tissue engineering has been the generation of biological substitutes which remodel into native tissue to replace affected bone. *In vivo* tissue regeneration depends on migration of stem cells into injured areas, their differentiation into specific cell types and their interaction with other cells that are necessary to generate new tissue. Therefore, optimized biomaterials are needed which allow survival and growth of mesenchymal stem cells, a subset of bone marrow stromal cells (BMSCs), which can migrate and differentiate into osteoblasts in bone tissue. Hypoxia-conditioned media (HCM) has a high chemo attractive capacity for BMSCs, as it harbors high concentrations of growth factors which are important to stimulate angiogenesis and cell migration. It can be derived from BMSCs but also from skin fibroblasts which can be easily obtained from patients in individualized therapy approaches. Scaffold functionalization with a central growth factor depot enhances hBMSC infiltration as well as ingrowth of tubular endothelial structures providing a strategy to stimulate *in situ* colonization with cells from the surrounding tissue. For *in vivo* testing, a 4 mm wedge shaped osteotomy of the distal metaphyseal area was generated in the femur of osteoporotic rats. Six weeks after implantation of mineralized collagen scaffolds loaded with HCM, bone defect healing was characterized histomorphometrically revealing an enhancing effect on vascularization and new bone formation. In our work, we demonstrated that allogenous growth factor mix derived from HCM is suitable to attract cells with regenerative potential, induces vascularization *in vitro* and has been shown to enhance bone defect healing *in vivo*.



Recent Publications

1. Quade M, *et al.,* (2018) Strontium-modification of porous scaffolds from mineralized collagen for potential use in bone defect therapy. Materials Science & Engineering C Materials Science & Engineering 84:159-167.
2. Gabrielyan A, *et al.,* (2017) Metabolically conditioned media derived from bone marrow stromal cells or human skin fibroblasts act as effective chemo attractants for mesenchymal stem cells. Stem Cell Research &Therapy 8(1):212.
3. Quade M, *et al.,* (2017) Central growth factor loaded depots in bone tissue engineering scaffolds for enhanced cell attraction. Tissue Engineering Part A 23(15-16):762-772.
4. Gabrielyan A, *et al.,* (2014) Hypoxia-conditioned media allows species-specific attraction of bone marrow stromal cells without need for recombinant proteins. BMC Veterinary Research 10(1):56.
5. Alt V, *et al.,* (2013) A new metaphyseal bone defect model in osteoporotic rats to study biomaterials for the enhancement of bone healing in osteoporotic fractures. Acta Biomaterialia 9(6):7035–7042.

Biography

Anastasia Gabrielyan studied Biology at TU Dresden and is currently a PhD student at the University Hospital Carl Gustav Carus, Dresden. Her research has been published in reputed journals.

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Young Researchers Forum Day 1

Verónica Uribe-Etxebarria, J Stem Cell Res Ther 2018, Volume 8
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Notch/Wnt cross-signalling regulates stemness of dental pulp stem cells through a link between core pluripotency factors, metabolism and epigenetics

Verónica Uribe-Etxebarria
University of the Basque Country, Spain

Dental pulp stem cells (DPSCs) from adult teeth express neural crest (NC) markers together with core transcriptional factors associated with stem cell pluripotency, such as Oct4a, Sox2, c-Myc, Rex1, Stella/Dppa3, Ssea1/Fut4, Lin28 and Nanog. The possibility to boost the natural stemness features of DPSCs by mild methods that do not involve gene and/or chromatin modification or gene transfection, is highly desirable for cell therapy. Canonical Wnt and Notch are two highly conserved developmental signalling pathways that are involved in NC emergence and stem cell self-renewal. We determined that both pathways coordinate to regulate the expression of core pluripotency and NC factors in DPSCs. Pharmacological inhibition of the Notch pathway for 48 h, by the γ-secretase inhibitor DAPT, abolished the expression of NC and core factors. This pluripotency network seems to be connected with metabolism which is mainly glycolytic and highly oxidative. Epigenetics plays also a relevant role preventing DNA from methylation and increasing acetylation marks in histones. Genetic, metabolism and epigenetics would be connected by complex networks which allow cell reprogramming. In addition, it induced a silencing of the canonical Wnt signalling and a clear reduction in the stemness potential of DPSCs, as shown by a reduced ability to generate mature, fully differentiated osteoblasts and adipocytes. Conversely, pharmacological activation of the Wnt pathway for 48 h, by either the glycogen synthase kinase 3 beta BIO or the human recombinant protein Wnt-3a, not only largely increased the expression of NC and core factors, but also increased the efficiency of DPSCs to differentiate into mature osteoblasts and adipocytes. These results showed that a short preconditioning activation of Wnt/Notch signalling by small molecules and/or recombinant proteins enhanced the stemness and potency of DPSCs in culture, which could be useful for optimizing the therapeutic use of these and other tissue-specific stem cells.

Biography

Verónica Uribe-Etxebarria is a PhD student at the University of the Basque Country and she has done part of her thesis at The Institute of Cancer Research and Biodonostia Health Research Institute. She has published two papers in *Frontiers in Physiology* and *European Cells and Materials*.

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Pooja Vinayak Shahapurkar et al., J Stem Cell Res Ther 2018, Volume 8
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Beyond immortality: Understanding cancer stem cells

Pooja Vinayak Shahapurkar and **Ganapathi Bhat Mugulthimoole**
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The cancer stem cells (CSC) are tumorigenic cells which phenotypically and functionally resemble stem cells and which are responsible for failures in conventional therapies and relapses. Consequently, genesis of cancer depends on the type of progenitor stem cells affected in stem cell hierarchy and the varying degree of stemness. The ability of CSC to possess the intrinsic stem like property enables them to produce more CSCs, ultimately bearing a tumorigenesis. They possess numerous biological properties covering hypoxia, unstable phenotype, multipotency and vigorous self-renewal leading to leukemogenesis. They express unique surface markers based on the type of cancer and are endowed with tumorigenic capacity sustaining growth. The epigenetic or genetic alteration giving rise to falsifications in normal cell signaling pathways such as Wnt/β-catenin, Notch, Hedgehog, etc. may also result in cancer cells behaving like stem cells. Promising therapeutic strategies hostile to CSCs involve steering the self-renewal pathways of CSCs, disrupting the communication between CSCs and their microenvironment. Stem cell niche becomes vulnerable to a plethora of carcinogenic mutations, injuries or insult. Importantly, the oncogenic transformation of these cells is highly potent. The classical example of CSC is blast crisis in chronic myeloid leukemia, where with the current available treatment, only the burden of blast cells can be kept in control till the chemotherapy works. However, there is no treatment to attack the blast producing CSCs, owing to their extremely malignant potential and drug-resistant properties. CSCs signify and strengthen objectives of the essence for evolving innovative anticancer drugs and therapeutic stratagems.

Biography

Pooja Vinayak Shahapurkar is working as Clinical Research Fellow in the Department of Medical Oncology and Stem Cell Transplant at Jaslok Hospital and Research Centre Mumbai, India. She is a Post-graduate from Cranfield University, UK and has gained basic laboratory work experience in Biochemistry, Immunology, Haematology and Microbiology lab. She is conversant with concepts of hematopoietic stem cell mobilisation, harvest, storage and transplant. She has to her credit few scientific write-ups published for international conferences along with chapters and is familiar with essentials of scientific publications and presently part of s research project entitled, "Isolation of T regulatory cells in heterogeneous population".

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Notes:

Juliette Peltzer et al., J Stem Cell Res Ther 2018, Volume 8
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Effect of mesenchymal stromal cells on T cells in a septic context: Immunosuppression or immunostimulation?

Juliette Peltzer[1], **Sebastien Le Burel**[1], **Cedric Thepenier**[1], **Laetitia Boutin**[2], and **Jean-Jacques Lataillade**[1,2]
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[2]University Hospital of South Paris, France

Sepsis is a complex process, including a first wave of damage partially due to the body's response to pathogens, followed by a phase of immune cell dysfunction. The efficacy of a pharmacological approach facing a rapidly evolving system implies a perfect timing of administration, this difficulty could explain the recent failure of clinical trials. Mesenchymal stromal cells (MSCs) are usually defined as immunosuppressive and their beneficial effects in preclinical models of acute sepsis have been shown to rely partly on such ability. If nonregulated, this phenotype could be harmful in the immunosuppressed context arising hours after sepsis onset. However, MSCs being environment sensitive, we hypothesized that they could reverse their immunosuppressive properties when confronted with suffering immune cells. Our objective was to evaluate the effect of human MSCs on activated human lymphocytes in an in vitro endotoxemia model. Peripheral blood mononuclear cells (PBMCs) underwent a 24-h lipopolysaccharide (LPS) intoxication and were stimulated with phytohemagglutinin (PHA) in contact with MSCs. MSCs induced a differential effect on lymphocytes depending on PBMC intoxication with LPS. Unintoxicated lymphocytes were highly proliferative with PHA and were inhibited by MSCs, whereas LPS-intoxicated lymphocytes showed a low proliferation rate, but were supported by MSCs, even when monocytes were depleted. These data, highlighting MSC plasticity in their immunomodulatory activity, pave the way for further studies investigating the mechanisms of mutual interactions between MSCs and immune cells in sepsis. Thus, MSCs might be able to fight against both early sepsis-induced hyper-inflammatory response and later time points of immune dysfunction.

Biography

Juliette Peltzer research aims to understand the coordinated relationships between metabolic and contractile pathways occurring during the differentiation of muscle satellite cells. In 2008, she joined Prof. Lataillade's laboratory specialized in cell therapy using mesenchymal stromal cells in different contexts and especially in humans in the case of radiation burns. She was first in charge of the characterization of perinatal MSCs, which we believe to be a good candidate for allogeneic cell therapy. Then they started to work on septic shock requiring extremely short processing times and therefore the use of immediately available cells from allogenic banking.

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