2nd International Conference

"The future of regenerative medicine in Africa"

2nd International Conference on Tissue Engineering and Regenerative Medicine (ICTERM)

and

The launch of African Tissue Engineering and Regenerative Medicine International Society (ATERMIS)

Host Institutions:

Tshwane University of Technology,

Vaal University of Technology

Rice University, Houston, Texas

VUT

Vaal University of Technology

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RICE

WELCOME TO SOUTH AFRICA
2nd INTERNATIONAL CONFERENCE ON TISSUE ENGINERRING AND REGENERATIVE MEDICINE

Dear Friends and Colleagues

Following the huge success of the 1st International Conference on Tissue Engineering and Regenerative Medicine organized in 2014 by Prof Motaungin Pretoria, South Africa,it is a wonderful, exciting and a great honour to extend a very warm and friendly welcome to all invited guests, sponsors, delegates and friends to Vanderbijlpark for the 2nd International Conference on Tissue Engineering and Regenerative Medicine (ICTERM)with the theme "The future of regenerative medicine in Africa".

This Conference will also serve as a platform to launch the Tissue Engineering and Regenerative Medicine International Society (TERMIS) in Africa. Currently there is TERMIS- Europe, TERMIS-Asia and TERMIS-USA. It will be a great occasion to launch TERMIS-Africa.

The ICTERM aims to bring together distinguished clinicians and scientists from around the world who work in the following areas: stem cell, cartilage, bone and biomaterials tissue engineering. This will enhance the interaction between young aspiring scientists and students from academia and national laboratories. The talks will cover basic studies through translational efforts and clinical trials and will address novel topics. During the five-day conference, we will listen to well-known experts in the field as they discuss recent advances, challenges and breakthroughs in the field of tissue engineering. The conference will feature keynote addresses, a number of plenary sessions, invited talks and contributed lectures focusing on specific views of tissue engineering. Furthermore, there will be several poster sessions, and the two best posters and oral presentations will be selected for an award.

I encourage you to actively participate in the conference and attend all sessions and ask probing questions to help our young scientists improve their work. I especially encourage all young scientists, the future of the continent to fully participate. It is hoped that ICTERM 2017 will make a meaningful contribution to the existing knowledge base in this field and motivate talented young people to pursue the field of tissue engineering. Lastly we wish you an informative and enjoyable time at the 2nd ICTERM conference.

Enjoy the conference and have a wonderful stay in the Vaal Triangle. Thank you for your support: it is greatly appreciated.

Professor Keolebogile Shirley Motaung
Chair, 2nd ICTERM 2017.

Scientific Committee

Prof. KeolebogileShirley Motaung (Chair)
Prof.Tony Mikos
Prof. Danie du Toit
Prof.Ugo Ripamonti
Prof. Sue Kidson
Dr. Carola Niesler
Dr.Mari Van de Vyver
Dr. Marianne Mureithi
Prof. Samie Amidou
Dr. Kevin Dzobo
Prof. Kathy Myburgh
Prof.Hari Reddi
Prof. Michael Pillay
Prof. Michael Pepper
Dr. Cano Ssemakalu
Dr. Janine Scholefield
Prof. Heidi Abrahamse
Prof. Berhanu Abegaz
Prof. Mkhululi Lukhele
Dr. Blessing Aderibigbe
Dr. Venant Tchokonte-Nana
Prof. Iqbal Parker

WE ARE GRATEFUL TO THE SPOSORS OF ICTERM 2017

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ACKNOWLEDGEMENTS

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Prof. Keolebogile Motaung
Prof. M Pillay
Dr. Cano Ssemakalu
Dr.Franca Nneka Alaribe
Mr. Prajesh Bhikha
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Mr. Tebogo Mokae
Ms Manani Hlongwane
Mr J. Maepa
Mr Moeketsi Monthsitsi
Ms Lily Molekoa

ICTERM 2017 Programme

26-30 July 2017

Vanderbijlpark, South Africa

PROGRAMME:

WEDNESDAY, JULY 26

16:00 **Registration**

PROGRAMME DIRECTORS

Prof. Keolebogile Motaung: Tshwane University of Technology, Pretoria, South Africa
Prof. Michael Pillay: Vaal University of Technology, Vanderbijlpark, South Africa
Prof. Antonios Mikos: Rice University, Houston, Texas, USA

18:00 - 18:15 Welcome address Emfuleni Local Municipality: Introduction by Prof. K P Dzvimbo
Executive Mayor Cllr Simon M. Mofokeng

18:15 - 19:00 Opening and Welcome address: Introduction by the Executive Dean of the Faculty of Applied and Computer Sciences, Prof. B.R. Mabuza.
Vice-Chancellor & Principal of VUT: Professor Emeritus (Anthropology) UNISA, Prof.G. N. Zide

Introduction by Deputy Vice Chancellor Teaching, Learning and Technology , Prof. S. Mukhola.
Vice-Chancellor & Principal of TUT: Prof. L. Van Staden

19:00 - 19:40 Plenary Lecture: Introduction by Prof. Antonios Mikos
Prof. Yasuhiko Tabata, Kyoto University, Japan
Tissue Regeneration Therapy Based on Biomaterial Technology of Dual Drug Release

19:40 - 20:20 Plenary Lecture: Introduction by Prof. Antonios Mikos
Prof. Wagner William, University of Pittsburgh, USA
Elastic, Soft and Temporary: Designing Biodegradable, Thermoplastic Elastomers for Applications in Regenerative Medicine

20:20 - 20:35 Vote of Thanks
Deputy Vice Chancellor Academic and Research of VUT: **Prof. K. P. Dzvimbo**
Acting Deputy Vice Chancellor Postgraduate Studies, Research & Innovation of TUT: ***Dr A.E. Nesamvuni***

20:35 **Reception and Dinner**

Thursday July 27, 2017

Scaffolds, Stem Cells, Tissue Engineering and Regenerative Medicine

Chairpersons:	**Prof. Michael Pillay**: Vaal University of Technology, Vanderbijlpark, South Africa **Prof Mkhululi Lukhele,** University of the Witwatersrand, Johannesburg, South Africa
08:00 - 08:25	Coffee and Registration
08:30 - 09:30	**Keynote Lecture:** Future Perspectives of Regenerative Medicine: **Prof John Jansen,** Radboud University Medical Center, Netherlands
09:30 - 09:45	Preliminary antibacterial evaluation of PEG/carbopol/mastic gum-based gels containing cavacrol: **Zintle Mbese,** University of Fort Hare, Alice, South Africa
09:45 -10:00	Preparation and characterization of polyaspartamide-based nanocarriers containing antimalarials: **Zandile Mhlwatika**, University of Fort Hare, Alice, South Africa
10:00 -10:15	Design of Polymer-Drug Conjugates for Combination Therapy for Controlled Delivery of Antimalarials: **Sibusiso Alven**, University of Fort Hare, Alice, South Africa
10:15 - 10:30	**Tea / Coffee Break**
10:30 - 11:30	**Keynote Lecture:** From Molecules to the Clinic - Austrian Cluster for Tissue Regeneration (ACTR): **Prof. Redl H,** Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Austria
11:30 - 11:45	Development and in vitro studies of nanocarriers for combination therapy: **Tobeka Naki,** University of Fort Hare, Alice, South Africa
11:45 - 12:15	A low cost bioprinter for alginate-based hydrogel microextrusion: **Prof. Earl Prinsloo**, Rhodes University, Grahamstown, South Africa
12:15 - 12:30	Myogenesis in a dish: investigating the complexity of skeletal muscle regeneration: **Venter C**. University of KwaZulu-Natal, Pietermaritzburg, South Africa
12:30-13:30	**Lunch**
Chairpersons:	**Prof. Kathy Myburgh:** Stellenbosch University, Stellenbosch, South Africa **Prof. Danie du Toit:** Tshwane University of Technology, Pretoria, South Africa
13:30 - 14:30	**Keynote Lecture:** Superhydrophobic Surfaces for Blood Contacting Medical Devices: **Prof. Ketul Popat,** Colorado State University, USA
14:30 – 15:00	Establishment of assays for culture and manipulation of haematopoietic stem cells: **Dr. Marianne Mureithi,** University of Nairobi, Nairobi, Kenya
15:00 - 15:30	Hijacking basic science to solve an African problem: When stem cells meet genome engineering: **Dr Janine Scholefield,** BTRI, CSIR/ UCT, South Africa
15:30-15:45	Influence of Low Intensity Laser Irradiation on Isolated Human Adipose Derived Stem Cells, in Combination with Growth Factors and in a Co-culture Environment, and Differentiation into Smooth Muscle Cells: **Natasha Hodgkinson**, University of Johannesburg, Doornfontein, South Africa
15:45– 17: 30	**Tea / Coffee Break (Poster Session** (presentation of posters with even numbers)
18:00	**Launch ATERMIS**

Friday July 28, 2017

Stem Cell and Tissue Engineering

Chairpersons:	**Prof. Keolebogile Motaung:**Tshwane University of Technology, Pretoria, South Africa **Dr Marianne Mureithi:** University of Nairobi, Nairobi, Kenya
08:00 - 08:25	**Coffee and Registration**
08:30 - 09:30	**Keynote Lecture:** Computational Modeling of Receptor-Ligand Interactions: **Prof. Lydia E. Kavraki**, Rice University, Texas, USA
09:30 –9:45	A hybrid microfluidic system for regulation of neural differentiation in induced pluripotent stem cells: **Zahra Hesari,** Guilan University of Medical Sciences, Iran
09:45 - 10:00	The fate of systemic and local administered adipose-derived mesenchymal stromal cells to modulate wound repair: **Karlien Kallmeyer**, University of Pretoria, South Africa
10:00 - 10:15	Comprehensive transcriptomic profile of adipogenic differentiation in human adipose derived stromal cells: **Melvin Anyasi Ambele**, University of Pretoria, South Africa
10:15 - 10:30	**Tea / Coffee Break**
10:30 - 11:30	**Keynote Lecture**: Development of a Tissue-Engineered Tumor Model: **Prof Antonios Mikos**, Rice University, Texas, USA
11:30 - 11:45	The search for the side population in human adipose-derived stromal cells: **Elize Wolmarans**, University of Pretoria, South Africa
11:45 - 12:15	Fibroblast-Derived Extracellular Matrix Induces Chondrogenic Differentiation in Human Adipose-Derived Mesenchymal Stromal/Stem Cells in Vitro: **Dr Kevin Dzobo**, ICGEB/ University of Cape Town, South Africa
12:15 - 12:30	Effect of adipogenesis on mitochondrial health and networks: **Rose Kadye**, Rhodes University, Grahamstown, South Africa
12:30 - 13:30	**Lunch**
Chairpersons:	**Dr Janine Scholefield,** BTRI, CSIR/ UCT, South Africa **Dr Kevin Dzobo**, ICGEB/ University of Cape Town, South Africa
13:30 – 14:30	**Keynote Lecture:** The Meniscus: from obscurity to significance in knee joint health and disease: **Prof. Adetola Adesida**, University of Alberta, Edmonton, Canada
14:30 - 15:00	Cis-vaccenic acid induces differentiation and up-regulates gamma globin synthesis in K562, JK1 and transgenic mice erythroid progenitor stem cells: **Dr Idowu A. Aimola**, Ahmadu Bello University, Zaria, Nigeria
15:00 - 15:30	Cellular processing with the Biosafe Sepax - a South African perspective: **Stephen Marrs**, Haemotec, South Africa
15:30-15:45	Molecular Mechanistic Interpretation of the Molecular Attributes Inherent to the Performance of Biomedical Material Archetypes: **Pradeep Kumar,** University of the Witwatersrand, Johannesburg, South Africa
15:45-17:30	**Tea / Coffee Break and Presentation of posters with even numbers.**
17:30	Braai and networking

Saturday July 29, 2017

Stem Cell and Tissue Engineering

Chairpersons: **Prof. Antonios Mikos**: Rice University, Texas, USA
Dr. Blessing Aderibigbe: University of Fort Hare, Alice, South Africa

08:00 - 08:25 Coffee and Registration

08:30 - 09:30 **Keynote Lecture:** Approaching the Complexity of Product Development in Tissue Engineering **Dr.Peter C. Johnson**, President and CEO Scintellix, LLC, Raleigh, NC,USA

09:30 – 9:45 Effect of Pleurostylia capensis plant extracts in C2C12 Myoblast cells: **Nokukhanya Cebekhulu**, Mangosuthu University of Technology, and Durban, South Africa

09:45 - 10:00 The effect ofPleurostylia capensis crude extracts on porcine adipose derived mesenchymal stem cells for chondrogenic differentiation: **Mapula Razwinani**, Tshwane University of Technology, Pretoria, South Africa

10:00 - 10:15 The Dose and Time Dependent Effects of HGF on Myf-5 and MyoD and Expression in Quiescent Primary Human Myoblasts: **Niccolo Passerind'Entreves**, Stellenbosch University, South Africa

10:15 - 10:30 **Tea / Coffee Break**

10:30 - 11:30 **Keynote Lecture:** 3D Printing for Engineering Complex Tissues: **Prof. John P. Fisher,** University of Maryland, USA

11:30 –11:45 MSC / PDEC interaction: a requirement for a functional beta cell in an injured adult pancreas:
Dr. Venant Tchokonte-Nana, Stellenbosch University, South Africa

11:45 - 12:00 An approach to establishing a comparative index by comparing primary myoblasts of two subjects in vitro.
Kirankumar Gudagudi, Stellenbosch University, South Africa

12:00 - 12:15 Kolaviron shows anti-proliferative effect and down regulation of Vascular Endothelial Growth Factor-C and Toll like Receptor-2 in Wuchereria bancrofti infected blood lymphocytes: **Dr. Aliyu Muhammad,** Ahmadu Bello University, Zaria, Kaduna State, Nigeria

12:15-12:30 Evaluation of Antimicrobial activities of extract from Pyrenacantha grandiflora Baill. [ICACINACEAE]:
Prof Samie Amidou,University of Venda, Thohoyandou, South Africa

12:30 - 13:30 **Lunch**

C**hairpersons:** **Prof. Samie Amidou:** University of Venda,Thohoyandou, South Africa
Dr Venant Tchokonte-Nana: Stellenbosch University, South Africa

13:30 – 14:30 **Keynote Lecture:**Degeneration and Repair of Rotator Cuff Muscle after Tendon Tear: **Prof. Johnna S. Temenoff**, Georgia Tech and Emory University, Atlanta, GA, USA

14:30 - 15:00 Development of sdf-1 alpha gene-activated collagen chondroitin sulfate scaffold for angiogenic therapy of chronic wounds: **Dr Michael B. Keogh**, RCSI, Dublin 2, Ireland

15:00-15:30 Identification of wild legume-derived lectins that could enhance burn wound healing: **Dr. Farisai Chidzwondo**, University of Zimbabwe, Zimbabwe

15:30-16:00 **Tea / CoffeeBreak**

16:00 - 17:00 **Dr. Joe Molete.** Director: VUT Southern Gauteng Science and Technology Park (SGSTP).

Tour of the Science Park.

17:00 - 18:00 **Poster Session** (presentation of posters with even numbers)

19:00 Gala Dinner and Awards Ceremony

Sunday July 30, 2017
Breakfast and Departure

Plenary Lectures

Tissue Regeneration Therapy Based on Biomaterial Technology of Dual Drug Release

Yasuhiko Tabata

Institute for Frontier Life and Medical Sciences, Laboratory of Biomaterials, Department of Regeneration Science and Engineering, Institute for Frontier Life and Medical Sciences Kyoto University 3-8-16 Biwadai, Uji-city, Kyoto 6110024, Japan. Tel: 9097013519; Mobile: +81-75-751-4121; Fax: +81-75-751-4646; Email: yasuhiko@infront.kyoto-u.ac.jp

For successful tissue regeneration therapy for the natural self-healing potential for patients, it is indispensable to manipulate the inherent ability of cells for their proliferation and differentiation which physiologically contributes to the self-healing potential. As a trial to achieve cell-based tissue regeneration, cells present in the body should be activated to promote their regeneration potential by any method. Biomaterial technology plays an essential role in creating the local environment which allows cells to activate their ability for tissue regeneration. If a key protein of a bioactive drug is supplied to cells at the right site, the right time period or at the appropriate concentration, their potential will be enhanced to naturally induce cell-based tissue regeneration.

Biodegradable hydrogels have been explored for the controlled release of drugs, growth factors, chemokines, and low-molecular-weight compounds, to succeed in the protein-induced cells activation for regeneration therapy of various tissues. The hydrogel system can not only release one type of drug, but multiple (e.g. two) types of drugs in different concentrations or time profiles. Such a dual release of drugs could further enhance the potential for cell proliferation and differentiation for tissue regeneration and repair. In case cells are not present around the target site for regeneration, it is necessary to enhance cell recruitment to the target site. For example, the controlled release of a chemokine protein can enhance the in vivo recruitment of stem cells, followed by the local functional activation of cells recruited by another drug released for an enhanced cell-based tissue regeneration. Inflammation is one of the essential host responses to pathologically modify the process of tissue regeneration. It is no doubt that without inflammation, no tissue regeneration takes place. In this study, tissue regeneration was naturally promoted by positively regulating the inflammation process through the local release of an anti-inflammatory drug. The positive regulation of inflammation further enhanced the therapeutic efficacy of tissue regeneration which is induced by the biomaterials technology of drug release. This paper discusses the significance of dual drug release in regenerative medicine.

Elastic, Soft and Temporary: Designing Biodegradable, Thermoplastic Elastomers for Applications in Regenerative Medicine

William R. Wagner

Director McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh USA. Email: wagnerwr@upmc.edu

As biomaterials, thermoplastic elastomers are valued for the ease with which they can be processedand for their soft tissue-like mechanical behavior. For applications such as insulating coatings for cardiac pacing leads ordiaphragmsfor blood pumps, preventing biodegradation has been a primary design concern. However, in regenerative medicine and drug delivery applications, controlled biodegradation of such elastomers into non-toxic byproducts is desired. Efforts have thus been focused on the design and processing of biodegradable, thermoplastic elastomers to achieve properties required in a range of settings. Some of these applications include:

- temporary mechanical support for the failing ventricle after a myocardial infarction,
- scaffolding for the creation of tissue engineered cardiac valves and valve leaflets,
- coatings for biodegradable vascular stents,
- temporary hollow fiber membranes for acute drug delivery to wound beds,
- transient mechanical support for vein segments used in arterial bypass procedures,
- tissue engineered blood vessels, and
- constructs for abdominal wall repair.

Molecular design parameters have been utilized to tune mechanical and degradation properties and to introduce reactive groups for subsequent biofunctional surface modifications. In the processing steps, composites with natural materials, such as extracellular matrix digests and components, have been generated. Fiber processing to control microstructure and mechanical behavior has also been utilized to mimic specific active biological tissues. This presentation will highlight the design, processing, and application of these materials to address clinical needs created by disease, trauma and congenital conditions.

SCAFFOLDS, STEM CELLS, TISSUE ENGINEERING AND REGENERATIVE MEDICINE

SESSION PRESENTATIONS

THURSDAY, JULY 27, 2017
08:30-12:30
CHAIRPERSONS:

Prof. Michael Pillay, Vaal University of Technology, Vanderbijlpark , South Africa
Prof.Mkhululi Lukhele, University of the Witwatersrand, Johannesburg, South Africa

Future perspectives of regenerative medicine

John A. Jansen

John A. Jansen, DDS, PhD, Department of Biomaterials, Radboud University Medical Center, Dentistry 309, PO Box 9101, 6500 HB Nijmegen, Email: john.jansen@radboudumc.nl

Over the last decades, great progress has been made in medicine in understanding disease processes and the development of new treatment strategies as well as methods. However, we have also become aware that not all diseases are curable. The treatment of such incurable diseases will benefit more from innovations in the area of health management instead of searching for the preeminent treatment method, where the final goal is a prolonged increase in the quality of life of the patient. Finally, this strategy offers the best perspective on affordable care for an aging society, where everybody wishes to be active as long as possible. Therefore, the goal of regenerative medicine is not to aim at the curing of diseases, but to strive for the life-long well-being of the patient. This seems to be a more realistic goal and inspiring challenge for health care in the 21th century. In the subsequent research strategy, two themes are very relevant:

Disease management: this deals with the maintenance and restoration of the functioning of (medically compromised) patients, but also deals with defining the maximum achievable function to prevent overtreatment (and overloading) of the patient.

Tailored medicine: Serious attention for the patient whereby patient focused/centered therapy, which offers the patient the possibility to control independently his/her health and also to manage this health with the health care provider. Therefore new diagnostic technologies are needed, as well as technologies to test the effectiveness of drugs. In this lecture, the above-mentioned issues will be discussed and examples will be provided.

Preliminary antibacterial evaluation of PEG/carbopol/mastic gum-based gels containing cavacrol

Zintle Mbese

University of Fort Hare 2200, Golf Course, Alice, South Africa Tel: 0835509301; Mobile: 040- 602 2266; Fax: 086 2313 187; Email: 201208394@ufh.ac.za

PEG/Carbopol/mastic gum-based gel was prepared from carbopol, polyethylene glycol, reduced graphene oxide, mastic gum and loaded with silver nanoparticles and cavacrol. FTIR spectra of the gels revealed C=O absorption at 1660 cm-1 confirming the incorporation of reduced graphene oxide into the gels. UV-Vis analysis of all gels showed maximum absorption at 245 nm. Antibacterial analysis revealed that the gels are effective against selected bacteria suggesting that they are potential therapeutic agents for wound dressing.

Preparation and characterization of polyaspartamide-based nanocarriers containing antimalarials

Mhlwatika Z and Aderibigbe, B. A.

University of Fort Hare AL-G Ntlabati 2-MA Floor: 1 Room: UGNFA 30 University of Fort Hare, Department of chemistry. Privatebag x1314 5700. Mobile: +27785193064; Tel: +27406022266; Fax: +27862313187; Email: 201103519@ufh.ac.za

Malaria is a chronic disease caused by a female Anopheles mosquito parasite. The greatest problem faced by malaria control programs worldwide is drug resistance to malaria parasites. To overcome drug resistance, malaria is treated by combination therapy. In this research, polymer-drug conjugates containing two antimalarials or two antimalarials and an antibiotic were prepared and characterized by FTIR, NMR, SEM/EDX, XRD, TGA and TEM which confirmed the successful isolation of the conjugates. The SEM images of the conjugates revealed a predominant interwoven morphology suggesting they are potential drug delivery systems for long term drug delivery.

Design of Polymer-Drug Conjugates for Combination Therapy for Controlled Delivery of Antimalarials

S. Alven and B. A. Aderibigbe

University of Fort Hare, Department of chemistry Thyali 1 Room 17, UFH, Alice 5700 Mobile: +27730900785 Tel: +27 40 602 2266 Fax: +27 86 2313 187 Email: 201214199@ufh.ac.za

Malaria is a serious and chronic disease that is endemic in the tropical regions. The currently used antimalarial drugs suffer from drug resistance, toxicity and poor water solubility which limit their pharmacological efficacy. To overcome drug resistance, malaria is treated by combination therapy which involves the combination of two or more antimalarial drugs. In this research, combination therapy was explored using polymer-drug conjugates containing 4-aminoquinoline, 8-aminoquinoline with folic acid and antibiotics. The conjugates were characterized by Scanning Electron Microscope (SEM), Fourier transform infrared Spectroscopy (FTIR) and 1HNMR. The characterization confirmed the successful incorporation of the antimalarial drugs into the polymers.

From Molecules to the Clinic - Austrian Cluster for Tissue Regeneration (ACTR)

Redl H.

Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Austria. Email:Office@TRAUMA.LBG.AC.AT

The ACTR integrates facilities of the Ludwig Boltzmann Institute for Trauma (LBI Trauma) and 20 other research groups of 8 universities in Austria. The cluster offers state-of-the-art facilities for tissue engineering including (stem/endothelial) cell research. With its fully translational approach, an interdisciplinary team including MD/VetMD, located partly in hospitals and a GMP facility provides an optimal research environment. ACTR covers - Neuroregeneration, Soft Tissue Repair, Cartilage/Tendon and Bone/Ligament Regeneration as well as competence centers for molecular biology, miRNA analysis, polymer synthesis, bioprinting, preclinical in vivo facilities incl. imaging, morphology. In particular the LBI Trauma has a long tradition in bioadhesives and hemostats e.g. plasma derived fibrin matrix and its special use for growth factor and cell delivery as well as a gene activated matrix. Several experimental and clinical studies show efficacy for extracorporeal shock wave therapy as a means to accelerate tissue repair and regeneration in various wounds and non-bone healing cases. However, the biomolecular mechanism by which this treatment modality exerts its therapeutic effects is only partially resolved which is a central research topic in the cluster. Another goal in our group is to use „medical garbage "for regenerative purposes (fat, placenta). In the orthopaedic field, of particular interest is the replacement of broken ligaments by degradable silk fibroin constructs which are replaced by endogenous ligament structures. The ACTR also provides special training opportunities (PhD program for bone and joints as well as support for the Biomedical Engineering programs).

Development and in vitro studies of nanocarriers for combination therapy

Tobeka Naki

University of Fort Hare Alice 5700-832474424, Tel: +27 (0) 40 602 2266; Mobile: +27 (0) 86- 2313 187; Email: tobekanaki@gmail.com

Polymer-based carriers are used for encapsulation and delivery of bioactive agents so as to reduce drug toxicity, for targeted drug delivery and to overcome drug resistance. In this study, platinum, procaine and bisphosphonate were incorporated onto polyamidoamine-based nanocarriers to form polymer-drug conjugates. The conjugates exhibited cytotoxic effects which was selective to the cancer cell lines whereas the free drugs were non-specific. The current findings indicate that these polymer-drug conjugates possess the potential for development of therapeutics for the treatment of cancer.

A low cost bioprinter for alginate-based hydrogel microextrusion

John R Honiball, Sidne Fanucci, Earl Prinsloo,

Rhodes University, Biotechnology Innovation Centre, 7 George Street, Grahamstown, 6139 South Africa. Tel: +27718711334; +27466038082; Email: e.prinsloo@ru.ac.za

Bioprinting aims to introduce the precision and reproducibility of additive manufacturing technologies to tissue engineering. Based on this we investigated the potential for modifying a commercially available RepRap Prusa iteration 3 (i3) three-dimensional (3D) printer, by replacing the fused filament fabrication capability with a microextrusionprinthead to enable computer controlled precision deposition of sodium alginate-based bioinks. Using adipose-derived human mesenchymal stromal stem cells (ad-HMSC) and human umbilical vein endothelial cells (HUVEC), the potential for fabricating vascularised adipose tissue was investigated. Cell viability assays and confocal laser scanning microscopy revealed that ad-HMSC remain viable post printing compared to HUVEC cultures which exhibited reduced cell survival. Here, we present data from direct bioink deposition and freeform reversible embedding of suspended hydrogel (FRESH) printing for optimisation of 3D spatial control of printed hydrogel constructs.

Myogenesis in a dish: investigating the complexity of skeletal muscle regeneration

Venter C. and Niesler CU.

Discipline of Biochemistry, School of Life Sciences, University of KwaZulu-Natal, Pietermaritzburg, South Africa Email: niesler@ukzn.ac.za

Skeletal muscle wound repair and regeneration is associated with multiple cell types where each type play distinct roles in regulating satellite cell activation and myogenesis. Macrophages secrete a host of inflammatory cytokines that activate and regulate the proliferation of satellite cells, and also modulate their differentiation. Fibroblasts differentiate to myofibroblasts and secrete cytokines and extracellular matrix (ECM) factors that form a scaffold for wound repair. Macrophages and fibroblasts therefore work together with myoblasts to facilitate wound repair. In order to understand the regulation of myogenesis by macrophages and fibroblasts, previous in vitro studies have primarily focused on the use of conditioned media or co-culture systems that physically separate the cell populations. The current study developed a simple and inexpensive co-culture method that allows for physical contact between cell types; in addition, a novel method was developed to quantitatively assess myoblast alignment prior to fusion. The effect of macrophages and fibroblasts on myoblast proliferation, migration, alignment and fusion was then determined.J774A.1 macrophages and LMTK fibroblasts were found to promote the proliferation of C2C12 myoblasts in a cell dependent manner; macrophages had a maximal effect at 80 x 103 cells, whereas fibroblasts promoted maximum proliferation at 20 x 103 cells. Macrophages and fibroblasts both promoted myoblast migration with maximal effects at 80 x 103 cells. Co-culturing a combination of macrophages (40 x 103) and fibroblasts (40 x 103) with myoblasts revealed that fibroblasts did not alter the pro-proliferative effects of macrophages on myoblasts; however, macrophages were able to decrease the pro-migratory effects of fibroblasts on myoblasts.

Analysis of alignment demonstrated that fibroblasts did not significantly affect myoblast/myotube alignment, while macrophages promoted alignment in a cell density-dependent manner with a maximal effect at 80 x 103 cells. Macrophages had no significant effect on myoblast fusion at 5 x 103, but increasing the number of cells beyond this significantly decreased myoblast fusion with the lowest percentage fusion at 80 x 103 macrophages. Co-culture with 5 or 10 x 103 fibroblasts significantly increased myoblast fusion; however, further increases in fibroblast number abrogated this effect.

In conclusion, we have developed a novel co-culture technique that better represents in vivo cell interactions by allowing for cell-cell contact and facilitating variable numbers. We show that macrophages are more important for promoting myoblast proliferation, while fibroblasts have a prominent role in promoting myoblast migration. We have also created a novel method to quantify alignment and further go on to show that macrophages play a distinct role in promoting myoblast/myotube alignment prior to fusion, but are required to resolve for successful fusion to occur. Fibroblasts, on the other hand, are required at low numbers to promote myoblast fusion.

SCAFFOLDS, STEM CELLS, TISSUE ENGINEERING AND REGENERATIVE MEDICINE

SESSION PRSENTATIONS and POSTERS

THURSDAY, JULY 27, 2017
13:30-16:00

CHAIRPERSONS:

Prof. Kathy Myburgh: Stellenbosch University, Stellenbosch, South Africa
Prof. Danie du Toit: Tshwane University of Technology, Pretoria, South Africa

Superhydrophobic Surfaces for Blood Contacting Medical Devices

Ketul Popat

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Many materials used for implants have excellent biocompatibility with different tissues in the body. However, when in contact with the blood, the occurrence of the incidents such as platelet/leukocyte adhesion and activation leads to further thrombosis and sometimes failure of these implants. It is well known that platelet functionality can be modulated by the surface chemistry and texture. Very few studies have investigated the effect of superhydrophobicity on hemocompatibility. Superhydrophobic surfaces are extremely repellent to water (contact angle for water is greater than 150˚) and water droplets easily roll off from the surfaces. In this study, we have developed surfaces with different superhydrophobic coatings. The surfaces were characterized using contact angle goniometry and X-ray photoelectron spectroscopy (XPS), and platelet adhesion and activation was investigated using fluorescence microscopy and scanning electron microscopy (SEM). The results indicate significantly better hemocompatibility of superhydrophobic surfaces as compared to unmodified surfaces.

Superhydrophobic Surfaces for Blood Contacting Medical Devices

Ketul Popat

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Many materials used for implants have excellent biocompatibility with different tissues in the body. However, when in contact with the blood, the occurrence of the incidents such as platelet/leukocyte adhesion and activation leads to further thrombosis and sometimes failure of these implants. It is well known that platelet functionality can be modulated by the surface chemistry and texture. Very few studies have investigated the effect of superhydrophobicity on hemocompatibility. Superhydrophobic surfaces are extremely repellent to water (contact angle for water is greater than 150˚) and water droplets easily roll off from the surfaces. In this study, we have developed surfaces with different superhydrophobic coatings. The surfaces were characterized using contact angle goniometry and X-ray photoelectron spectroscopy (XPS), and platelet adhesion and activation was investigated using fluorescence microscopy and scanning electron microscopy (SEM). The results indicate significantly better hemocompatibility of superhydrophobic surfaces as compared to unmodified surfaces.

Establishment of assays for culture and manipulation of haematopoietic stem cells

Marianne W. Mureithi, Patrick Mwaura, Matrona Akiso, Peninah Wairagu, Robert Langat, Bashir Farah and Omu Anzala

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Although combination antiretroviral therapy can dramatically reduce the circulating viral load in those infected with HIV, replication-competent virus persists. To eliminate the need for indefinite treatment, there is growing interest in creating a functional HIV-resistant immune system through the use of gene-modified hematopoietic stem cells (HSCs). Here, we proposed to establish assays for isolation and maintenance of cord blood and adipose tissue-derived stem cells for better understanding of communicable diseases such as HIV/AIDS and pave the way for long term research into applications of these stem cells to address various areas namely: cardiovascular diseases, diabetes, cancer therapy, wound healing and tissue regeneration. Pregnant women about to deliver at Mbagathi District hospital were invited to participate in the study and informed consent was obtained. One hundred and fifty millilitres of blood was collected from the umbilical cord and the placenta immediately after parturition. Cord Blood Mononuclear Cells (CBMCs) were then isolated and the cells viability tested. Adipose-derived stem cells were also isolated from adipocytes obtained from adipose tissues following plastic surgery performed at Kenyatta National Hospital (KNH). Our preliminary data indicated that most of the CMBCs and adipocytes isolated were viable for culture and expansion of the cells into hematopoietic stem cells. In conclusion, this pioneering stem cell research project will enhance the potential to offer single cell therapies to create a functional HIV-resistant immune system.

Hijacking basic science to solve an African problem: When stem cells meet genome engineering,

Janine Scholefield

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It is well established that the genetic diversity of the African diaspora is not accounted for in the largely Caucasian clinical trials established in developed nations, resulting in severe adverse drug reactions (ADR), estimated to cause as many as 1 in 12 hospital admissions. This leads to a decline in compliance which can be fatal in many scenarios, but is of particular concern within the context of South Africa's high HIV burden, where lifelong ART regimens are required to avoid disease progression and death. Therefore, established drugs need to be retested across the sub-Saharan population. However, the time and cost associated with these potential retrials make this a less attractive prospect for large international pharmaceutical companies. There is therefore, a need to bridge the gap between expensive and time consuming clinical trials on the sub-Saharan population and finding novel testing models to minimise ADR.

The development of appropriate cellular models which are representative of the genotypes and haplotypes endemic to Southern Africa may negate the requirement for clinical re-trials and help to predict, based on simple PCR or sequencing tests which drugs will be best tolerated in vivo. Such cellular models need to retain basic characteristics, i.e. comparisons between proficient and poor drug metabolism phenotypes must be made with the knowledge of the exact contributing genetic change. These can then be used to characterise accurate indicators of drug metabolism. Therefore it is critical to investigate the development of advanced physiologically relevant cellular models that can be used in a high-throughput format. The CSIR has established cutting edge iPSC technology which would allow us to generate infinite amounts of hepatocytes – the cell type most affected in, and indicative of, ADRs. In addition to which, we have established genome engineering technology which allows us to precisely and discretely introduce mutations known to exist in the African population with which to re-evaluate drug toxicity. We are currently engineering stem cells to incorporate a highly prevalent African single nucleotide polymorphism which leads to the poor metabolism of the anti-retroviral efavirenz – considered a standard drug in the fight against HIV in South Africa. With these engineered and physiologically relevant cells, which are highly superior to currently available testing models, we can propel the reassessment of drug screening into an African-centric domain

Influence of Low Intensity Laser Irradiation on Isolated Human Adipose Derived Stem Cells, in Combination with Growth Factors and in a Co-culture Environment, and Differentiation into Smooth Muscle Cells

Natasha Hodgkinson and Heidi Abrahamse

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Human adipose derived stem cells have shown great potential for use in regenerative medicine due to their differentiation potential. Growth factors such as transforming growth factor (TGF-β1) and retinoic acid (RA) play a significant role in cell differentiation. In addition, low intensity laser irradiation (LILI) has also shown to influence the behavior of stem cells. Our investigations included the effect of LILI in combination with RA on the differentiation of ADSCs into smooth muscle cells, as well as the co-culture of ADSCs and a commercial smooth muscle cell line (SKUT-1) exposed to LILI and a combination of RA and TGF-β1. In the first experiment ADSCs were exposed to a 363 nm diode laser at a fluence of 5 J/cm2 and differentiated using RA. The second set of experiments involved co-culture of the ADSCs and the SKUT-1 cells at a ratio of 1:1, treated with growth factors RA and TGF-β1, and then exposed to LILI (636 nm and 5 J/cm2). Morphological changes were assessed using inverted light microscopy and differential interference contrast microscopy. Cellular viability and proliferation was assessed by optical density, trypan blue and adenosine triphosphate luminescence. Cell markers of both the ADSCs and the differentiated cells were assessed using flow cytometry and real-time reverse transcriptase polymerase chain reaction (RT-PCR). LILI alone did not induce differentiation of ADSCs to SMCs, however, RA did induce differentiation within 14 days, and was confirmed by changes in morphology, as well as, expression of SMC markers. In the co-culture experiment, LILI showed increased proliferation of the co-cultured cells, and the expression of SMC markers increased in the groups exposed to LILI in combination with growth factors, while the ADSC markers decreased.

STEM CELLS AND TISSUE ENGINEERING

SESSION PRSENTATIONS

FRIDAY, JULY 28, 2017
08:30-12:30
CHAIRPERSONS:

Prof. Keolebogile Motaung: Tshwane University of Technology, Pretoria, South Africa
Dr Marianne Mureithi:University of Nairobi, Nairobi, Kenya

Computational Modeling of Receptor-Ligand Interactions

Lydia E. Kavraki

Rice University, Department of Computer Science and Bioengineering

Computational methods have been largely used in the study of protein-ligand complexes, to perform virtual screening of potential protein inhibitors. Molecular docking, for instance, can predict both the structure of the protein-ligand complex and the corresponding binding energy. These methods are known to be reliable for small drug-like ligands, but their accuracy and efficiency greatly decays for larger ligands such as peptidomimetics, peptides, or larger ligands that are encountered in tissue engineering applications. For instance, some peptidomimetics known to inhibit important transcription factors have up to 25 rotatable bonds or degrees of freedom (DoFs), far exceeding the capacity of standard docking tools. As an alternative, our group has developed DINC, a meta-docking method for the incremental docking of large ligands. DINC is based on a divide and conquer approach and the popular AutoDock algorithm. However, instead of docking the whole ligand at once, DINC reduces the problem complexity by incrementally docking larger and larger overlapping fragments of the original ligand. This process is repeated incrementally, until the whole ligand is reconstructed and docked. At each step, only a small number of DoFs is sampled, ensuring efficiency. The method has been implemented and is now freely available through a webserver (http://dinc.kavrakilab.org/). DINC allows docking predictions for large and flexible ligands and opens the way to use computational docking in tissue engineering applications.

A hybrid microfluidic system for regulation of neural differentiation in induced pluripotent stem cells

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Controlling cellular orientation, proliferation and differentiation is valuable in designing organ replacements and directing tissue regeneration. In the present study, we developed a hybrid microfluidic system to produce a dynamic microenvironment by placing aligned PDMS microgrooves on the surface of biodegradable polymers as physical guidance cues for controlling the neural differentiation of human induced pluripotent stem cells (hiPSCs). The neuronal differentiation capacity of cultured hiPSCs in the microfluidic system and other control groups was investigated using quantitative real time PCR (qPCR) and immunocytochemistry. The functionally of differentiated hiPSCs inside the hybrid system's scaffolds was also evaluated on the rat hemisected spinal cord in acute phase. The implanted cell's fate was examined using tissue freeze section and the functional recovery was evaluated according to thelocomotor rating scaleof Basso, Beattie and Bresnahan (BBB). Our results confirmed the differentiation of hiPSCs to neuronal cells on the microfluidic device where the expression of neuronal-specific genes was significantly higher compared to those cultured on the other systems such as plain tissue culture dishes and scaffolds without fluidic channels. Although the survival and integration of implanted hiPSCs did not lead to a significant functional recovery, we believe that the combination of fluidic channels with nanofiber scaffolds provides a great microenvironment for neural tissue engineering, and can be used as a powerful tool for in-situ monitoring of differentiation potential of various kinds of stem cells.

THE FATE OF SYSTEMIC AND LOCAL ADMINISTERED ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS TO MODULATE WOUND REPAIR

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Introduction: There is increasing interest in the use of adipose-derived mesenchymal stromal cells (ASCs) for wound repair. However, the fate of the administered cells is still poorly defined. Prior to assessing the benefit of ASCs in in vivo models of wound repair, this study set out to establish the location and survival of ASCs in vivo when administered either systemically or locally using both bioluminescence imaging (BLI) and histological analysis.

Methods: ASCs were transduced with a dual lentivector which expresses both firefly luciferase (Fluc) and green fluorescent protein (GFP). To determine the behaviour of ASCs, a model of physiological wounds in rats was used. Wounds on the dorsal aspect of the hind paws were created bilaterally in all animals. Two modes of application was assessed: 2x10^6 ASCs systemically into the tail vein, and 10^5 ASCs locally into the corners of the wound bed. ASC distribution and survival was followed in animals by BLI and histological analysis at 3h, 24h, 48h, 72h, 7 and 15 days post ASC injection.

Results: In animals treated systemically, ASCs were detected in the lungs with a decrease in signal from 3h to 48h, but no luminescent signal or GFP staining was detected in the wounds. However, locally administered ASCs remained strongly detectable for at least 7 days at the injection site. At the histological level, locally administered ASCs were detectable by GFP staining at the injection site. Interestingly a few ASCs seemed to migrate into the wound area as early as 48h post injection.

Conclusion: Using this physiological wound model we have observed that GFP/Fluc labelling allowed ASCs to be identified in vivo. When administered systemically, the majority of ASCs were filtered out in the lungs. Locally administered ASCs on the other hand remained and survived at the wound site for at least 7 days. Therefore systemic administration of ASCs for local wound repair in the clinical setting is questionable. To fully understand the role of ASCs in the context of wound repair, further studies using different administration methods in pathological wound models of increased severity should be performed.

Comprehensive transcriptomic profile of adipogenic differentiation in human adipose derived stromal cells

Melvin Anyasi Ambele, [1,2] Carla Dessels,[2] Chrisna Durandt[2] and Michael Sean Pepper[2]

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Adipogenesis is driven by changes in gene expression in adipose derived stromal cells (ASCs). Accumulation of excess adipose tissue as a result of adipocyte differentiation leads to obesity, which is a risk factor for type-2 diabetes, cardiovascular disease and cancer. We have employed transcriptomic techniques to systematically study the process of adipogenic differentiation in ASCs in vitro to be able to identify genes with a role in human adipogenesis that could potentially be manipulated to control this process with an overall goal of combating obesity. AffymetrixHuGene 2.0 ST arrays were used to study the changes in gene expression profile that characterize ASC adipogenic differentiation on days 1, 7, 14 and 21. A total of 61, 124, 138 and 149 significantly up-regulated genes (fold change ≥4, $p<0.05$ and FDR <0.5) were observed on days 1, 7, 14 and 21, respectively. The transcription factors (TFs) KLF15, LMO3, FOXO1 and ZBTB16 were up-regulated throughout the differentiation process. In silico analysis identified SIRT1 AKT1, HDAC1 & NCOR2 as functional partners that strongly interact with these TFs. Conversely, CEBPA, PPARG, ZNF117, MLXIPL, MMP3 and RORB were TFs identified to be up-regulated only from day 14 to 21. This coincides with adipocyte maturation, suggesting these TFs could serve as potential biomarkers characterizing this stage in adipogenesis. In a similar manner, genes significantly up-regulated only from day 1 to 7 and day 7 to 21 were identified and could serve as early-stage and general adipocyte differentiation biomarkers, respectively. RT-qPCR confirmed the observed gene expression changes from the microarray experiments. Strikingly, genes that were up-regulated during adipogenesis were enriched for neural and blood vessel development, migration of leukocytes, tumor growth, invasion and metastasis. Furthermore, pathway analysis revealed common genes shared by both adipocyte differentiation and certain obesity related pathophysiological conditions such as cancer, cardiovascular and metabolic diseases. Therefore, this study has identified potential biomarkers for different stages in human adipogenesis, which could be explored further in in vivo studies to identify potential candidates for combating obesity and obesity-related pathophysiological conditions by interfering with the process of adipogenesis.

Development of a Tissue-Engineered Tumor Model

Antonios Mikos

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Three-dimensional (3D) tumor models are gaining traction in the research community given their capacity to describe different cues of the tumor microenvironment absent in monolayer cultures. Accordingly, 3D tumor models are readily available for mechanistic studies of tumor biology and for preclinical drug screening. However, these systems often overlook biomechanical stimulation, another fundamental driver of tumor progression. To address this issue, we cultured Ewing sarcoma (ES) cells on electrospunpoly(ε-caprolactone) 3D scaffolds within a flow perfusion bioreactor. Flow-derived shear stress provided a physiologically relevant mechanical stimulation that promoted insulin-like growth factor-1 (IGF1) production, resulting in a shear stress-dependent drug response to IGF-1 receptor (IGF-1R) blockade. Given the central role of the IGF1/IGF-1R pathway in ES progression, these findings are particularly relevant and provide a mechanistic explanation for variable response to IGF-1R targeted therapies observed in ES patients.To elucidate the concerted effects of biomechanical stimulation and stromal cell signalling on ES phenotype and drug sensitivity, we then introduced mesenchymal stem cells (MSCs) in the model. Strikingly, ES cells became insensitive to IGF-1R blockade due to MSC-mediated activation of interleukin-6/transcription factor Stat3 pathway, a signalling pathway heavily involved in acquired drug resistance in several malignancies. In these conditions, ES-acquired resistance was overcome only by IGF-1R/Stat3 dual targeting.In conclusion, the use of a 3D tissue-engineered model enables the precise description of biomechanical stimuli and the detection of tumor- and/or stroma-specific mechanisms within a controlled environment. While these aspects are normally convoluted during in vivo testing, the use of a 3D tumor model allows the understanding of the specific impact of different microenvironmental cues on tumor progression and drug response. Furthermore, culture conditions and tumor/stroma ratios can be adjusted to determine drug response at different stages of disease progression, in contrast to time-consuming animal experiments, where tumorigenesis occurs over a much longer timescale.

The search for the side population in human adipose-derived stromal cells

Elize Wolmarans, Chrisna Durandt and Michael S. Pepper

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Adult stem cells are responsible for self-renewal in adult mammalian tissues and exist in various tissues in the human body including adipose tissue. Adipose-derived stromal cells (ASCs) can be defined as a heterogeneous population of cells, isolated from adipose tissue, with multipotent stem/progenitor cells that have the capacity to differentiate into various cell types. Increasing interest has been shown in the use of these cells in cell-based therapies. An inherent characteristic of human ASCs that is poorly understood is their heterogeneity. Very little is known about the various sub-populations that make up the isolated ASC population. It is assumed that one of the sub-populations includes stem/progenitor cells. Currently, the stem cell field lacks cell-surface markers that can be used to unambiguously identify a population of true stem cells within heterogeneous populations, and the search for specific markers is a major theme in research in this area. A strategy that has been used with success for isolating a primitive sub-population from a heterogeneous cell population in hematopoietic stem cells is the side population (SP) assay. The assay is based on the differential ability of cells to efflux a fluorescent dye, attributed to the expression of one or more members of the ATP-binding cassette (ABC) transporter protein family. It is theorized that the degree of efflux activity of SP cells correlates with their maturation state, such that cells exhibiting the highest efflux activity are the most primitive. We adapted and optimized the SP assay in house and the assay was used to study the efflux capacity of human ASCs with the focus on possibly identifying and isolating a sub-population. Results revealed no SP present in human ASCs. In addition, the results revealed the absence of expression of one of the most well-known ABC transporter proteins linked to the SP phenotype. These negative results suggest that the SP assay is not the optimal assay for studying heterogeneity in ASCs, and that other methods will have to be employed in order to find the elusive stem cell population in human ASCs.

Fibroblast-Derived Extracellular Matrix Induces Chondrogenic Differentiation in Human Adipose-Derived Mesenchymal Stromal/Stem Cells in Vitro

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Mesenchymal stromal/stem cells (MSCs) represent an area being intensively researched for tissue engineering and regenerative medicine applications. MSCs may provide the opportunity to treat diseases and injuries that currently have limited therapeutic options, as well as enhance present strategies for tissue repair. The cellular environment has a significant role in cellular development and differentiation through cell–matrix interactions. The aim of this study was to investigate the behavior of adipose-derived MSCs (ad-MSCs) in the context of a cell-derived matrix so as to model the in vivo physiological microenvironment. The fibroblast-derived extracellular matrix (fd-ECM) did not affect ad-MSC morphology, but reduced ad-MSC proliferation. Ad-MSCs cultured on fd-ECM displayed decreased expression of integrins alpha 2 and beta1 and subsequently lost their multipotency over time, as shown by the decrease in CD44, Octamer-binding transcription factor 4 (OCT4), SOX2, and NANOG gene expression. The fd-ECM induced chondrogenic differentiation in ad-MSCs compared to controlad-MSCs. Loss of function studies, through the use of siRNA and a mutant Notch1 construct, revealed that ECM-mediated ad-MSCs chondrogenesis requires Notch1 and beta-catenin signalling. The fd-ECM also showed anti-senescence effects on ad-MSCs. The fd-ECM is a promising approach for inducing chondrogenesis in ad-MSCs and chondrogenic differentiated ad-MSCs could be used in stem cell therapy procedures.

Effect of adipogenesis on mitochondrial health and networks

Rose Kadye, Pascalene Houseman and Earl Prinsloo

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Mesenchymal stem cells (MSCs) are multipotent stem cells considered as a viable option for cell based therapy because of their ability to differentiate and give rise to multiple cell types such as bone, cartilage and adipose. Studies have shown that a cells energy requirements and mitochondrial biogenesis are modified depending on proliferation or differentiation; mitochondria can be a major limiting factor in ensuring the differentiation potential of MSCs. These changes in mitochondrial biogenesis affects the mitochondrial networks, structure, membrane potential, substrates and products. Therefore, this study aimed to investigate such changes during the adipogenic differentiation of adipose derived human MSCs. Using mitochondrial potentiometric dye JC-1, DCF-DA and immunohistochemistry, mitochondrial DNA, distribution, membrane potential and mitochondrial networks were analysed. The results of this study show that upon adipogenic differentiation of hMSCs, mtDNA, ROS and the mitochondrial transcription factor A (TFAM) increased, mitochondrial mass increased, the mitochondrial membrane potential become more polarised, its networks become more tortuous, while the branches decreased in thickness but increased in length and neutral lipids drastically increased. These results suggest that as mitochondrial biogenesis increased, mitochondria became healthier and its networks became more fragmented when human mesenchymal stem cells were differentiated into white adipocytes.

STEM CELLS AND TISSUE ENGINEERING

SESSION PRSENTATIONS AND POSTERS

FRIDAY, JULY 28, 2017
13:30-16:30
CHAIRPERSONS:

Dr. Janine Scholefield, BTRI, CSIR/ UCT, South Africa
Dr.Kevin Dzobo, ICGEB/ University of Cape Town, South Africa

The Meniscus: from obscurity to significance in knee joint health and disease

Adetola Adesida

Associate Professor of Surgery, University of Alberta, Department of Surgery, Edmonton, Canada

From obscurity to significance in knee joint health and disease, the meniscus can no longer be ignored or regarded as vestigial tissue structures within the knee joint. Its discovered association with high incidence of early onset of osteoarthritis post-surgical resection has brought it to the forefront of orthopaedic research. Since meniscus is susceptible to repeat injuries and has limited reparative capacity, particularly in the avascular inner zone (the largest portion of meniscus tissue), treatment of meniscus injuries typically focuses on non-operative management whenever possible. However, when pain is persistent and catching of the meniscus in the injured knee occur, surgical resection of the damaged meniscus is inevitable. Although the consensus to retain and not resect injured meniscus is appreciated, only a small subset of meniscus injuries are considered amenable to repair, making partial or complete meniscectomy a widespread practice. The downstream effect of injury and repair on mechanical function and biological health of the meniscus are however not well understood. New and emerging research findings suggest that injured meniscus may hold both biomechanical and biological signs/ signatures that could potentially predict the knee organ's susceptibility to tissue degeneration and ultimately early onset of osteoarthritis. My talk will provide an overview of the latest research findings on unravelling the role of knee meniscus biology and its interaction with meniscus biomechanics in both health and disease, as well as present an overview of new findings from ongoing meniscus research in my cell-based tissue engineering laboratory at the University of Alberta, Canada.

Cis-vaccenic acid induces differentiation and up-regulates gamma globin synthesis in K562, JK1 and transgenic mice erythroid progenitor stem cells

Idowu A.Aimola[1,2,4] HajiyaM.Inuwa[1,2,] AndrewJ.Nok[1,2], AishalMamman[3],James J.Bieker[4]

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Gamma globin induction remains a promising pharmacological therapeutic treatment mode for sickle cell anemia and beta thalassemia. However,hydroxyurea remains the only FDA approved drug which works via this mechanism. In this regard,we assayed the γ-globin inducing capacity of Cis-vaccenicacid (CVA). CVA induced differentiation of K562, JK1 and transgenic mice primary bone marrow hematopoietic progenitor stem cells. CVA also significantly up-regulated γ-globin gene expression in JK-1and transgenic mice bone marrow erythroid progenitor stem cells (TMbmEPSCs) but not K562 cellswithout altering cell viability.Increased γ-globin expression was accompanied by KLF1 suppression in CVA inducedJK-1 cells. Erythropoietin induced differentiation ofJK-1cells 24h before CVA induction did not significantly alter CVA induced differentiation and γ-globin expression inJK-1cells. Inhibition of JK-1 and transgenic mice bone marrow erythroid progenitor stem cells Fatty acid elongase5 (Elovl5) and Δ9 desaturase suppressed the γ-globin inductive effects of CVA.CVA treatment failed to rescue γ-globin expression in Elovl5 and Δ9-desaturase inhibited cells 48h post inhibition in JK-1cells.The data suggeststhat CVA directly modulates differentiation of JK-1 and TMbmEPSCs, and indirectly modulates γ-globin gene expression in these cells. Our findings provide important clues for further evaluations of CVA as apotential fetalhaemoglobin therapeutic inducer.

Cellular processing with the BiosafeSepax - a South African perspective.

Stephen Marrs

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The BiosfeSepax cell separation device is a fully automated, mobile, closed system for the safe, efficient and consistent processing of umbilical cord blood, bone marrow, peripheral blood or other cell based products. Automated technologies are now widely accepted as an essential part of ensuring the quality and viability of the isolation step that has a direct impact on the number of cells that are ""recovered"" from the initial sample.

The role in which the Sepax technology is used in Laboratories in South Africa will be discussed. Some case studies will be presented where the Sepax was used in regenerative applications.

Molecular Mechanistic Interpretation of the Molecular Attributes Inherent to the Performance of Biomedical Material Archetypes

Pradeep Kumar

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The elucidation of mechanism(s) behind the performance of biomaterial-based complex assemblies presents a significant challenge to biomaterial scientists around the world with most of the studies only providing "qualitative estimation" based on "theoretical experience" and "quantitative experimental results". Molecular mechanics simulations were employed for the "quantitative elucidation" of the mechanism inherent to multi-elemental biomaterial archetypes and a unique "in vitro–in vivo–ex vivo–in silico" performance-correlation profile was developed. HyperChemTM 8.0.8 and ChemBio3D Ultra 11.0 were employed for 3D Structure generation wherein the molecular structures were drawn in their syndiotactic stereochemistry and natural angle conformation. The overall steric energy was minimized through MM+, AMBER 3 and MMFF94 force fields in conjugation with Polak–Ribiere conjugate gradient method (novel progressive convergence strategy). An analytico-mathematical representation of potential energy surfaces was designed with total energy composed of bond stretching, angle, and torsional contributions as bonding and van der Waals interactions, H-bonding and electrostatic functions as non-bonding energies. The reactional profiles for component molecules and their complexes were elucidated by exploring the spatial disposition of the various component molecular attributes. The presentation will include 10 most recent and important molecular tectonic findings related to 1) porosity-controlled multi-elemental mucoadhesive system (Pharm Res cover page); 2) catalytic action of enzymes on a biomatrix; 3) reactional profile and cross-linking mechanism of ovalbumin and genipin; 4) fabrication of anisotropic neurodurable scaffold via molecular disposition of persulfate-mediated polymer slicing and complexation; 5) multi-macromolecular alginate-hyaluronic acid-chitosan polyelectrolyte complex; 6) anti-inflammatory and bioresponsivebehavior of an biocomposite intraocular implant; 7) formation of interpolyelectrolyte, hydrated and crosslinked polymer morphologies; 8) molecular simulation approach to the biomaterials bioadhesivity; 9) interfacially plasticized electro-responsive and -activated hydrogel; and 10) biomacromolecular interactions of an interpenetrating proteo-saccharide hydrogel network (biomaterial-protein interactions).

To date we have successfully demonstrated and published the role of molecular mechanics energy relationships towards the interpretation and understanding of the mechanisms that control the formation, fabrication, selection, design, performance, complexation, interaction, sterospecificity, and preference of various multi-elemental biomaterial archetypes for biomedical applications.

Publications to be presented:

1. Adeleke et al. Pharm Res 2015, 32, 2384–2409.
2. Bawa et al. J Control Release 2013, 166, 234–245.
3. Govender et al. Pharm Res 2016, 33, 3057–3071.
4. Kumar et al. Int J MolSci 2012, 13, 13966-13984.
5. Bijukumar et al. AAPS PharmSciTech 2016, 17(5), 1075-1085.
6. du Toit et al. Pharm Res 2014, 31, 607-634.
7. Ngwuluka et al. J Biomed Mater Res A 2015, 103A, 1077–1084.
8. Reddy et al. J Drug DelivSciTechnol 2017, 37, 123-133.

STEM CELLS AND TISSUE ENGINEERING

SESSION PRSENTATIONS

SATURDAY, JULY 29, 2017

08:30-12:30
CHAIRPERSONS:

Prof. Antonios Mikos: Rice University, Texas, USA
Dr. Blessing Aderibigbe: University of Fort Hare, Alice, South Africa

Approaching the Complexity of Product Development in Tissue Engineering

Peter C. Johnson, MD

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The raison d'être of our work in tissue engineering is to better serve patients having illnesses that lend themselves to tissue replacement and/or repair. This is a daunting task. The patient lives at the end of what can be described as a long string of related and unrelated hurdles, any one of which may thwart the delivery of tissue engineering technology in an effective manner. The resistances (R) in a series electrical circuit illustrate a simple example of the problem:

R1 -> R2 -> R3 -> R4 –> R5 -> R6 -> User -> R7

In tissue engineering, R1 might be considered the compendium of technical risks associated with the development of the physical 'product.' R2 might be considered the risks associated with financing early development. R3 could be the risk of preclinical or clinical failure during testing. R4 might be the risk of lack of regulatory clearance, R5 might be the risk of reimbursement failure and R6 might be the risk of lack of adoption by caregivers or by complex hospital and distribution systems such a Group Purchasing Organizations. R7 would be the risk of technology failure during post-market surveillance. There are many sub risks in the continuum but these represent the major zones of risk.

As a result of these linked risks, business models in our field need, in many cases, to be contrived at the onset of technology development itself. This implies that early technology developers – generally academics – need to become quite well versed in both clinical applications and business methods, the latter including financing, regulatory, reimbursement and distribution issues. Recently published work indicates that there is a wide – and understandable - gap in this awareness among academics. Work is ongoing to further explore gap areas in which educational forums and supplemental education can bring progress. However, there appears to be an immediate need for consortia of business and academic talent to enable filtering of opportunity and augmentation of 'risk hurdling' as we bring these important technologies forward.

Effect of Pleurostylia capensis plant extracts in C2C12 myoblasts

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Bone fractures accounting for 8.9 million fractures per year globally are a persistent challenge in orthopaedics. In South Africa there is no conclusive epidemiological data, but the medical cost of healing a fracture is in the region of about R50000.00.Medicinal plants have been in use since time immemorial and the existence of traditional and complementary medicine is known to be a fertile ground for western medicine and has drawn curiosity in the bone tissue engineering arena for their recently discovered osteoinductive and osteogenic capability in several studies. Locally Pleurostyliacapensis extracts are popular for their multipurpose remedies; traditionally for a ritual body wash, cosmetic use, steam bath, and purgative against symptoms of witchcraft, mental illness, and colic in babies, epilepsy and antibacterial and anti-inflammatory properties. This study aimed at investigating the osteoconductive and osteoinductive properties of P.capensis plant extracts in C2C12 myoblast cells.

C2C12 myoblast cells were purchased from American Type Culture Collection 5x10^4 (ATCC no.CRL-1772). The cells were transferred to each well of a 24 well plate in Dulbecco's modified Eagles medium (DMEM) supplemented with heat inactivated 10% fetal bovine serum (FBS), 2.5 mM L-Glutamine, 100 µg/mL streptomycin and 100 U/mL penicillin. After 24 hourswhen attachment and about 80% confluence was attained, the medium was substituted with 1% FBS/DMEM and 1% antibiotic cocktail. Each sample was assayed in triplicate. The medium was changed after two days and incubated at 37°C in an atmosphere containing 5% CO2. Cells were treated with 15 µg/ml, 30 µg/ml and 50 µg/ml concentrations of the bark and root extracts of the plant. The treated cells were thereafter assessed for their morphology and subsequently observed under an inverted florescence microscope at the excitation wavelength of 352 nm. Their viability was confirmed with an automated cell counter utilizing 0,4% Trypan blue staining solution to determine total cell count, live cell count and percentage of live cells after treatment at 2, 4, and 8 days of differentiation. Finally cell proliferation and differentiation were evaluated by MTT,ALP, BMP-2 assays. There was a correlation between cell shape, proliferation and phenotypic expression of cells at the variable concentrations. The cell morphology of treated C2C12 was distinct from that of untreated cells. Quantification of the ALP and BMP-2 content expressed indicated an enhanced osteocyte cell differentiation and maturation. Extracts of P. capensis were found to significantly enhance the cell proliferation, differentiation and considerably up-regulated the expression ALP and BMP-2 osteocyte activity in vitro. The results obtained are considered sufficient for further studies aimed at isolating and identifying the active compounds.

The effect of Pleurostylia capensis crude extracts on porcine adipose derived mesenchymal stem cells for chondrogenic differentiation

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Adipose derived mesenchymal stem cells (ADMSCs) are one of the most recent used cells for tissue engineering and regenerative medicine because they can beeasily harvested, have the ability to proliferate considerably and differentiate into any other cell type. There is very little evidence is using crude extracts from medicinal plants for ADMSCs differentiation. There is a growing interest in the ability of traditional medicines to promote chondrogenesis. The aim of this study was to determine whether crude extracts from the bark and roots of P. capensiswill differentiate pADMSCs into chondrocytes.

ADMSCs were isolated from porcine knee joint and grown to confluence passage-0. Exactly 5x104 cells/ml of ADMSCs were cultured in 96 E-plate well bottoms in α-MEM medium supplemented by 10% fetal bovine serum in a humidified 5% CO2 atmosphere at 37°C for 24, 48 and 72 hours. Too assess cell proliferation, the MTT assay and xCELLigence system was used. Micro-mass culture was used to induce the cartilage differentiation. About 2.5×105 cells/ml passage 0 cells were pelleted at 300 g for 5 min and cultured for 21 days. Crude extracts of P. capensisat 5, 15, 30, 50 and 100 µg/ml concentrations were used and transforming growth factor (TGF)-β3 was used as positive control. Expression levels of type II collagen mRNA was determined in the cell culture supernatant. The crude extracts of P. capensisshowed proliferation of ADMSCs at 5, 15 and 50 µg/ml concentration at 24 hr. After 48 and 72 hrs of incubation; cell viability was above 70% as compared to untreated control cells. This indicates that the ADMSCs are differentiating. Metachromatic nature of the matrix was demonstrated by the toluidine blue staining method. To best of our knowledge this study is the first to evaluate the influence of P. Capensis crude extracts on ADMSCs growth kinetics and differentiation. Our results demonstrated that P. Capensis crude extracts had increased cell proliferation and differentiation of ADMSCs into chondrocytes, increased cell proliferation and stimulated the secretion of type II collagen.

The dose and time dependent effects of HGF on Myf-5 and MyoD and expression in quiescent primary human myoblasts

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Satellite cells are progenitor cells that persist in adult muscle in a quiescent state. Upon injury, growth or hypertrophy, satellite cells become activated, proliferate and differentiate into myoblasts. Hepatocyte growth factor (HGF) induces activation of quiescent satellite cells in vivo. Also, HGF binding to its receptor, c-Met, leads to transcription of key myogenic regulatory factors, Myf-5 and MyoD.The response of satellite cellsto HGF is variableand dependent on time and concentration, although published results are inconsistent. Previous studies have not standardised initial conditions prior to interventions, thus complicating comparisons and conclusions. Therefore, it is still somewhat unclear whether HGF treatment may have a role in regenerative medicine. The aim was to determine the time and concentration dependent effects of HGF on satellite cells in vitro by analysing key myogenic regulatory factor gene expression and protein levels after first standardising myoblast characteristics. Primary human myoblasts (PHMs) explanted from human muscle biopsies were expanded and stocks frozen. Stock PHMs were defrosted, proliferated and placed in specialised media for 10 days to synchronise. PHMs were then characterised using multicolour flow cytometry and cell cycle analyses to elucidate their differentiation vs. quiescence status prior to intervention. Intervention with rh-HGF included 4 conditions: 2 different concentrations and 2 different durations. The myogenic regulatory factors, Myf-5 and MyoD were analysed using Western blotting, while their mRNA expression levels were analysed using qPCR.

Effects of 10 d culture in specialised media: PHMs maintained viability and an undifferentiated morphology. Muliticolour flow cytometry analyses of satellite cell markers indicated that 98% of PHMs remained positive for CD34 confirming their undifferentiated state. Activation and proliferation markers CD56 and Ki-67, decreased from 26% to 2% and from 85% to 46%, respectively. While Myf-5 expression remained constant (~98%) for this period, MyoD expression dropped from 20% to 9%. Cell cycle progression was reduced: The percentage of G1-phase cells increased from 58% to 87%, while S-phase cells dropped from 42% to 10%. The majority of PHMs were thus deemed quiescent. Effects of treating quiescent PHMs with rh-HGF: Treatment lead to significant ($p<0.0001$) time (24 h and 48 h) and concentration (2 ng/mL and 10 ng/mL) dependent increases in endogenous HGF protein. c-Met receptor content increased significantly ($p<0.01$) only with exposure to high dose HGF (10 ng/mL) within 24 h. MyoD mRNA expression decreased (~2 to 3-fold) with all HGF conditions, however Myf-5 mRNA expression did not decrease significantly in any treatment or time point. MyoD protein decreased only after 48 h in both HGF concentrations, compared to untreated control, while Myf-5 did not decrease significantly in any treatment or time point. These data confirmed time and concentration dependent effects of HGF on myoblasts. More specifically, stable baseline conditions allowed elucidation of HGF's different extent of effect on MyoD and Myf-5 expression. Finally, the dose-dependent effects on MyoD and Myf-5 also differed at protein level, indicating that myogenic regulatory factors do not respond uniformly to HGF.

3D PRINTING FOR ENGINEERING COMPLEX TISSUES

John P. Fisher

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The generation of complex tissues has been an increasing focus in tissue engineering and regenerative medicine. With recent advances in bioprinting technology, our laboratory has focused on the development of platforms for the treatment and understanding of clinically relevant problems ranging from congenital heart disease to preeclampsia.We utilizestereolithography-based and extrusion-based additive manufacturing to generate patient-specific vascular grafts, prevascular networks for bone tissue engineering, dermal dressings, cell-laden models of preeclampsia, and bioreactors for expansion of stem cells. Furthermore, we have developed a range of UV crosslinkable materials to provide clinically relevant 3D printed biomaterials with tunable mechanical properties. Such developments demonstrate the ability to generate biocompatible materials and fabricate diverse structures from natural and synthetic biomaterials. In addition, one of the key challenges associated with the development of large tissues is providing adequate nutrient and waste exchange.By combining printing and dynamic culture strategies, we have developed new methods for generating macrovasculature that will provide adequate nutrient exchange in large engineered tissues. Finally, the use of stem cells in regenerative medicine is limited by the challenge in obtaining sufficient cell numbers while maintaining self-renewal capacity. Our efforts in developing 3D-printed bioreactors that mimic the bone marrow niche microenvironment have enabled successful expansion of mesenchymal stem cells by recapitulating the physiological surface shear stresses experienced by the cells. This presentation will cover the diverse range of materials and processes developed in our laboratory and their application to relevant, emerging problems in tissue engineering.

MSC / PDEC interaction: a requirement for a functional beta cell in an injured adult pancreas

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The islet, the endocrine portion of the pancreas, develops from an invagination of the pancreatic duct epithelial cells (PDECs) into the surrounding tissue. The contact of the PDECs with mesenchymal cells (MSCs) may be an essential drive for endocrine cell fate. During pancreatic development, cells that express Neurogenin-3 (Ngn3) biomarker are precursors of insulin producing beta cells. These precursors have been reported in the neogenesis of islets from adult tissues following the surgical ligation of the main pancreatic duct (PDL). But the capacity of these precursors to induce the appropriate signals to complete the entire neogenesis program has been questioned. We studied the fate of co-culture of PDECs and MSCs from the ligated adult pancreas and established the exact location of adult stem- or progenitor-like cells that give rise to beta cells. PDECs were cultured in direct contact with or without MSCs in serum-containing culture media. The cytomorphology of the cells in co-cultures was determined and the immunocytochemical study of the cells was carried out using anti-Ngn3, anti-Insulin and anti-cytokeratin-7 (CK7) antibodies. Both the PDEC/MSC- and PDEC/MSC+ cultures showed out pocketing from duct epithelium by the end of the second week, which are distinct as cell clusters only in PDEC/MSC+ cells later in week four, exhibiting numerous branching ducts. Co-expression of Ngn3 with insulin was observed in both cultures from the second week. However, characterizations of these Ngn3+ cells in the PDEC/MSC+ culture revealed that these cells also co-expressed a CK7 biomarker. This study provides new evidence of the ductal epithelial nature of beta cells in injured adult pancreas; and that the mesenchymal stromal cells are required to sustain Ngn3 expression for beta cell maturation and function.

An approach to establishing a comparative index by comparing primary myoblasts of two subjects in vitro.

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Primary cells are isolated from live beings. Humans or animals may have different physiological states or may have adapted differently to living conditions prior to tissue harvesting and cell isolation. This may cause variability in the primary cells isolated from different individuals even with no experimental intervention. It is therefore important to understand individual variability and yet, no clearly defined protocols exist to assess primary cells' characteristic behaviour in vitro. When performing in vitro experiments, during which cells are exposed to treatments that affect the cellular function at the genomic and protein level, a key aspect that influences their responses may be the timing of treatment. This study aimed to establish a baseline method with which primary human myoblasts can be compared to each other. Since cells in vitro go through cell cycle phases (G1, S, G2 and M), we hypothesised that a useful "Comparative Index" could use the phase as a marker and an objectively quantifiable parameter as a comparator. Since the highest amount of mRNA for downstream application can be isolated after G1, we targeted the "S" phase of the cell cycle.

Primary human myoblasts (PHMs) isolated from skeletal muscle biopsies of two young and healthy male subjects were compared: S6 and S9. PHMs were allowed to migrate off incubated explants of the biopsies for the initial harvesting. Incubation was done 3 times for S6 resulting in a stock of PHMs called S6.3, whereas one incubation was sufficient to harvest PHMs from S9, resulting in a stock called S9.1. Subsequently these stocks were defrosted. 500,000 cells were plated in "proliferation media" prepared with Ham's F10 at intervals of 2 hours for 2 to 24 hours of subsequent culture. Once harvested cells were counted using an automated cell counter (Countess, Invitrogen, USA) and 250,000 cells were taken for mRNA isolation and the rest were used for cell cycle analysis using flow cytometry (FACSAria, Becton Dickinson Biosciences, USA) and propidium iodide staining (BD Cell cycle kit). After lysing myoblasts with Tripure, RNA was isolated using a kit (High Pure, Roche, Switzerland) and quantified using Nanodroplite (Thermofischer, Germany). Comparing the different timepoints, "S6.3" had the highest number of cells (~23%) in "S" phase at 22 hours. With respect to mRNA, the highest concentration of mRNA was also isolated at the 22-hour timepoint (8848 ng). In contrast, "S9.1" did not attain a peak proportion of cells in "S" Phase between 2 and 22 hours, as we could see even at the 24-hour time point the proportion of cells in the S phase was still increasing. mRNA content was 7780 ng at 22hr. This preliminary study sought to establish a protocol to use as a comparative index for primary human myoblasts taken from frozen stocks. The preliminary data suggests that S9.1 cells have a slower rate of proliferation compared to S6.3 and this difference indicates that the method developed was able to distinguish between the two myoblast stocks

Kolaviron shows anti-proliferative effect and down regulation of Vascular Endothelial Growth Factor-C and Toll like Receptor-2 in Wuchereriabancrofti infected blood lymphocytes

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The anti-proliferative effect and down regulation of vascular endothelial growth factor C and toll like receptor-2 by kolaviron on Wuchereria-bancrofti infected peripheral blood lymphocytes were investigated. Blood was collected from consenting volunteers in Talatamafara, Nigeria, between the hours of 10pm to 12am, and microscopically identified for microfilariae. Wuchereriabancroftipositive samples were cultured for 72 hours with Doxycycline (2µg/ml) and kolaviron (5µg/ml) in vitro. The mitotic index, expression of vascular endothelial growth factor-C (VEGF-c), and toll like receptor- 2 (TLR-2) were determined using standard procedures. The mitotic index was significantly ($P<0.05$) reduced in the kolaviron treated group compared to negative control. Kolaviron also significantly ($P<0.05$) down regulated the expression of VEGF-c and TLR-2 when compared to the untreated group. In both cases, the effects of kolaviron was not significantly different ($P<0.05$) to that of doxycycline. Furthermore, strong positive correlations between the mitotic index, VEGF-c and TLR-2 expressions were observed.The study suggests that kolaviron rich portion of Garcinia kola exhibited anti-proliferative effect and down regulation of VEGF-c and TLR-2 in Wuchereriabancrofti infected blood. Thus, the results from this study might have unravelled the potency of kolaviron in the management of complications associated with lymphatic filariasis.

Evaluation of Antimicrobial activities of extract from PyrenacanthagrandifloraBaill.

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Microbial drug resistance has reached the level of a crisis with the emergence of multi-drug resistant bacterial organisms. This has led to the search for new antimicrobial compounds and plants are considered as one of the most promising sources for new antimicrobials. Despite the relatively small area ofthe Venda region of South Africa, medicinal plants such as Pyrenacanthagrandiflora are used widely for the treatment and management of diarrhea, gastrointestinal related infections,dysentery, inflammation and tooth pain. The goal of our research was to evaluate the antimicrobial efficiency of P. grandiflora tubers against fifteen bacterial and eleven fungal strains.

Plant extracts were obtained using five solvents separately: Boiled andcold water, methanol, dichloromethane, chloroform and ethyl acetate. The hole-plate assay was used for initial evaluation of antimicrobial properties of plant materials. Minimum inhibitory concentrations (MIC) of the most active plant extracts were determined by the broth microdilution method. The hole-plate assay revealed that the highest antibacterial activity (18 mm zone of growth inhibition)was against Micrococcus kristinae with the ethyl acetate extract. The MIC of all the plant extracts showed antimicrobial activity against all test strains at a range of 0.06-7.5 mg/ml. All extracts showed positive results in Minimum fungicidal concentration (MFC)testing and hot water extract appeared to be more active against Cryptococcus neoformans with the MFC value of 0.06 mg/ml. The methanol extract also showed to be active against most test strains includingCandida tropicalis with the minimum fungicidal concentration value of 3.75 mg/ml. The antimicrobial activity of Pyrenacanthagrandifloratubers vary with test strain and the type of solvent used for extraction. This study providessome scientific evidence that this plant could be useful in the treatment of certain diseases as is currently practiced in the Venda communities. Further studies are needed to identify active constituents as well as the toxicity of the extracts. We plan to combine the extract with nano-particles to further increase the activity of the extracts of this plant and improve its delivery.

STEM CELLS AND TISSUE ENGINEERING

SESSION PRSENTATIONS AND POSTERS

SATURDAY, JULY 29, 2017

13:30-16:00
CHAIRPERSONS:

Prof. Samie Amidou: University of Venda,Thohoyandou, South Africa
Dr Venant Tchokonte-Nana: Stellenbosch University, South Africa

Degeneration and Repair of Rotator Cuff Muscle after Tendon Tear

Johnna S. Temenoff

Coulter Department of Biomedical Engineering, Georgia Tech and Emory University, Atlanta, GA, USA

Tears to the rotator cuff tendons result in degenerative changes to the attached muscle, primarily due to muscle unloading. After tendon tear, increasing fibrous and fatty infiltration, along with overall muscle atrophy, can be observed, which may not be corrected even after reattachment of the tendon, and can lead to lack of functional recovery for patients. We have recently adopted a rat model of massive rotator cuff tear in our laboratory. Histological, biochemical, and cellular changes to the muscle and tendon after tendon transection were characterized. Subsequently, delivery of stromal-derived factor-1-releasing micro-particles to the muscle were undertaken to modulate local recruitment of cells after injury. Such an approach may represent an effective strategy to encourage endogenous repair of muscle after rotator cuff tears.

Development Oo Sdf-1 Alpha Gene-Activated Collagen Chondroitin Sulfate Scaffold for Angiogenic Therapy of Chronic Wounds

Ashang Luwang, L.[1,4]Raftery, R.M,[1] O'Brien, F.J, [1,2,3] Keogh, M.B[4].

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Wound healing strategies involving biomaterial scaffolds often fail due to core cell necrosis caused by a lack of neovascularisation. Within our lab, a collagen glycosaminoglycan scaffold with high porosity and controlled pore size has been developed (1, 2). Stromal derived factor-1 alpha (SDF-1α) is a chemokine of high therapeutic interest for chronic wound healing, as it is known to play a major role in the migration, recruitment, and retention of circulating endothelial progenitor cells and contributes to neovascularization. However, exogenous supplementation of recombinant proteins in tissue regeneration is limited by their relatively short half-life, degradation by proteases and the time-dependent nature of cell homing to the site of injury (3). Non-viral gene therapy can be used to manipulate cells to function as local factories for sustained production of growth factors. The incorporation of genes within a 3D biomaterial scaffold, a gene-activated scaffold, is being increasingly explored as a platform for enhancing the therapeutic effects of biomaterial scaffolds. (4). Such a scaffold is expected to act as a depot for genes while simultaneously offering structural support and matrix for tissue ingrowth (5). The objectives of this study were to use polyethyleneimine (PEI) as a vector to deliver plasmid DNA (pDNA) encoding SDF-1α to mesenchymal stem cells in 2D monolayer and within a 3D collagen glycosaminoglycan (Coll-GAG) scaffold. Conditioned media from these cells was then used to assess the vessel-forming ability of human umbilical vein endothelial cells (HUVECs).

Branched PEI was mixed with 2μg of SDF-1α pDNA to yield a polyplex with N/P ratio of 10. The polyplexes were added to MSCs in monolayer or soak-loaded onto freeze-dried coll-GAG scaffolds to produce gene-activated scaffolds. Rat MSCs were expanded to at passage 5 before use in both 2D and 3D transfection studies. Protein expression was quantified using SDF-1α specific ELISA. Conditioned media from transfection culture was used to assess tubule-forming ability by HUVECs on Matrigel. Rat MSCs transfected with PEI-pSDF-1α produced the highest amount of SDF-1α protein on day 3, which decreased gradually with time. Conditioned media derived from the 3rd day of culture in 3D was found to promote significantly higher tubule formation by HUVECs as compared to non-transfected control. The gene-activated scaffold developed in this study represents a promising therapeutic approach for promoting angiogenesis and skin repair. The specific binding of the locally produced SDF-1α proteins to CXCR4 receptors on the cells are expected to trigger a myriad of signalling events and facilitate in the wound repair process in vivo (6). Ongoing experiments focus on assessing mature vessel formation in 3D scaffolds both in vitro and in vivo.

Identification of wild legume-derived lectins that could enhance burn wound healing

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Lack of adequate power supply has led to rural Africa having the highest number of paediatric burn injuries. Scarring that occurs during burn wound healing in children causes severe acceptance challenges in school and playground settings. Given the resource constraints of Zimbabwe's health systems, which cannot afford cutting edge regenerative medicine therapies, there is need to seek frugal innovations that solve intractable health problems using natural resources. Wound-healing is a complex process that needs to be manipulated so that the process is regenerative rather than scar-forming. Traditionally, natural products such as honey, Aloe vera and other plant extracts have been widely used in the treatment of wounds but validation of efficacy is lacking. The aim of the project is to identify, purify and characterize mitogenic and anti-inflammatory lectins from Zimbabwean wild legumes and to investigate the effect of these carbohydrate-binding proteins on the growth pattern of skin keratinocytes in 2D and 3D cultures. Our approach uses methods in regenerative medicine by culturing keratinocyte stem cells in the laboratory as models that allow us to safely and ethically test efficacy of different compounds and analyse results using growth curves and migration experiments. We will build on preliminary studies which identified two lectins from wild legume seeds; the Pterocarpusangolensis mannose-specific and the Bauhinia petersianagalactose-specific lectins, to investigate their effect on the growth pattern of keratinocyte cell cultures

POSTERS:

Poster 1
Regulation of neural differentiation in induced pluripotent stem cells using a hybrid microfluidic system

Zahra Hesari

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A valuable design in organ replacements and directing tissue regeneration necessitates controlling cellular orientation, proliferation and differentiation. In the current investigation, we developed a hybrid microfluidic system to produce a dynamic microenvironment by placing aligned PDMS microgrooves on surface of biodegradable polymers as physical guidance cues for controlling the neural differentiation of human induced pluripotent stem cells (hiPSCs). The capacity of cultured hiPSCs for neuronal differentiation in the microfluidic system and other control groups was investigated using quantitative real time PCR (qPCR) and immunocytochemistry. The functionally of differentiated hiPSCs inside hybrid system's scaffolds was also evaluated on the rat hemisected spinal cord in acute phase. Implanted cell's fate was examined using tissue freeze section and the functional recovery was evaluated according to the Basso, Beattie and Bresnahan (BBB) locomotor rating scale. Our results confirmed the differentiation of hiPSCs to neuronal cells on the microfluidic device where the expression of neuronal-specific genes was significantly higher compared to those cultured on the other systems such as plain tissue culture dishes and scaffolds without fluidic channels. Although survival and integration of implanted hiPSCs did not lead to a significant functional recovery, we believe that combination of fluidic channels with nanofiber scaffolds provides a great microenvironment for neural tissue engineering, and can be used as a powerful tool for in-situ monitoring of differentiation potential of various kinds of stem cells.

Poster 2
Generation of iPSCs from long-term cryopreserved human neonatal fibroblasts in feeder-free condition and their comprehensive characterization

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A new approach for pluripotent stem cell generation is the attempt to induce conversion of the adult somatic cells into induced pluripotent stem cells (iPSCs) by introducing specific transcription factors. iPSCs have two essential biological properties, they are pluripotent and possess long term cell-renewal capacity. Additionally, iPSCs can be derived from patient-specific somatic cells, thus bypassing ethical and immunological issues. The aim of our study was to reprogram long-term cryopreserved human neonatal fibroblasts by method using lipid nano-particle technology in combination with Epi 5 reprogramming vectors. The obtained iPSCs were characterized by several sophisticated methods of molecular biology and microscopy. Distinct colonies of iPSCs started to appear by day 20 after reprogramming. The presence of iPSCs colonies was shown by alkaline phosphatase (AP) live staining. After manual picking the colonies and their subsequent passaging, they did not lose the ability to form embryoid bodies; they were positive for AP, Tra-1-60, and SSEA-5. Moreover, the obtained iPSCs expressed pluripotency markers Oct4, Sox2 and Nanog, and the expression levels of chondrogenic, osteogenic and adipogenic markers were significantly higher in comparison to control ($p < 0.05$). In summary, we have demonstrated that long-term cryopreserved human neonatal fibroblasts can be reprogrammed into iPSCs and after further analysis concerns on their biological safety they may be used as patient-specific cells in regenerative medicine.
Supported by grant APVV no. 14-0032.

Poster 3
Regeneration of myocardial cells using mesenchymal stem cell derived exosome

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The application of mesenchymal stem cells (MSCs) in regenerative medicine has been broadly studied over the last decades. Cardiovascular diseases are the leading cause of morbidity and mortality with nearly half resulting from myocardial infarction (MI). Due to modern medicine and surgery the mortality rate has declined. However, regeneration of cardiac cells are limited and inadequate to functionally regenerate damaged heart tissue. Cardiac cells present throughout the infarction site die rapidly due to apoptosis and the microenvironment surrounding the damaged site is not promising for cell survival and renewal. The molecular mechanism of how ischemic myocardium initiates repair and remodelling are known by the secretion of soluble factors playing a major role in communication to distant tissues such as bone marrow. The regeneration of cardiac cells based on MSCs are considered as one of the most promising candidates for reducing tissue injury, protection of tissues from further adverse effects and enhancing tissue repair through paracrine activity by trophic factors with diverse properties. The regenerative capacity of MSCs has been focused on the ability that these cells would differentiate and replace damaged cardiac cells through direct cell-to-cell interaction. Recently, actively secreted membrane vesicles derived from mesenchymal stem cells, such as exosomes are being recognized as new candidates for cardiac regeneration effects.

Poster 4
Potential therapeutic effects of Eucomisautumnalis aqueous extracts on the proliferation and differentiation of porcine adipose derived mesenchymal stem cells

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Articular cartilage defects are common, causing significant pain and morbidities. So far, tissue engineering techniques using mesenchymal stem cells offer a promising modality for cartilage repair. In this study, the potential for Eucomisautumnalis aqueous extracts to induce the differentiation of porcine adipose-derived mesenchymal stem cells (pADMSCs) into chondrocytes was investigated.

Porcine MSCs were harvested and isolated from adipose tissue and grown up to passage 0. The prepared cells were treated with E. autumnalis aqueous extracts and transforming growth factor (TGFβ3) in vitro. The cells were then examined microscopically and also stained with safranin O and toluidine blue to observe their growth and morphology. Gene expression analysis was also used to assess chondrogenic differentiation. The results showed that the cell viability and proliferation of ADMSCs was unaffected on day one and three. However, a significant increase in cell viability and proliferation of ADMSCs was evident on day seven. Interestingly, the porcine ADMSCs were observed to have firstly attached to the surface before proliferating. The results also revealed that E. autumnalis aqueous extracts and TGFβ3 were able to induce chondrogenesis of ADMSCs as observed in the morphology of the resultant cells. The resultant cells upregulated gene expression of SOX 9 and at the same time downregulated gene expression of collagen type II and X.

These findings suggest that porcine ADMSCs could differentiate into chondrocyte-like cells driven by the plant extracts. These results show the potential role that E. autumnalis could play towards cartilage regeneration and repair.

Poster 5
The role of Capparis separia crude extracts in porcine articular cartilage

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The plant Capparissepiaria known as Himsra in Ayurveda is a profusely branched woody climber that belongs to the family Capparidaceae. It has been reported to possess various properties such as anti-inflammatory, analgesic, blood purifier, cardiotonic and used in the management of liver disorder, as a treatment for skin diseases, tumours and inflammation. Nevertheless, there are no reports on the efficacy of C. sepiaria in the management of osteoarthritis (OA), which is a degenerative joint disease. OA decreases overall quality of life, is a major cause of pain, morbidity, activity limitation and represents a substantial financial public health burden. Given the nature of OA, a long lasting treatment will likely be essential to arrest or slow its progression. Therefore there is an urgent need for drugs with good efficacy and low toxicity that can regenerate or repair articular cartilage. The present study is set out to address the role of C. Sepiaria on tissue engineering of articular cartilage. Articular chondrocytes were isolated from superficial and middle zone of the porcine knee, cultured as monolayers in serum free chemically defined medium overnight. After cells have attached the media was changed to serum-free DMEM/F-12 medium with insulin transferrin selenium and treated with different concentrations (5, 15, 30, 50 and 100 µg/ml) of C. Sepiaria root extracts and TGF-β1 (3 ng/ml) for four days. Morphological observations were performed under an inverted light microscope for both surface and middle zones. DNA was measured using CyQuant cell proliferation assay. The results showed that cells treated with 5, 30 and 100 µg\ml in surface zone were growing adherently in a healthy status like the positive control TGF-β1, while for middle zone only 50 and 100 µg\ml were growing. In CyQuant assay, a significant increase in cell proliferation was evident for 30µg/ml and 5µg/ml in surface and middle zone, respectively. In conclusion, C. sepiaria root extracts induced the proliferation of chondrocytes and thus it is not toxic in both surface and middle zone of the porcine articular cartilage.

Poster 6
Preparation and characterization of polyamidoamine drug conjugates containing ferrocene and platinum analogues

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Polymer drug conjugates are a promising drug delivery technology useful for alleviating the problems of toxicity and drug resistance of the currently used chemotherapeutic drugs.In the current study, polyamidoamine drug conjugates containing ferrocene and platinum analogues were prepared using Michael addition polymerization. The drug conjugates were characterized by Fourier transform infrared (FTIR) spectroscopy, H1 NMR, scanning electron microscopy (SEM), transmission electron microscopy TEM and EDX. The techniques showed successful preparation of the conjugates though the degree of drug conjugation varied as indicated by EDX and AAS data. The drug conjugates are currently being evaluated for cytotoxicity activity on HeLa and breast cancer cell lines.

Poster 7
Wharton's Jelly-Derived Mesenchymal Stromal Cells and Fibroblast-Derived Extracellular Matrix Synergistically Activate Apoptosis in a p21-Dependent Mechanism in WHCO1 and MDA MB 231 Cancer Cells In Vitro

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The tumour microenvironment plays a crucial role in tumour progression and comprises tumour stroma which is made up of different cell types and the extracellular matrix (ECM).Mesenchymal stromal cells (MSCs) are part of the tumour stroma and may have conflicting effects on tumour growth. In this study we investigated the effect of Wharton's Jelly-derived MSCs (WJ-MSCs) and a fibroblast-derived ECM (fd-ECM) on oesophageal (WHCO1) and breast (MDAMB 231) cancer cells in vitro. BothWJ-MSCs and the fd-ECM, alone or in combination, downregulate PCNA, cyclin D1, Bcl-2, Bcl-xL, and MMPs and upregulate p53 and p21. p21 induction resulted in G2 phase cell cycle arrest and induced apoptosis in vitro. Our data suggest that p21 induction is via p53-dependent and p53-independent mechanisms inWHCO1 andMDA MB 231 cells, respectively. Vascular endothelial growth factor, Akt, and Nodal pathways were downregulated in cancer cells co-cultured with WJ-MSCs. We also demonstrate that WJ-MSCs effects on cancer cells appear to be short-lived whilst the fd-ECM effect is long-lived. This study shows the influence of tumour microenvironment on cancer cell behaviour and provides alternative therapeutic targets for potential regulation of tumour cells.

Poster 8
Apigenin compound on different zones of porcine articular cartilage

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Apigenin (AP) is a flavonoid commonly isolated from plants such as chamomile, parsley and celery. It has compelling anti-inflammatory, anti-oxidant properties and has a potential to prevent and treat arthritic disorders and also inhibits the release of cartilage degradative enzymes resulting in osteoarthritis, of which have been proven in experiment models. The aim of this study was to investigate the effects of AP on superficial and middle zone of porcine articular cartilage.

Porcine stifle joints, obtained from local abattoir were dissected aseptically. The superficial zone cartilage slices of the femoral condyles were harvested using a dermatome and middle zone slices were removed using a custom cutting jig. Dissected cartilage wasdigested with 0.2 % collagenase-P and released chondrocytes were cultured as monolayer for xCELLigence (Days 1, 4, 7 and 11) and MTT proliferation assays (Days 1, 4 and 7), reverse transcriptase PCR (qRT-PCR) for gene expression (Days 4 and 7); as well as micromass culture for CyQUANT cell proliferation (Days 1, 4 and 7), glycosaminoglycan assay (Day 14), histology and immunohistochemistry (Day 21) in a serum free, apigenin treated medium at 5, 10, 20, 50 and 100 µM.

Apigenin significantly stimulated chondrocyte proliferation in both superficial and middle zones of porcine articular cartilage enormously at 5, 20 and 50 µM based on MTT assay, CyQUANT assay with an increase from day 1 to 7, collagen type II immunolocalization (immunohistochemistry) and histology analysis. xCELLigence showed more proliferation on superficial zone than middle zone. Glycosaminoglycan assay revealed more GAG content at 5 & 10 µM AP concentrations on both AC zones and at 100 µM on middle zone. On chondrocyte qRT-PCR assay, gene expression was observed prominently on day 4 compared to day 7, which suggests a decrease in gene expression after a week of chondrocyte incubation. This study revealed the importance of apigenin in the proliferative ability of chondrocytes at different concentration, in different zones ofporcine articular cartilage.

Poster 9
Herbal scaffolds in stem cell therapy: Differentiation of porcine adipose derived stem Cells.

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The significance and the potential of in vitro cell culture studies are great considering the need for more cost efficient development of new drugs, time efficient treatment of cancer patients, and an understanding of developmental biology and mechanisms of stem cell differentiation. Cells, growth factors and scaffolds are the fundamental issues for tissue engineering. If porcine derived adipose stem cells (pADSCs) can effectively proliferate and differentiate when cultured on a herbal scaffold, it will be a potential candidate for an in vivo environment with possible profound impact on therapeutic application of herbal scaffolds. This study evaluated the in vitro differentiation capacity and anti-inflammatory effect of fabricated herbal scaffolds on pADSCs. To this effect, herbal scaffolds were developed by incorporating medicinal plant extracts (Eucomisautumnalis and Pterocarpusangolensis) and natural biopolymers (Alginate and chitosan) using a lyophilization technique. A standard sterility test on the scaffolds before in vitro use showed the ultraviolet radiation with 75% (v/v) ethanol to be suitable. pADSCs cultured on the herbal scaffolds were further monitored for in vitro proliferation and differentiation using different biological, immunological and genetic techniques. The identity of pADSCs were confirmed by positive FACs analysis of mesenchymal stem cell surface markers CD44, CD90 and CD105 (≥ 85%). Their multi potency was further evaluated by trilineage differentiation of pADSCs toward adipocyte, osteoblast and chondrocyte with immunostaining. Scanning electron microscope (SEM) revealed that the herbal scaffolds possess an extremely porous structure than control (non-herbal scaffold). Protein content was found to be significantly high in P. angolensis scaffold at day 1 to day 21 than in E. autumnalis and non-herbal scaffold. SEM and immunofluorescence results also revealed more attachment of cells at day 7, 14 and 21 on herbal scaffolds than non-herbal scaffolds. Expression of TNF alpha, IL-6 with ELISA assay and gene expression of collagen type 11, SOX9 and glycociaminoglycans (GAG) with RT-PCR will confirm the anti-inflammatory nature and mRNA expression/chondrogenic nature of the pADSCs cultured on the herbal Scaffolds. This study indicates that pADSCs would have great therapeutic potential as seeding cells for in vivo transplantation to treat various inflammatory diseases and bone injuries when co-applied with medicinal plants, chitosan/alginate bio-scaffolds.

Poster 10
Hexanoyl- and acetyl-glycol chitosan derivatives for functional pancreatic islet cell spheroid

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Pancreatic islet transplantation has considered as a tremendous strategy for the treatment of type 1 diabetes mellitus, providing insulin independence to patients. However, clinical success of islet transplantation is limited due to donor insufficient, immune response, and hypoxic stress after implantation procedure. Particularly, the oxidative stress is a major obstacle to long-term islet survival. About 70% of transplanted islets undergoes oxidative stress one day after transplantation because transplanted islets lose their own vasculature and revascularization requires more than two weeks. This hypoxia induces the apoptosis in the centers of islets due to their relative large size (80~300 μm). Therefore, generating small size of islets is important to prevent nutrient- and oxygen-deprived states. In this study, we present a novel, potent method to generate islet spheroid using hexanoyl glycol chitosan (HGC) and acetyl glycol chitosan (AGC). In brief, 24 well-plate was coated by AGC (5%) and trypsinized islet single cell was cultured in AGC-coated dish with a HGC (0.5%) supplementation. The results demonstrated that small size (31 nm) of islet cluster was generated in AGC-coated dish with a HGC supplementation while relative large size (96 nm) of islet cluster was formed in untreated control dish. In addition, this small size of islets shows good insulin secretion ability, however, islets totally lost their function in the control group. Taken together, we newly developed the technology that can generate functional, small islets. This technique would enable successful islet transplantation by suppressing the hypoxia-induced rejection of islet grafts.

Poster 11
Evaluation of the antioxidant, cytotoxicity and anti – HIV activities of four commonly used Venda medicinal plants and their formulations.

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Medicinal plants form an important part of the Southern African cultural heritage. Indigenous populations, for example the Vha-Venda people, tend to use medicinal plants in formulations rather than western medicines for health and survival. The present study was aimed at assessing the antioxidant and cytotoxicity activities of four Venda medicinal plants and their formulations and to assess the anti –HIV activity of the medicinal plant formulations

Peltophorumafricanum (roots), Pterocarpusangolensis (bark), Terminaliasericea (roots) and Ximeniacaffra (roots) were collected from the Thohoyandou area. The collected plant parts were extracted with methanol and water, respectively. From the Individual plant extracts, five formulationswere designed per solvent used. All the plant extracts and their formulations (a total of 18) were assessed for their abilityto scavenge free radical 1, 1-diphenyl-2-picrylhydrazyl (DPPH) using a spectophotometer. The toxicity of the 18 plant samples was against human lymphatic endothelial cells (HLEC) was determined using the CellTiter 96 Non-Radioactive Cell Proliferation Assay. All 10 plant formulations were assessed for their anti-HIV activity using the Reverse Transcriptase Colorimetric Assay kit. All plant extracts and formulations exhibited good antioxidant activity against DPPH and the methanolic formulation showed the best antioxidant activity with IC50of 0.094 ± 0.33µg/ml. Some extracts showed toxicity, such as the aqueous X. caffra, mixture 2 which inhibited 26% and 51% of the cells at 12.5mg/ml and 3.125mg/ml, respectively. Peltophorumafricanum and mixture 5 inhibited 34%, 54% and 43% toxicity at 3.125mg/ml, 6.25mg/ml and 12.5 mg/ml respectively against Human Lymphatic Endothelial cells growth. For anti- HIV inhibition, all formulations at 200µg/ml exhibited higher percentage of HIV-1 reverse transcriptase inhibition with methanolic mixture 3 being the best overall at 97.5% activity whilst aqueous mixture 5 was the least active with 63.03% inhibition activity. Moreover, the best anti-HIV activity at 100µg/ml was exhibited by methanolic mixture 3 at 71% inhibition.The results from the study indicated that thecertain formulations were more effective indicating potential synergistic effect of the plants. They showed good antioxidant activities, and good cell proliferation activities and good anti-HIV activities. The low toxicity of these mixtures is an important findings that should guide the design of more efficient product for the control of certain infectious and non-communicable diseases.

Poster 12
Plants today drugs tomorrow: Cordia grandicalyx a possible future anti–hypoglycaemic?

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The use of medicinal plants has evolved over the years and human kind has depended on them for treatment and management of diseases. Dependence on plants is mainly due to the fact that they contain phytochemical compounds of interest, some of which have been used for development of several drugs now in the market. This has led to a belief that plants have a potential to be used as possible future drugs. Inflammation is the body's response mechanism to protect itself against any harmful pathogens or stimuli and thus initiation of a healing process, but can also cause damage to tissues or cells. Diabetes mellitus and cancer are some of the diseases known to be related to inflammation.

Plants were collected in Mashishimale village and 2g of plant leaves were extracted in 20ml of different solvents polarities viz; deconcoction (water), acetone, ethyl acetate, chloroform and n-hexane. Glucose uptake assay, Glut 4 translocation and cytotoxicity assay were analysed using the C2C12 and Vero monkey cells. Based on the results it was observed that C. grandicalyx resulted in the decrease of glucose concentration in medium and the water extracts demonstrated no stimulation of Glut-4 translocation though it demonstrated good antioxidant activity. The findings that aqueous extracts had no good activity, does not support their traditional uses in treating diabetes, but efficacy cannot be ruled out since promising activity was observed with both glucose uptake and antioxidant activity. The findings indicate that either C. grandicalyx regenerates the membrane of the cells or either uses a different mechanism to improve uptake of glucose by the cells. The findings of the study indicate that studies of this nature are useful and guide in screening of plants for discovery of compounds. Furthermore, the identity of the active ingredients may be important to establish the mechanisms used by this plant.

Poster 13
Comparison of osteogenic capacity of OSTA MaxigroTM and OSTA RegigroTMin C2C12 myoblast cell line.

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Bone defects are the most common problems encountered in clinical orthopaedic practice and they often result from trauma, malignant disease, fractures and prostatic replacement. Currently, research is focused on developing bio-ceramics with morphological structure like that of normal bone to promote bone regeneration. OstaMaxigro™ and OstaRegigro™ collected from OSTA Technology South Africa, are natural bone minerals which were derived from a bovine extract resulting in a highly purified mineral structure which is comparable to that of human bone. This study set to establish how high surface area bio-ceramics (greater than 80 m2 area) differentiate into the bone regeneration process compared to lower surface area bio-ceramics.To facilitate the use of OSTA MaxigroTM and OSTA RegigroTMfor bone regeneration, an experiment was performed using C2C12 myoblast cells to determine their proliferation rate when treated with OSTA MaxigroTM and OSTA RegigroTM. 5x104 cells/mlof C2C12 wereculturedin a 24 well plate in a medium of Dulbecco's modified Eagle's medium /F-12 (DMEM/F12 with Pen/Strip and Fungizone), supplemented with heat inactivated 10% foetal bovine serum (FBS) (Life Technologies) and 1% Antibiotic cocktail (Penicillin and Fungizone) (Life Technologies). After24-hours of incubationat 37°C in a 5% CO2 atmosphere,attachment and about 80% cell confluence was obtained.Cells were then treated with(3mg\ml, 5mg\ml and 10mg\ml) concentrations of OSTA RegigroTM in a media containing1% FBS in triplicates. After 2, 4 and 8 days of incubation, cells were assayed for cell viability and proliferation using Trypan Blue exclusion test andcell morphology was observed with an inverted Leica DM IL LED light microscope (Leica microsystems, Switzerland). The results showed that cells treated with 5mg\ml were proliferating adherently in a healthy status higher than that of the positive control. In conclusion, OSTA RegigroTM induces higher C2C12 proliferationrate as compared to BMP-2 as a control.

Poster 14
Analysis of different biomaterial as Scaffolds in bone tissue engineering

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In tissue engineering for larger bone defects the use of mesenchymal stem cells has to be combined with the use of scaffold materials .The culture of multipotentmesenchymal stem cells on natural biopolymers holds great promise for treatments of connective tissue disorders in human and Veterinary medicine. However, the safety and performance of such therapies relies on the systematic in vitro evaluation of the developed stem cell-biomaterial constructs prior to invivo implantation. This study evaluated two biomaterials; B30 (70% silica+ 30% collagen) andB30Sr20 (50% silica+ 30% collagen, 20% strontium) a biocompatible composite polymer, as a scaffold for adipose mesenchymal stem cells (MSCs) for application in bone tissue engineering.The quality of biomaterials was measured by analyzing cell adhesion ***(DAPI staining)*** and cell proliferation ***(MTT assay)*** in conjunction with the scaffold materials. Live cell imaging for cell viability (cell migration) after plating of the materials with cells in culture dishes were done using ***florescence microscopy.*** Cell morphology on the biomaterials was investigated using ***scanning electron microscopy***. Furthermore, osteogenic differentiations were tested by driving the cells into the osteogenic lineage using specific growth and differentiation factors. Osteogenic differentiation were analysed by detecting typical morphological changes, by specific staining procedures ***(Alizarin red method)*** as well as using molecular biological techniques ***(qualitativePCR)***.The biomaterials characterized using scanning electron microscopy (SEM) demonstrated that only B30 induced fiber bundling of cells. Furthermore B30 were shown to be-cytocompatible, supporting cellular adhesion, and allowed for osteogenic differentiation ofMSCs under pellet culture than fluid shear stress culture. No significant differences were observed in proliferation potential for cells seeded either with B30 or B30Sr20 in both culture conditions. Generally, it could be concluded that cells on the B30 scaffold were viable and metabolically more active than B30Sr20 and culturing the MSCs with B30 under pellet culture condition has shown more promising results than in fluid shear stress. These findings demonstrate that the combination of a B30 (silica-collagen-xerogels) and MSCs are promising constructs for bone tissue engineering applications

Poster 15
Entamoeba in South Africa: correlations with the host Microbiome, parasite burden and first description of E. bangladeshi outside of Asia.

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A high prevalence of Prevotellacopri is a biological marker of a symptomatic Entamoebahistolytica infection. The goal of this work was to verify this Asian finding in a S. African population and to examine the association of this biological marker with other related Entamoeba species common in our study population. A comprehensive assay was used which included probes to identify E. bangladeshi, first described in Bangladesh, which had not previously been described outside the Asian continent.A total of 484 stool samples were collected between November 2013 to June 2015 (rural=227) and (urban=257), from both diarrheal and non-diarrheal participants. DNA was extracted and a highly sensitive qPCR assays and amplicon sequencing of selected samples were used to detect and quantitate Entamoebaspp, Prevotellacopri and Enterobacteriaceae. Approximately 27% (n=129) of the collected study samples were positive for Entamoeba species. The prevalence of E. histolytica was 6.4% (31/484), E. dispar 8% (38/484), and E. bangladeshi 4.5% (22/484) (co-infections accounted for 2.3% (11/484) of the cases). Up to 10% (49/484) of samples were not initially identified at the species level by the qPCR assay. The amplicons of 34 of the 49 unassigned Entamoeba were purified and sequenced. Of these 10 were E. histolytica (adjusted prevalence 8.5%) and one E. bangladeshi (adjusted prevalence 4.75%) the remainder proved to be derived from E hartmanni (2.6%), which was not discriminated against by the Entamoeba genus probe.Entamoeba moshkovskii was not identified in this population. A high parasite burden and expansion of the P. copri level was associated with diarrhea due to E. histolytica. Entamoeba bangladeshi, first discovered in an urban cohort in Bangladesh, was identified in urban and rural S. African settings. This is the first description of E. bangladeshi outside of Bangladesh. We were also able to observe changes in the host microbiome and the parasite burden associated with E. histolytica infections in S. African diarrhea cases versus infected asymptomatic controls but not with E. bangladeshi or the non-pathogenic E. dispar.

Cancelled Speakers Abstracts
Bio-functional Surface and Materials for Regenerative Medicine

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Biomaterials have been developed in regenerative engineering to perform multiple functions including rapid expansion of stem cells, delivery of therapeutic cells or drugs, or endogeneous induction of cell/tissue response upon implantation. Although synthetic biodegradable materials have been widely used in regenerative medicine, they are mostly hydrophobic and showed poor interactions with cells and native tissue. Therefore, many efforts have been made to develop bio-functional materials that can exhibit chemical, physical, biological, and structural characteristics similar to those of native extracellular matrix (ECM) milieu. ECM is composed of a number of biomacromolecules including structural as well as functional proteins, glycosaminoglycans, and proteoglycans, which are assembled together to form complex 3-dimensional network. Furthermore, the 3-dimensional network sequesters soluble factors by affinity-based binding, which are released under activated conditions such as wound healing and tissue repair. Cells are bound to these ECM components, which in many cases, are implicated in critical cell fate process such as adhesion, proliferation, differentiation, and survival. In this presentation, the discussion will be focused on our approaches to develop cell-interactive bio-functional surfaces and materials for modulation of cell function, which can be used as direct implantable scaffolds for induction of tissue regeneration or as a substrate for delivery of cell sheet.

Bioengineering of Direct Cellular Reprogramming

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Direct cell reprogramming or transdifferentiation, where adult cells are reprogrammed from one lineageto another without going through an intermediate stem cell-like stage, produces cells promising for regenerative medicine. It obviates the use of embryos and minimizes the risk of teratoma formation associated with the in vivo application of induced pluripotent stem cells. Direct reprogramming can also produce cells for disease modelling and drug screening. I will discuss our recent effort to convert human endothelial progenitors (hEPC) into induced smooth muscle cells (iSMC),hEPC into induced skeletal myocytes (iSkM),human fibroblasts into induced cardiomyocyte-like cells (iSML), and murine fibroblasts into induced neurons (iN). I will describe various approaches of achieving direct cell reprogramming using transcription factor overexpression, microRNA delivery, molecular pathway manipulation, and CRISPR/dCas9-based transactivation either separately or in combination. This will be presented from the perspective of how biomaterials and biomedical engineering researchers can help advance this exciting field.

Microspheres / hydrogel composites for tissue engineering applications

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Hydrogels are important biomedical materials for cell delivery and associated tissue engineering applications. However, the use of hydrogels for regeneration of certain tissues, such as bone, has been hampered by the mass depletion of cells after encapsulation, due to the lack of a proper interface between hydrogel matrices and osteo-progenitor cells. Efforts to graft bioactive molecules as cell attachment moieties have achieved limited success, and novel strategies are greatly demanded to meet the challenges arising from different fields of regenerative medicine. In this study, we report two gel-based composite systems, namely hydrogel / microcarrier (GC) and hydrogel / nanoaggregate (GN) hybrids, which work as a suspension of injectable cell-laden microcarriers or nanoaggregates in hydrogel. Our in vitro and in vivo investigations show that these injectable microscopic anchors not only provide platforms for cellular focal adhesion but also facilitate the cells to overcome gel entrapment and fully spread out into their native morphology. Such hydrogel composites could be competent vehicles for the conveyance of anchorage-dependent cells (ADCs) and regeneration of bone and other tissues. Our study has provided a solution for the settlement and commitment of ADCs in hydrogels. First, we have addressed the importance of anchorage-dependence to the delivered ADCs in 3D environment, and elicited that the lack of integrin ligation to "cellular anchors" is responsible for cell apoptosis in conventional 3D hydrogel. Second, we have found that GC system could facilitate both survival and differentiation of osteo-progenitor cells, while maintaining their favorable spread morphology in hydrogel matrices. Third, we have demonstrated a hydrogel/nanoaggregate composite for therapeutic cell delivery, in which potential cytotoxicity of nanoparticles could be effectively prevented by confining the nanoaggregates with hydrogel encapsulation, while, reversely, these functional nanoaggregates managed to promote delivered ADCs to maintain high viability and favorable spreading morphology in the system. Both GC and GN models presented preserve all the advantageous features of hydrogels as cell vehicles/scaffolds, and combine unique advantages of microcarriers and promising features of nanoparticles, respectively. In the future, we expect to see GC, GN or similar models being expanded to various applications of regenerative medicine, wherever the mass transfer of therapeutic anchorage-dependent cells are in great demand.

Hexanoyl- and acetyl-glycol chitosan derivatives for functional pancreatic islet cell spheroid

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Pancreatic islet transplantation has considered as a tremendous strategy for the treatment of type 1 diabetes mellitus, providing insulin independence to patients. However, clinical success of islet transplantation is limited due to donor insufficient, immune response, and hypoxic stress after implantation procedure. Particularly, the oxidative stress is a major obstacle to long-term islet survival. About 70% of transplanted islets undergoes oxidative stress one day after transplantation because transplanted islets lose their own vasculature and revascularization requires more than two weeks. This hypoxia induces the apoptosis in the centers of islets due to their relative large size (80~300 μm). Therefore, generating small size of islets is important to prevent nutrient- and oxygen-deprived states. To do that, in this study, we present a novel, potent method to generate islet spheroid using hexanoyl glycol chitosan (HGC) and acetyl glycol chitosan (AGC). In brief, 24 well-plate was coated by AGC (5%) and trypsinized islet single cell was cultured in AGC-coated dish with a HGC (0.5%) supplementation. Results demonstrated that small size (31 nm) of islet cluster was generated in AGC-coated dish with a HGC supplementation while relative large size (96 nm) of islet cluster was formed in untreated control dish. In addition, this small size of islets shows good insulin secretion ability, however, islets totally lost their function in the control group. Taken together, we newly developed the technology that can generate functional, small islets. This technique would enable successful islet transplantation by suppressing the hypoxia-induced rejection of islet grafts.

Advances in Tissue Engineering Ceramic Scaffolds and Bone Surrogates using 3D Printing

David Prawel Ph.D.

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Additive manufacturing (a.k.a. 3D Printing) is a revolutionary technology that has only recently exploded into the global vernacular, after decades of pioneering work in research labs and corporate R&D centers. It is already playing a huge role in nearly all aspects of science, technology, and industry. Like many technologies, it is fascinating, engaging, and powerful. Unlike many technologies, 3D printing is truly improving lives, and transforming the way we do research and think about tissue engineering and regeneration. For more than two decades researchers have been using viscosity extrusion methods to create countless forms of tissue engineering scaffolds. Powder sintering and binder-jetting methods emerged to address early challenges and have advanced the field yet further. More recently, photopolymer-based solutions are showing promise in tissue engineering, as material choices and the demand for higher accuracy increase, while the cost of these devices decreases. In this session, I will present an overview of the most common 3D printing methods for tissue engineering ceramic scaffolds and bone surrogates. I will discuss the latest research and some of our research activities in this area.

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