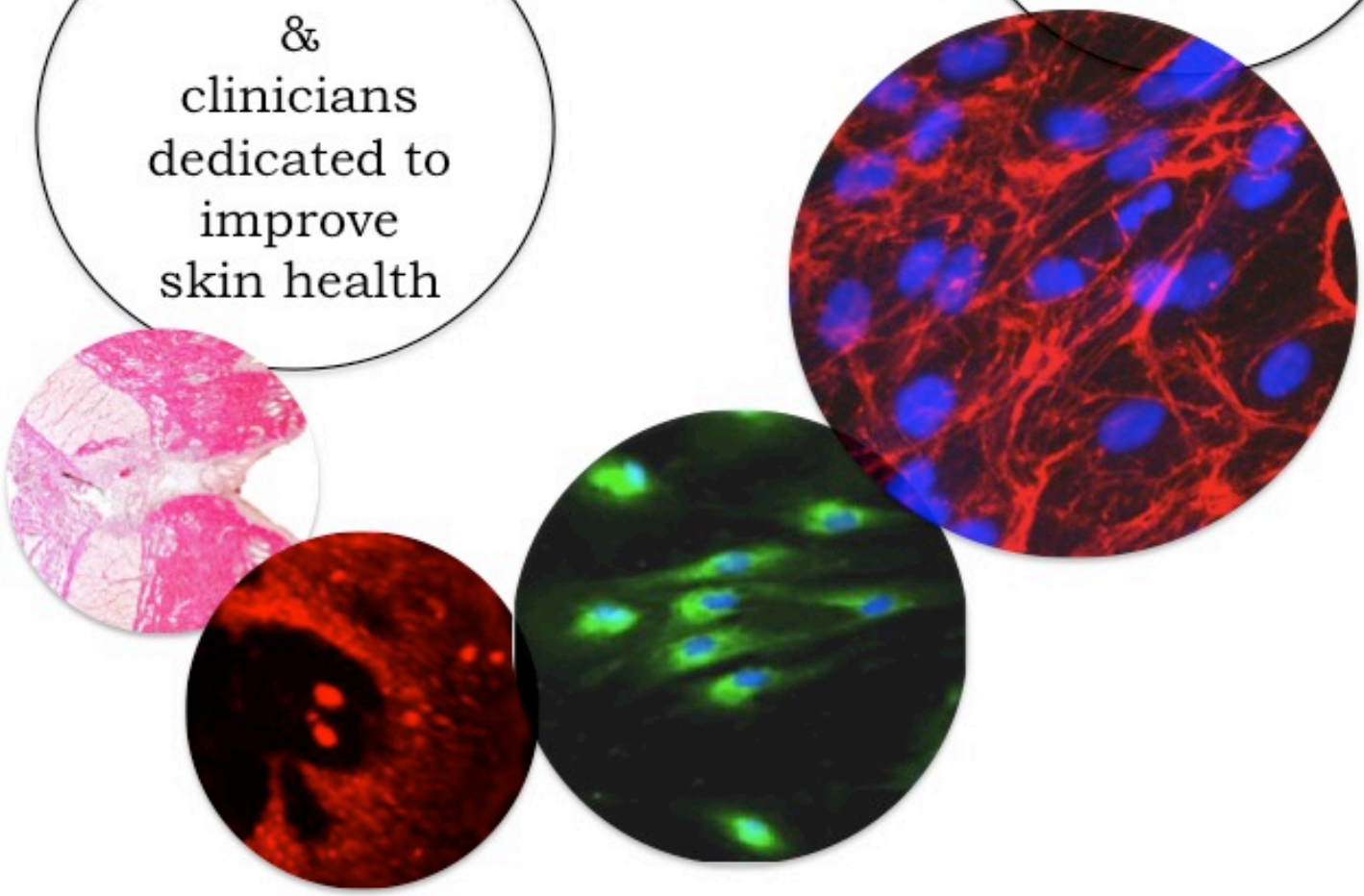
Skin Research Group Canada

4th Annual Symposium

May 17 – 18, 2017 | Montreal, QC

PROGRAM
&
ABSTRACTS

Researchers
&
clinicians
dedicated to
improve
skin health



https://www.skinresearchgroup.org

Dear Skin Research Group Symposium Participants,

Welcome to the 4th annual Skin Research Group Canada (SRGC) symposium 2017.

It is our pleasure to welcome you all to Montreal for the SRGC symposium hosted at the McGill New Residence Hall in Montreal, Quebec, on May 17-18, 2017. The SRGC represents a multidisciplinary group of new and established investigators from basic and clinical research disciplines, who are focused on skin repair, healing and restoration.

The SRGC symposium is the premiere annual meeting for scientists and clinicians interested in skin tissue healing and repair in Canada and provides an excellent forum for them to interact and exchange knowledge and ideas and network with patient groups and industry partners. This year's symposium features speakers from across Canada and cover current hot topics in the field of skin basic and clinical research. It also encourages and recognizes the work of young scientists, postdoctoral fellows, and graduate students in the field of skin research by providing them the opportunity to present their work at scientific sessions. Prizes will be awarded for best trainee oral and poster presentations.

The SRGC 2017 organizing committee members look forward to seeing you all in Montreal in May 2017!

Anie Philip
Conference Co-Chair

Stéphane Roy
Conference Co-Chair

ORGANIZING COMMITTEE

Anie Philip, PhD (co-chair)
Professor
Department of Surgery
McGill University

Stéphane Roy, PhD (co-chair)
Professor
Faculties of Medicine and Dentistry
University of Montreal

Boris Hinz, PhD
Professor
Laboratory of Tissue Repair and Regeneration, Matrix Dynamics Group
Faculty of Dentistry
University of Toronto

Veronique Moulin, PhD
Professor
Department of Surgery
LOEX
Université Laval

Dieter P. Reinhardt, PhD
Professor
Faculties of Medicine and Dentistry
McGill University

Kenneth Finnson, PhD
Research Associate,
Department of Surgery
McGill University

LOCAL ORGANIZERS

Fadi Sader

Jean François Denis

Muthu Lakshmi Muthu

Rongmo Zhang

Heena Kumra

Joseph Di Paolo

Shufeng Zhou

Faegheh Ghanbari Divshali

Emily Buck

Rayan Fairag

JUDGING COMMITTEE

ORAL PRESENTATIONS

Aziz Ghahary, PhD (Chair)
Director of BC Professional
Firefighters' Burn and Wound Healing Research Group

Saeid Amini Nik, MSc, MD, PhD
University of Toronto
Sunnybrook Research Institute

Andrew Leask, PhD
Schulich School of Medicine & Dentistry
Western University

Anie Philip, PhD
Department of Surgery
McGill University

QUICK-SHOT PRESENTATIONS

Veronique Moulin, PhD (Chair)
LOEX, Université Laval

Dieter P. Reinhardt, PhD
Faculties of Medicine and Dentistry
McGill University

Boris Hinz, PhD
Faculty of Dentistry
University of Toronto

Stéphane Roy, PhD
Faculties of Medicine and Dentistry
University of Montreal

POSTER PRESENTATIONS

Francois Berthod, PhD (Chair)
Laval University

Julie Fradette, PhD
LOEX Division of Regenerative Medicine
CHU de Québec Research Centre-Université Laval

Kenneth Finnson, PhD
Department of Surgery
McGill University

Denis Jean-François, PhD
Faculties of Medicine and Dentistry
University of Montreal

EVENT PROGRAM	
Wednesday, May 17	
5:00pm - 6:00pm	**Registration and poster setup**
6:00pm - 7:00pm	**Cocktails/ Reception & Poster viewing**
7:00pm - 7:15pm	**Welcome Remarks** *Anie Philip, McGill University, Montreal, QC* *Stéphane Roy, University of Montreal, Montreal, QC*
7:15pm - 8:30pm	**Representatives from Patient support groups.**
7:15pm	**"**Canadian Skin Patient Alliance and Research Initiatives" **Kathryn Andrews-Clay** Executive Director/Directrice générale Canadian Skin Patient Alliance/Alliance canadienne des patients en dermatologie Canadian Association of Psoriasis Patients/Association canadienne des patients atteints de psoriasis
7:30pm	"Canadian Association of Psoriasis Patients and Research Initiatives" **Morris F Manolson** Board member/Membre du conseil d'administration Canadian Skin Patient Alliance/Alliance canadienne des patients en dermatologie Canadian Association of Psoriasis Patients/Association canadienne des patients atteints de psoriasis Professor and Associate Dean of Graduate and Post Graduate Studies at the Faculty of Dentistry, University of Toronto
7:45pm	**Marie Hudson** Canadian Scleroderma Research Group (CSRG) Associate Director for Clinical Research, Lady Davis Institute Associate Professor, Department of Medicine, McGill University
8:00pm	**Sabrina Hanna** Directrice executive | Executive Director Fondation Sauve Ta Peau | Save Your Skin Foundation
8:15pm	"Burns: perspectives from past to present" **Sue-Ling Chang** Association des grands brûlés *F.L.A.M*
8:30pm – 9:00pm	**Panel Discussion** **Patient Group Representatives and Trainee**
Thursday, May 18	
8:00am - 8:30am	**Light Breakfast and Registration**
8:30am - 8:45am	**Welcome Remarks** ***Anie Philip**, McGill University, Montreal, QC* ***Stéphane Roy**, University of Montreal, Montreal, QC*

8:45am – 10:30am	**Plenary Session 1** *Moderators: Dieter P. Reinhardt and François Berthod*
Invited Speakers:	
8**:45am**	"Can Immune Cells Become Skin Cells In Large Skin Injury?" ***Aziz Ghahary**, Director of BC Professional Firefighters' Burn and Wound Healing Research Group, Vancouver, BC.*
9:15am	"CCN1 Expression By Fibroblasts Is Required For Dermal Fibrosis And Melanoma Metastasis" ***Andrew Leask**, University of Western Ontario, London, ON.*
Trainee Presentations:	
9:30am	"An Innervated And Vascularized Immunocompetent Tissue-Engineered Skin To Study Cutaneous Neuroinflammation" ***Quentin Muller**, CNRS, LOEX, Université Laval, Québec, QC.*
9:40am	"Acellular Dermal Matrix Modulates Phenotype Of Adipose-Derived Stem Cells As A Treatment For Chronic Wounds" ***Reza Jalili**, ICORD, University of British Columbia, Vancouver, BC.*
9:50am	"Role Of Microfibrillar Protein Interactions In ECM Assembly And Function" ***Heena Kumra**, McGill University, Montreal, QC.*
10:00am – 10:15am	COFFEE BREAK
10:15am – 12:00am	**Plenary Session 2** *Moderators: Andrew Leask & Veronique Moulin*
Invited Speakers:	
10:15am	"Why Do We Care So Much About The Skin In Scleroderma? Isn't This A Systemic Disease?" ***Murray Baron**, Jewish General Hospital, Montreal, QC.*
10:45am	"Myeloid Cells Steer Mesenchymal Stem Cells Into The Wound Bed: A Mechanism For Elderly's Deficient Healing" ***Saeid Amini Nik**, Sunnybrook Research Institute, University of Toronto, ON.*
Trainee Presentations:	
11:00am	"Mimicking Cutaneous Melanoma Microenvironment Using Tissue-Engineered Skin" ***Jennifer Bourland**, LOEX & Universite Laval, Quebec, OC.*
11:10am	"Comparative Study Of Cell Source On The Functional Characteristics Of Human Reconstructed Connective Tissues Engineered Under Serum-Free Conditions" ***Meryem Safoine**, LOEX, Université Laval.*
11:20am	"A Salamander-Derived Protein (Sdp) As An Inhibitor Of TGF-β Signaling And Fibrotic Responses" ***Ahmed Al-Qattan**, McGill University, Montreal, QC.*

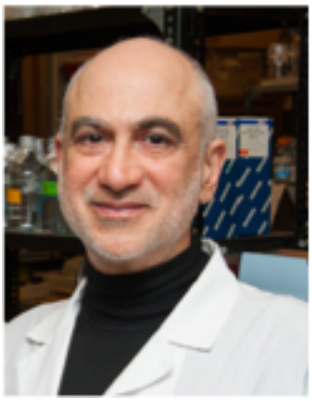
Trainee Quick-shot Presentations:	
11:30am	"Electrospun Polyurethane-Gelatin Scaffolds for Manufacturing Skin Substitute" ***Mohammadali Sheikholeslam**, Sunnybrook Research Institute, University of Toronto, ON.*
11:35am	"Comparison of Loading Methods of an Antibiotic in Electrospun PLGA Fibers" ***Emily Buck**, Materials Engineering, McGill University*
11:40am	"Anti-Bacterial Efficacy Of Silver Doped Sol-Gel Derived Borate Glass For Wound Healing Applications" ***Shiva Naseri**, McGill University**,** Montreal, QC.*
11:45am	"Development Of A Serum Free Medium Optimized For Human Epithelial Cell Culture" ***Sergio Cortez Ghio**, Université Laval & LOEX, Québec, QC.*
11:50am	"A Surgical Device to Study the Efficacy of Bioengineered Skin Substitutes in Mice Wound Healing Models" ***Andrea-Kaye Datu**, Sunnybrook Research Institute, Toronto, ON**.***
11:55am – 1:00pm	LUNCH BREAK
1:00pm – 2:10pm	**Plenary Session 3** *Moderators: Aziz Ghahary and Julie Fradette*
Invited Speakers:	
1:00pm	"Role of PARP1 in solar UVB-induced non-melanoma skin cancers" ***Girish Shah**, CHU de Québec, Université Laval, Québec, QC.*
1:30pm	"Building Innovative Wound Care Technology" ***Yunghan Au,** Swift Medical, Montreal, QC.*
Trainee Quick-shot Presentations:	
1:45pm	"Exosomes In The Acellular Wharton's Jelly Of The Human Umbilical Cord Enhances Skin Wound Healing" ***Nazihah Bakhtyar**, Sunnybrook Research Institute, Toronto, ON.*
1:50pm	"Cellular microRNA Regulation By Fibrillin-1 And Fibronectin Is Mediated Through Integrins" ***Rongmo Zhang**, McGill University, Montreal, QC.*
1:55pm	"FBLN4 And LTBP4 Cell Receptor Interactions" ***Hana Hakami**, McGill University, Montreal, QC.*
2:00pm	"Pullulan/Gelatin Scaffold: An Ideal Niche For Skin Regeneration" ***Nan Cheng**, Sunnybrook Research Institute, Institute of Medical Science, University of Toronto, ON.*
2:05pm	"Targeting TGF-β Pathway In Squamous Cell Carcinoma By CRISPR/ Cas9-Mediated Genome Editing" ***Shufeng Zhou**, McGill University, Montreal, QC.*
2:10pm – 2:30pm	COFFEE BREAK

2:30pm – 3:00pm	**Plenary Session 4** *Moderators: Saeid Amini Nik and Kenneth Finnson*
Invited Speakers:	
2:30pm	"Wound Healing Clinical Cases and Basic Science Concept Application to Clinical cases " ***Lucie Lessard**, McGill University, Montreal, QC.*
2:45pm	"Successful Treatment Of Atrophic Facial Leishmaniasis Scars By CO2 Fractional Laser" ***Huma Khurrum**, King Saud University, Riyadh, Saudi Arabia.*
3:00pm –3:15pm	**"Skin Research Group Canada: Past, Present and Future"** ***Anie Philip**, McGill University, Montreal, QC* ***Stéphane Roy**, University of Montreal, Montreal, QC*
3:15pm – 4:15pm **4:15pm**	**Panel Discussion:** *Invited Speakers, Trainees, Patient and Industry Representatives, Faculty.* **CONCLUDING REMARKS** by ***Andrew Leask**, University of Western Ontario, London, ON.*
4:30pm	**AWARD PRESENTATIONS**

INVITED SPEAKERS' BIOGRAPHIES

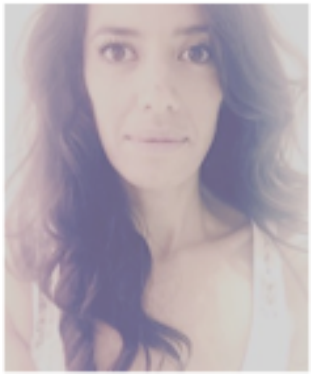
Mrs. Kathryn Andrews-Clay has worked with the Canadian Skin Patient Alliance (and the Canadian Association of Psoriasis Patients) as Executive Director since March 2015. Kathryn brings years of experience at the Senior Management level in both the public and voluntary health sectors. Prior to this role, Kathryn was a Director General at the Canadian Institutes of Health Research – last two years as Director of Institute Affairs and previously the Director of Partnerships & Citizen Engagement.

At CIHR, she led the very successful Institutes Model Review on behalf of the Governing Council in 2014 and won a Leadership Award for her commitment to collaborative and ethical partnerships in 2013. Kathryn was also the inaugural Executive Director of Leadership Ottawa, a program to develop community leaders at the local level. She has a wide range of skills including stakeholder engagement, financial management and strategic planning.



Dr. Morris F Manolson is a Professor and Associate Dean at the Faculty of Dentistry with a cross appointment in the Faculty of Medicine at the University of Toronto. His research focuses on preventing the excessive bone loss associated with osteoporosis, inflammatory arthritis and periodontal disease. In 2007, he received the "Quality of Life" award from the Institute for Musculoskeletal Health and Arthritis, and in 2008 he received the Canadian Institute of Health Research-Institute for Gender Health/Ontario Women's Health Council Senior Investigator Award, both in recognition of the importance of his work towards preserving bone health in arthritis and osteoporosis. He has served on grant and training scholarship reviewing committees for the Canadian Institute of Health Research and The Arthritis Society, was a member of the board of the Canadian Arthritis Network from 2007 to 2009 and served on the Scientific Advisory Committee for The Arthritis Society of Canada. His current research is funded by the Canadian Institute of Health Research and has produced three patent applications and over 50 peer reviewed papers, which have accumulated over 3000 citations from other refereed journals. He is currently a board member of the Canadian Association of Psoriasis Patients and of the Canadian Skin Patient Alliance.

Dr. Marie Hudson is a rheumatologist, epidemiologist, and Assistant Professor in the Department of Medicine at McGill University. She is a physician-scientist and member of the Center for Clinical Epidemiology and Community Studies at the Jewish General Hospital. She is a fellow of the Royal College of Physicians of Canada and is funded as a New Investigator by the Canadian Institutes of Health Research (CIHR).



Mme. Sabrina Hanna is the Executive Director of the Save Your Skin Foundation, a Canadian based patient advocacy group dedicated to skin cancer. Advocating on behalf of patients to promote an increasing awareness of melanoma and its treatment, Save Your Skin Foundation offers clear, qualified information across Canada. Sabrina works to bring accountability to process' directly impacting patients' lives and to facilitating education and preventative action programs within the organization. Sabrina graduated from Concordia University, in Montreal, with a Bachelor's of Science in Exercise Science. After receiving her B.Sc. she earned a certificate in public relations. Sabrina has dedicated her career to the not-for profit sector, beginning her professional career working in research at the Jewish General Hospital, and prior to joining the team at the Save Your Skin Foundation, served as the Director of Communications for the Dean of Libraries at McGill University in Montreal. She has been with the Save Your Skin Foundation since 2014.

Mme. Sue-Ling is a burn survivor. When she was 3 years old, a kitchen accident left various parts of her body scalded requiring several skin grafts. Since this accident occurred in South America during the seventies, at the time, support services for patients and families were inexistent which impacted the way her family dealt with the event. Because of this experience, she is passionate about optimizing patient care and supporting loved ones.

She currently serves as volunteer, and board member for the Association des Grands Brûlés F.L.A.M., an association based in Quebec City, that provides support to burn victims and loved ones. She collaborates on various projects and grants looking to optimize quality of life for all burn survivors.

Dr. Aziz Ghahary received his Ph.D in Medical Physiology from the University of Manitoba in 1988 and after 2 years as post - doctoral training, he accepted an assistant professorship position in the Department of Surgery at the University of Alberta in 1990. He was then promoted to associate and full professor in 1996 and 2003, respectively. In 2005, he was then, recruited by the Department of Surgery/ Plastic Surgery as a full professor and the director of the BC professional Firefighters' Burn and Wound Healing Research Group. During the last 12 years, 14 Ph.D. and 5 master students have been successfully graduated from his lab.

Funding and publications: Dr. Ghahary has been awarded more than 52 research grants from local, national and international granting agencies. He is one the well-funded investigator in UBC. He has published or co-published over 185 peer reviewed articles, presented over 220 abstracts and major presentations at national and international conferences.

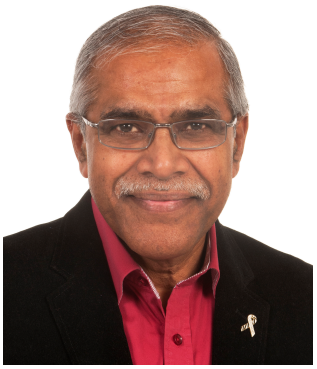
Discovery and Patents: Dr. Ghahary has 7 patents from which one is related to a protein called stratifin also known as 14-3-3 sigma. He then found a very high level of eta isoform of 14-3-3 protein in sera of patients with rheumatoid arthritis. This biomarker has now been patented and licensed to the biggest diagnostic company in US and Canada, Quest Diagnostic and Lifelab, respectively. The early RA diagnostic test called JOINTstat, is now available in Canada and US. This has been approved for diagnosis in Europe, Australia, Japan and New Zealand.

Dr. Murray Baron is the chief of the Division of Rheumatology at the Jewish General Hospital, where he has practiced since 1981. He graduated from McGill University's Faculty of Medicine and, after stints as a family doctor in Newfoundland and British Columbia, trained in internal medicine at the University of British Columbia and rheumatology at the University of Toronto. He is a Professor of Medicine at McGill University.

He runs a division with five full-time academic rheumatologists. Dr. Baron's primary research interest is in an uncommon rheumatic disease called scleroderma. In this disease, there is fibrosis of multiple organs leading to severe morbidity and increased mortality. Because the disease is rare, Dr. Baron has established the Canadian Scleroderma Research Group (CSRG). Over 15 rheumatologists from across Canada see patients once a year and enter a large amount of data into a central database. Biological specimens, such as blood and skin, are also collected. Research is performed on the data by clinical researchers at McGill and elsewhere, and on the bio-specimens at multiple laboratories that Dr. Baron has brought into his group.

In addition, Dr. Baron has established the International Systemic Sclerosis Inception Cohort (INSYNC). This new research group will focus attention on recent onset scleroderma to be able to better appreciate what happens from very early on in the disease.

Dr. Baron is the current president of the Scleroderma Clinical Trials Consortium, a body representing most of the world's clinical scleroderma researchers.



Girish M. Shah, Ph.D. Professor, Laval University, Faculty of Medicine

Senior Researcher, CHU de Quebec Laval University, Laboratory for Skin Research and Axe Neurosciences and Oncology, Quebec (QC), Canada

Dr. Shah's research is focused on identifying genetic and cellular factors that can influence the development of cancers or their resistance to therapy using two models of cancers, namely solar ultraviolet radiation-induced non-melanoma skin cancers (NMSC) and neuroendocrine tumors (NET).

For last 15 years, his team has identified novel roles of a nuclear enzyme poly(ADP-ribose) polymerase 1 (PARP1) in cellular responses to solar UVB-radiation induced non-melanoma skin cancers using cellular and animal models. His work resulted in identification of PARP1 as a key player in the removal of UV-induced DNA lesions in skin cells by the nucleotide excision repair pathway of DNA repair. His team has created a novel strain of albino hairless PARP1 knockout mice to study different pro-and anti-cancerous roles of PARP1 in UVB-induced skin cancers in mice.

His work on PARP1 in different cancers is supported over last two decades by various national agencies. He received an award for "Outstanding Achievement in Carcinoid/Neuroendocrine Tumor Research" in 2006 from the Carcinoid Cancer Foundation Inc. USA. More recently he has been serving on the Board of Directors and as a Chair of Scientific and Medical Advisory Board of Carcinoid Neuroendocrine tumor Society of Canada. His current research on the roles of PARP1 in neuroendocrine cancers is supported by the Canadian Cancer Society Research Institute and that on the roles of PARP1 in responses to UV radiation is supported by the Natural Sciences and Engineering Research Council of Canada through its Discovery and Discovery Accelerator Grants.

Dr. Lucie Lessard MD, CSPQ, FRCSC, FRCSC, FACS

Dr. Lessard is the Chief of the Division of Plastic and Reconstructive Surgery at the MUHC, McGill University, an Associate Professor and a Plastic Surgeon who specializes in Craniomaxillofacial surgery, trauma, cancer breast reconstruction and hand/microsurgery.

Dr. Lessard is a double board certified Royal College of Canada surgeon who has trained in Quebec as well as obtaining her specialty in Plastic Surgery at the Brigham and Women / Boston Children's Hospital Harvard under her great mentor Dr. Elof Ericsson and also trained in New York with Dr. Joseph MacCarthy.

She oversees both the pediatric and adult hospitals in a 9 hospital urban hospital centre and continues to work on the interface between craniofacial surgery and microsurgery to reintegrate disfigured patients (pediatric and adult, oncology and trauma) into society with her reconstructive skills.

Dr. Lessard is the head of BAHA/Ear Reconstruction for Congenital Problem at the Shriners Hosptial where she is the main Plastic Surgeon and has also developed a robust post-breast cancer breast reconstruction adult practice being the only female plastic surgeon in Canada at the chief level she has been sought out and has embraced this practice with extra sensitivity to the female form. Dr. Lessard excels and loves working on challenging problems with 3D solutions.

Simultaneously, Dr. Lessard has kept a basic sciences surgical research interest in surgical edema (rat model), craniofacial mandibular distraction osteogenesis and BMP bone morphogenetic proteins 2,4,7 (rabbit model) as well as wound healing basic sciences with TGF-beta.

Dr. Lessard is active as a teacher and participates fully in the training of all plastic surgery residents. She is the founding craniofacial surgeon and is the Director of the Post-Graduate Craniofacial Fellowship which began in 2010 and has been successful with fellows from all over the world.

Dr. Lessard has trained close to 100 residents in Plastic Surgery and continues to represent McGill nationally and internationally. She has been invited as Guest Speaker/Visiting Professor at the national and international level such as recent presentations at the Mayo Clinic (US), Kuwait, India, Brazil, and Saudi Arabia and Argentina.

Dr. Lessard is the first woman in a leadership position as a Chief of a Plastic Surgery Division in Canada and at McGill. She is a former President of the Group pour l'Avancement de la Microchirurgie (GAM) of the Canadian Society of Plastic Surgeons, is the current national delegate representing Canada for international matters voted by the Canadian Society of Plastic Surgeons (CSPS) board and was recently voted Chair of Education for the newly formed International Confederation of Plastic Surgery Society (ICOPLAST).

ORAL PRESENTATION
ABSTRACTS

Wednesday, May 17

Session: Representatives from Patient support groups

7:15 - 7:30pm

Title: Canadian Skin Patient Alliance and Research Initiatives
Kathryn Andrews-Clay
Executive Director/Directrice générale
Canadian Skin Patient Alliance/Alliance canadienne des patients en dermatologie
Canadian Association of Psoriasis Patients/Association canadienne des patients atteints de psoriasis

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This short presentation will introduce the role of the Canadian Skin Patient Alliance as it pertains to patient engagement and will highlight some recent projects that involved research. Kathryn will also touch on ways that patient groups and researchers can work together to bring patient perspectives to the research projects.

7:30 - 7:45pm

Title: Canadian Association of Psoriasis Patients and Research Initiatives
Morris F Manolson
Board member/Membre du conseil d'administration
Canadian Skin Patient Alliance/Alliance canadienne des patients en dermatologie
Canadian Association of Psoriasis Patients/Association canadienne des patients atteints de psoriasis
Professor and Associate Dean of Graduate and Post Graduate Studies at the Faculty of Dentistry, University of Toronto

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This presentation will build on the CSPA information and highlight the projects that CAPP has undertaken in the past few years. Morrie will highlight what he brings to the CAPP Board as a psoriatic arthritis patient and discuss the impact of skin research and new therapeutics on his personal life. He will talk about some of the student projects that CAPP funded last summer related to psoriatic diseases and how the organization is building on this initiative by adding a knowledge translation component as well as an open access policy. Here he will also present different ideas and examples of how patients can help skin researches.

7:45 - 8:00pm

Title: "TBA"
Marie Hudson
Canadian Scleroderma Research Group (CSRG)
Associate Director for Clinical Research, Lady Davis Institute
Associate Professor, Department of Medicine, McGill University

Abstract not available

8:00 - 8:15pm

Title: "TBA"
Sabrina Hanna
Directrice executive | Executive Director
Fondation Sauve Ta Peau | Save Your Skin Foundation

Abstract not available

8:15 - 8:30pm

Title: Burns: perspectives from past to present
Sue-Ling Chang
Association des grands brûlés F.L.A.M

Improvements in burn care have led to significant gains in survival. As the number of burn survivors increases, survivorship has become increasingly important. Therefore, programs that focus on this phase of the patient care continuum is becoming a priority. Although surviving a burn injury remains a major preoccupation for health professionals, burn survivors face a number of specific physical and psychological challenges that may significantly impact quality of life. Moreover, family members are often themselves traumatized by the events and are unequipped to deal with the aftermath.
The return to normalcy after a traumatic burn injury is a challenge but is possible. Sue-Ling Chang uses her own experience as a burn survivor and as a volunteer at a burn survivor association, to provide insight. She will discuss how the patient experience has evolved and what needs remain unmet.

Plenary Session 1

Keynote

8:45 - 9:15am

Title: Can Immune Cells Become Skin Cells In Large Skin Injury?

Y. Li, MD, PhD, RT. Kilani, Ph.D and **A. Ghahary, PhD**[1]

1 Director of BC Professional Firefighters' Burn and Wound Healing Research Group, Vancouver, BC

Introduction and Hypothesis: Upon any kind of dermal injury, keratinocytes and fibroblasts migrate from the edge of injury site to the wound site where they proliferate and promote wound healing. However, it is unlikely that these cells from the edges of large burn injury be able to migrate to a very long distance to cover the injury site. Here, we hypothesize that skin injury initiates a signal through which a subset of circulating immune cells become de-differentiated into stem like cells and these cells then become the major source of skin cells during the healing process.

Methods: The potential role of releasable factors from the proliferating fibroblasts on trans-differentiation of immune cells to multi-potent stem like cells was evaluated by culturing immune cells in fibroblast conditioned medium for 6 days. Cells were then examined for their morphology and the expression of a set of stem cell markers and their capacity to further differentiation into other cell types.

Results: The finding showed that culturing a subset of blood derived immune cells have the capacity to be de-differentiated into fibroblast like cells when co-cultured with proliferating fibroblasts. These cells were then identified to be fibroblast like cells with capacity to express a panel of stem cell markers such as alkaline phosphatase, formation of embryonic bodies, and expression of other pluripotent stem cells markers. Further, these cells showed a capacity to further differentiate into fibroblasts, osteocytes, adipocytes, smooth muscle cells, endothelial cells, neural cells. This finding was further confirmed in a mouse model by showing an easy detection of SSEA-1, a main marker for PSCs in wounded but not in normal tissues.

Conclusions: These data confirm that a subset of circulating immune cells have the capacity to become de-differentiated into PSCs within the wound environment and that these cells become the main source of skin cells in large wounds including burn. Applicability of Research to Practice: Identifying the factors responsible for conversion of immune cells to skin cells would make it possible to topically apply these factors to promote the healing and reduce inflammation in large burn injury.

Notes

Plenary Session 1

Invited Lecture

9:15 - 9:30am

Title: CCN1 Expression By Fibroblasts Is Required For Dermal Fibrosis And Melanoma Metastasis

Katherine Quensel[1], James Hutchenreuther[1], Krista Vincent[2], Lynne-Marie Postovit[2] and **Andrew Leask[1*]**

1. *Dentistry, University of Western Ontario*
2. *Oncology, University of Alberta*

Expression of the CCN family of matricellular proteins is dysregulated in fibroproliferative disorders. Previously we showed that fibroblast-specific expression of CCN2 (CTGF) is required for dermal fibrogenesis and melanoma metastasis. Herein, we show the related protein CCN1 (cyr61) is overexpressed in scleroderma active disease and in fatal melanomas (CCN1 expression negatively correlates with survival $p<0.007$ and with the extent of tumor stroma). Loss of CCN1 from fibroblasts results in progressive skin thinning correlating with reduced collagen protein. In skin from mice deficient in CCN1, production of collagen mRNA is not affected; however mRNA expression of genes collagen modifying enzymes (eg LOX, PLOD2 and P4H) is significantly reduced ($p<0,01$). Loss of CCN1 expression from fibroblasts results in resistance to bleomycin-induced skin scleroderma as visualized by induction of myofibroblasts, skin thickness and collagen levels ($p<-0.05$), Moreover, in a syngeneic model of melanoma metastasis. Loss of CCN1 expression from tumor stroma results in impaired metastasis to the lung ($p<0.01$), although tumor growth is unaffected. These results emphasize the fibrotic tumor stroma in playing an essential role in dictating the degree of metastasis of tumors. Also, our results stress the importance of CCN1 as a therapeutic target for fibroproliferative disease.

LAYMAN SUMMARY:

We want to develop therapies for fibrosis and melanoma. Our data suggest anti-CCN1 therapies might be used to block fibrosis and melanoma metastasis

Notes

Plenary Session 1

Trainee Presentation

9:30 - 9:40am

Title: An Innervated And Vascularized Immunocompetent Tissue-Engineered Skin To Study Cutaneous Neuroinflammation

Quentin Muller[1,2], Marie-Josée Beaudet[2], Evelyne Schaeffer[1], Christopher Mueller[1], François Berthod[2]# and Vincent Flacher[1]#

1. CNRS-UPR3572/LabEx Medalis « Immunopathologie et Chimie Thérapeutique », Institut de Biologie Moléculaire et Cellulaire, France;

2. LOEX, centre de recherche du CHU de Québec-UL, and Department of Surgery, Université Laval, Canada, # Equal contribution

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Background: Immune reactions in the skin are initiated by the cutaneous dendritic cells (DCs). The potential sensitizing effect of a compound can be predicted in vitro using human blood monocytes differentiated into DCs (Mono-DCs) or monocytic cell lines. However, these simplistic models remain inaccurate because the activation of cutaneous DCs by sensitizers may be triggered or modulated by microenvironmental interactions with multiple types of non-immune cells.

Objective: Our goal is to develop an immunocompetent tissue-engineered skin (TES) that will combine DCs with all structural and functional element of the skin, i.e. an epidermal barrier laid upon a dermis containing a network of endothelial capillaries and nociceptive nerve fibers.

Methods: Collagen-chitosan sponge were first seeded with fibroblasts and endothelial cells, then with precursors of nerve fibers derived from either human induced pluripotent stem cells (iPSC) or murine embryonic dorsal root ganglia (DRG). Finally, we introduced keratinocytes and Mono-DCs.

Results: We observed that in situ differentiated neurons grow axons towards the epidermis as usually observed in normal human skin what. What's more, the neurons derive from iPSC, express neuropeptides and calcium channel as normal nociceptive fibers. Moreover, Mono-DCs settled as expected beneath the epidermis and remained sessile for several weeks.

Conclusion: The model will be used to predict the irritant potential of chemical compounds, and the impact of nerves on DC activation. Further, the iPSC technology allows us to create a "one patient" TES with all cells from the same donor to start a personal medicine tool.

Notes

Plenary Session 1

Trainee Presentation

9:40 - 9:50am

Title: Acellular dermal matrix modulates phenotype of adipose-derived stem cells as a treatment for chronic wounds

Victoria McCann, Ali Farrokhi, Jasmine ZiJin Cheng, Aziz Ghahary, and **Reza Jalili***

**Professional Firefighters' Burn & Wound Healing Research Group, Division of Plastic Surgery, Department of Surgery, International Collaboration on Repair Discoveries (ICORD), University of British Columbia*

Chronic wounds contribute to increased morbidity and mortality and impose a significant financial burden on healthcare systems. The main goal of wound treatment is to achieve a rapid closure of the lesion and promote healing with minimal scaring. Extracellular matrix- based biomaterials such as acellular dermal matrices (ADM) are advantageous for treatment of chronic wounds due to their mechanical strength and retained biological activity when compared with synthetic polymer materials. Further recellularization of ADM with adipose-derived stem cells (ASCs) significantly increases its healing capacity. The aim of our study was to develop an ASC-populated ADM and assess its characteristics in vitro with the ultimate goal of promotion of wound healing. In this study, we introduced a novel method of de-cellularizing mouse skin and used this as an ADM scaffold to seed with human ASCs. We compared this 3D model to 2D ASC cultured at different time points. Combinations of positive (CD146, CD44, CD90, and CD73) and negative (CD31, CD34, CD45) markers were used as stem cell markers. Morphology and myofibroblast differentiation capacity of ASCs were also evaluated. Our results showed a significant reduction in expression of CD73 and CD44 in ASCs cultured on the 3D ADM compared to cells grown in 2D culture. We found that ASCs cultured under regular 2D conditions mainly shifted towards a myofibroblastic phenotype with increased myofibroblast marker α-smooth muscle actin (α-SMA), and ECM protein type I collagen. In contrast, ASCs cultured on ADM showed a more balanced differentiation pattern with maintenance of some stem cell markers such as CD146. Taken together, these findings show that ASC differentiation into myofibroblasts can be regulated by the 3D ADM. This ASC-ADM combination has good potential as a therapeutic approach to reduce fibrosis while maintaining the benefit of natural extracellular matrix wound coverage and the healing capacity of stem cells.

Notes

Plenary Session 1

Trainee Presentation

9:50 - 10:00am

Title: Role Of Microfibrillar Protein Interactions In ECM Assembly And Function

Heena Kumra[1]*, Valentin Nelea[2]*, Amelie Pagliuzza[1], Hana Hakami[1] and Dieter P. Reinhardt[1,2]

1 Faculty of Medicine and

2 Faculty of Dentistry, McGill University, Montreal, Canada

**Co-first authors*

Background: Elastogenesis is an intricate and well-orchestrated cellular mechanism which involves several extracellular matrix (ECM) proteins such as Fibulin-4 (FBLN4), Latent TGF-β binding protein-4 (LTBP4), Fibronectin (FN) and Fibrillin-1 (FBN1). These proteins play key roles in driving the assembly of tropoelastin into mature elastic fibers, which are essential for the elasticity of various soft tissues including skin and blood vessels.

Rationale: The aim of this study is to determine the structural and functional role of interaction of these ECM proteins in facilitating elastogenesis.

Methods and Results: Surface plasmon resonance spectroscopy (SPR) showed that recombinantly expressed LTBP4L (long isoform of LTBP4) and FBLN4 can each self-interact *in vitro*. Immunofluorescence demonstrated that both proteins assemble in cell culture. Deletion of FN using fibroblasts from *Fn* knockout mice disrupts the assembly of FBLN4 and LTBP4. To analyze if the dependency of FBLN4 and LTBP4 on FN is direct or is dependent on other ECM proteins which require FN for their assembly, fibroblasts from *Fbn1* knockout mice were utilized. Knocking out *Fbn1* (FN assembly is still intact) disrupts the assembly of LTBP4 but not of FBLN4. This data shows direct dependency of FBLN4 on FN for its assembly, whereas LTBP4 requires FBN1 which in turn is dependent on FN for its assembly. Next, we observed by SPR that FBLN4 interacts with LTBP4. This interaction induced an unexpected conformational change in the structure of LTBP4, as revealed by atomic force microscopy. Furthermore, this conformational change triggered an increased binding of LTBP4 to FBN1 but a decreased binding to FN, as shown by solid phase assays. Immunofluorescence analyses revealed that the conformational change in LTBP4 induced by FBLN4 also affected LTBP4 assembly/deposition in cell culture.

Conclusions: These results highlight new interactions between the elastogenic proteins FBLN4 and LTBP4, their structural and functional consequences, and their dependency on FN and FBN1. These data provide a new paradigm of how elastic fibers assemble.

Notes

Plenary Session 2

Invited Lecture

10:15 - 10:45am

Title: Why Do We Care So Much About The Skin In Scleroderma? Isn't This A Systemic Disease?

Murray Baron[1]

1 Jewish General Hospital, Montreal, QC.

Systemic Sclerosis (SSc, scleroderma) is indeed a systemic disease with elements of autoimmunity, vascular disease and organ fibrosis. The skin is involved in almost all patients, with the occasional exception. We are going through a remarkable period of rapid growth in the numbers of drug trials in scleroderma. Because there are so many manifestations of this disease, it has become very important to decide how to measure the response to drug therapy. Traditionally, the modified Rodnan skin score, a simple sum of the assessment of skin involvement at 17 sites in the body, has been used as a primary trial outcome measure. We will discuss the manifestations of the disease in, on or under the skin. We will answer some important questions about the skin in SSc: What is the natural history of the course of the skin score in SSc? Do changes in this skin score represent changes in other organs? Do changes in skin score predict morbidity and/or mortality? Does the skin score have a place in multidimensional outcome measure for trials in SSc? We will address these questions using data from the Canadian Scleroderma Research Group, a collaboration of clinicians and investigators from across Canada and Mexico, that has been collecting data since 2005 and now has over 1500 subjects in its database. We will concentrate on those patients usually enrolled in drug trials, ie patients with early disease and diffuse skin involvement. We will show how the baseline skin score and changes in the skin score over time may be associated with changes in organ involvement and subsequent morbidity and mortality.

Notes

Plenary Session 2

Invited Lecture

10:45 - 11:00am

Title: Myeloid Cells Steer Mesenchymal Stem Cells Into The Wound Bed: A Mechanism For Elderly's Deficient Healing

Marc G Jeschke, Abdikarim Abdullahi, Nancy. Yu, Casandra Belo, Marc Jeschke and **Saeid Amini Nik**[1]

1 Sunnybrook Research Institute, University of Toronto, *ON.*

Over the last decades, advancements have improved survival and outcomes of severely burned patients except for one population, elderly. The Lethal Dose 50 (LD50) burn size in elderly has remained the same over the past three decades, and so has morbidity and mortality, despite the increased demand for elderly burn care. We have already reported that elderly have a profound increased mortality, more premorbid conditions, and stay at the hospital for longer with a substantial delay in wound healing predominantly due to alteration in characteristics of progenitor cells. In order to unravel the mechanism of delayed skin healing, we compared skin-healing characteristics of old patients (as well as aged mice) with the young ones. Young (8 weeks old) and aged mice (>52 weeks) were subjected to 30% full thickness burn and their skin healing was monitored up to two weeks post burning. We report on the deficient recruitment of MSCs into the wound bed of aged animal, which is accompanied, with the lack of myeloid lineage cells in the wound bed of these animals. The lack of MSCs observed in aged animal was predominantly seen in CD90+ subpopulation of MSC. When MSCs express CD90, myeloid cells can steer them into the wound bed during skin injury and that is what skin of the aged animal is lacking.

Notes

Plenary Session 2

Trainee Presentation

11:00 - 11:10am

Title: Mimicking Cutaneous Melanoma Microenvironment Using Tissue-Engineered Skin

Jennifer Bourland [1,2,3], Julie Fradette[1, 2,3], François A. Auger[1, 2,3]

1 Centre de recherche en organogenese experimentale de l'Universite Laval / LOEX

2 Division of Regenerative Medicine, CHU de Quebec – Universite Laval Research Center

3 Department of Surgery, Faculty of Medicine, Universite Laval, Quebec, Qc, Canada

Melanoma incidence is constantly increasing in developed countries. Melanoma can spread through lymphatic or blood vessels. Mechanisms controlling the dissemination paths are poorly understood and models for studying melanoma physiopathology ex vivo are often inadequate. To address this, we hypothesized that the human tumor microenvironment can be mimicked in vitro to study melanoma biology.

Tissue-engineered skin was produced using primary dermal, epidermal and microvascular endothelial cells by the self-assembly approach without any exogenous biomaterial. Tumor microtissues were produced using the hanging drop method and added to the reconstructed skin. Six melanoma cell lines were used (A375, SK-MEL 28, WM983a, RPMI 7951, Malme-3M and WM983b). Tumor development was assessed by histology, immunofluorescence and confocal microscopy, while cytokine secretion profiles were determined by ELISA. WM983a and WM983b models were treated with vemurafenib. Response to treatment was assessed by quantification of Ki67-positive tumor cells.

We obtained a tissue-engineered skin displaying two distinct microvascular networks: a PDPN-CD31+ blood network, and a PDPN+ CD31+ lymphatic network. Histological analyses revealed tumor microtissue integration at the dermoepidermal junction. The pro-lymphangiogenic VEGF-C was detected in conditioned media from melanoma microtissues (662 pg/ml). CCL21, a chemoattractant secreted by lymphatic endothelium, displayed secretion levels that were 10-fold higher in microvascularized tissues compared to the non-microvascularized skin ($P \leq 0.001$).

Both cytokines are involved in the cross-talk between tumor cells and capillaries. The 3D melanoma model responded to vemurafenib with up to a 5-fold decrease of tumor cell proliferation. WM983a and WM983b models showed significantly different IC50 in response to treatment ($P \leq 0.01$). This unique 3D in vitro melanoma model mimics tumor microenvironment by combining blood and lymphatic capillaries with melanoma microtissues in a reconstructed skin.

Being responsive to vemurafenib treatment, it represents a valuable tool for studying mechanisms of metastasis and drug response in a fully human microenvironment.

Notes

Plenary Session 2

Trainee Presentation

11:10 - 11:20am

Title: Comparative Study Of Cell Source On The Functional Characteristics Of Human Reconstructed Connective Tissues Engineered Under Serum-Free Conditions

Meryem Safoine[1], Valérie Trottier[1], Kim Aubin[1], Marc-André Plourde Campagna[2], Jean Ruel[2] and Julie Fradette[1]

1. Centre de recherche en organogénèse expérimentale / LOEX, Division of Regenerative Medicine, CHU de Québec Research Center, Department of Surgery, Faculty of Medicine, Université Laval, Québec, Qc, Canada.

2. Bureau de design, Mechanical Engineering Department, Université Laval, Québec, Qc, Canada.

INTRODUCTION: Tissue engineering allows the production of human substitutes intended to be grafted. Several cell sources are considered for connective tissue reconstruction, with dermal fibroblasts (DFs) remaining the most used. In recent years, adipose-derived stem cells (ASCs) have gained major interest due to their minimal donor site morbidity and their secretome exhibiting a major therapeutic potential. The aim of this study was to investigate the effect of cell source on stromal reconstruction. We hypothesized that ASCs allow the production of human reconstructed connective tissues (rCTs) exhibiting enhanced functional properties compared to DFs.

METHODS: DFs and ASCs were used to engineer human connective cell-sheets which were superposed to form DFs-hrCTs and ASCs-hrCTs according to the self-assembly method. A commercially available GMP grade serum-free medium (SFM) was used for the entire tissue production limiting animal derivatives. The tissue structure was analyzed using Masson's trichrome staining and immunolabelings. Mechanical properties were evaluated using uniaxial tensile tests (Instron E1000) and secretory profiles were determined by ELISA to assess their biological functionality.

RESULTS: Both tissues displayed similar histological appearance and a diversified matrix composition [fibronectin, collagens type I and III, glycoproteins (tenascin C) and proteoglycans (decorin, perlecan)]. ASC-rCTs showed an enhanced matrix formation being 2.9x thicker than DFs-rCTs and a slightly but non-statistically significant increased contraction ($p = 0.0944$). Interestingly, the use of SFM compared to standard fetal bovine serum-containing medium increased ASCs-rCTs thickness by 4.4x and diminished contraction by 1.6x. Mechanical tests revealed comparable ultimate failure strength for both tissue types. Finally, ASCs-rCTs secreted 7x more angiopoietin-1 and PAI-1 than DFs-rCTs.

CONCLUSION: ASCs are a cellular type of choice for stromal reconstruction comparable and even superior to DFs especially regarding their secretion of pro-angiogenic molecules. Those reconstructed tissues have extensive surgical applications as graft substrates and can also provide stromal support for skin reconstruction.

Notes

Plenary Session 2

Trainee Presentation

11:20 - 11:30am

Title: A Salamander-Derived Protein (Sdp) As An Inhibitor Of Tgf-B Signaling And Fibrotic Responses

Ahmed Al-Qattan[1], Lucie Lessard[1] and Anie Philip[1]

1 *Divsion of Plastic Surgery, McGill University*

Fibrotic disorders of the skin such as scleroderma, hypertrophic scarring and keloids are characterized by excessive TGF-β signaling, leading to an increase in deposition of collagen and other extracellular matrix (ECM) components, resulting in functional impairment which is often debilitating. To date, the treatment options remain limited. The aim of this study is to examine the effectiveness of a salamander-derived protein (SDP) to inhibit TGF-β signaling and fibrotic responses in human skin fibroblasts (HSF). HSFs were treated with SDP in doses of 100pM,1nM and 10nM for 24 hrs and were then left untreated or treated with 20 pM of TGF-β. The inhibition of TGF-β-mediated pro-fibrotic responses was determined by measuring alpha smooth muscle actin (α-SMA), connective tissue growth factor (CTGF), collagen III and fibronectin protein production by Western blot as well as immunofluorescence and validated at the mRNA level by Quantitative PCR. Activation of the TGF-β pathway was determined by measuring the TGF-β receptor (ALK5) and phosphorylated Smad2/3 levels by using Western blot and immunofluorescence. Both the Western Blot and the immunofluorescence results revealed that the application of the SDP protein to HSFs in the presence of TGF-β successfully inhibited the fibrotic response shown by a decrease in the fibrotic factors such as α-SMA, collagen III, CTGF and fibronectin. In addition, immunofluorescence after 1 hour of treatment with SDP revealed a significant decrease in phosphorylated Smad2/3, and a decrease in the TGF-β receptor (ALK5), thereby inhibiting the TGF-β signaling pathway.

Our findings suggest that the salamander-derived protein exhibits marked anti-fibrotic effects in human skin fibroblasts.

Notes

Plenary Session 2

Trainee Quick-shot Presentations

11:30 - 11:35am

Title: Electrospun Polyurethane-Gelatin Scaffolds For Manufacturing Skin Substitute

Mohammadali Sheikholeslam[1,2] , Meghan Wright[4] , Marc Jeschke[1,2,3], Paul Santerre[4,5] and Saeid Amini-Nik[1,2,6]

1 Sunnybrook Research Institute,

2 Department of Surgery, Division of Plastic and Reconstructive Surgery,

3 Institute of Medical Science,

4 Translational Biology and Engineering Program, Ted Rogers Centre for Heart Research, Institute of Biomaterials & Biomedical Engineering,

5 Faculty of Dentistry

6 Department of Laboratory Medicine and Pathobiology, University of Toronto

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There is an immediate need for skin substitute despite significant developments in the management of severe skin loss. Gelatin is a low cost natural biomaterial, which is frequently used for tissue engineering applications and serve as a potential home for progenitor cells. However it suffers from a lack of sufficient mechanical strength and associated difficulties with handling. Polycarbonate urethanes (PU) are biodegradable elastomeric biomaterials with water and CO2 as final degradation products. These polymers can be spun into fibrous scaffolds, with excellent cell compatibility, controlled degradation, and non-toxic degradation products. We hypothesized that the addition of a small amount of PU to gelatin would improve the mechanical strength of electrospun gelatin. A new gelatin-based electrospun scaffold was fabricated for skin tissue engineering via the addition of PU. Screening different ratios of Gel and PU, we found that scaffolds generated with a mass ratio Gel80-PU20 exhibited no significant difference in average fiber size and fiber morphology, however the yield strength, and elongation of these scaffolds increased relative to 100% gelatin scaffolds (Gel100). These properties are essential for the optimal performance of the scaffold in vivo. Human dermal fibroblasts (HDF) were employed as one of the main cell sources in the dermis. More than 90% of the cells were viable, comparable to the Gel100 in an in vitro assay. Unlike the HDF cultured on Gel100 scaffolds, which showed an aligned orientation, HDF cultured on Gel80-PU20 had a random orientation, reminiscence of human skin. The depth of cell infiltration into the scaffold was similar for Gel100 and Gel80-PU20, as well as for commercial skin substitute material IntegraTM. The results show that Gel80-PU20 scaffold is an ideal 3D environment for essential cell component of skin and might serve as an ideal scaffold for manufacturing skin substitute using various skin progenitor cells.

Notes

Plenary Session 2

Trainee Quick-shot Presentations

11:35 - 11:40am

Title: Comparison Of Loading Methods Of An Antibiotic In Electrospun PLGA Fibers

Emily Buck [1], Vimal Maisuria [2], Nathalie Tufenkji [2] and Marta Cerruti [1]

1. *Materials Engineering, McGill University*
2. *Chemical Engineering, McGill University*

Electrospun scaffolds are proposed for use as wound dressings due to their high porosity and surface area to volume ratio. They can be given antibacterial properties by loading an antibacterial agent in the scaffold through one of many established methods. The most common loading method involves blending an antibacterial agent into the polymer solution before electrospinning; this creates a homogeneous scaffold in one step and allows for controlled release of the agent. However, it is not known whether this method has advantages over physisorbing the antibacterial agent onto the scaffold by simply dipping the electrospun fibers into a solution containing the agent. In this study, we compared the antibacterial properties of poly(lactic-co-glycolic acid) (PLGA) electrospun scaffolds containing a model antibiotic, ciprofloxacin (CIP), that was loaded by either blending with the polymer during electrospinning (scaffolds referred to as "CIP-BLEND") or by physisorption after electrospinning (scaffolds called "CIP-PHYSI"). We tested two CIP concentrations and quantified the initial loading of CIP in the scaffolds by high performance liquid chromatography (HPLC). The amount of CIP loaded in the two types of scaffolds was not significantly different, which allowed for a direct comparison of the CIP-loading methods. The antibacterial properties were tested using an agar disk diffusion assay and three bacterial strains, namely, Staphylococcus aureus ATCC 25923, Staphylococcus epidermidis ATCC 14990 and Pseudomonas aeruginosa PA14. For all bacterial strains, larger zones of clearance were observed around the CIP-PHYSI scaffolds than the CIP-BLEND scaffolds at both concentrations of CIP investigated. This indicated that the physisorbed CIP was more effective at killing bacteria than the blended CIP, which can be explained by faster CIP release from the CIP-PHYSI scaffolds than the CIP-BLEND scaffolds. The results of this study suggest that physisorbing antibiotics could be applied to create more effective antibacterial electrospun scaffolds for use as wound dressings.

Notes

Plenary Session 2

Trainee Quick-shot Presentations

11:40 - 11:45am

Title: Anti-Bacterial Efficacy Of Silver Doped Sol-Gel Derived Borate Glass For Wound Healing Applications

Shiva Naseri[1], William C Lepry[1], Vimal B Maisuria[2], Nathalie Tufenkji[2], Showan N Nazhat[1]

1. *Department of Mining and Materials Engineering, McGill University, Montreal, QC.*
2. *Department of Chemical Engineering, McGill University, Montreal, QC.*

A major issue in chronic wounds such as ulcers in diabetic patients is infection and repeated tissue insults. Therefore, novel therapies are required to accelerate the healing process. While silver ions are known for their anti-bacterial properties, elevated concentrations are toxic to mammalian cells [1] and their use in pure silver salt form causes damage to skin tissues. Recently, bioactive glasses have been studied for wound healing applications. Doping of these glasses enhances their chemical and biological properties, including controllable ion release, anti-bacterial or angiogenic properties [2]. Research has also shown that sol-gel glasses are more suitable for biomedical applications when compared to their melt-quench equivalents due to inherent porosity and higher surface area, leading to greater control over degradation rates [3]. In this study, amorphous sol-gel derived silver doped borate glasses (AgBGs) of the composition 60B2O3-36CaO-(4-X)P2O5-XAg2O where X= 0, 0.3, 0.5 and 1 (mol%), developed for wound healing applications, were investigated for their anti-bacterial properties. AgBGs were characterized by their high surface areas with nano range porosities leading to rapid dissolution and ion release rates.

Anti-bacterial activity of AgBGs against Escherichia coli and Staphylococcus aureus was evaluated through bacteria growth curves and cell viable count methods. The results demonstrated that AgBGs are highly effective against bacteria associated with wounds resulting in dose dependent efficacy, and correlating with silver ion release rates and quantities. In sum, therapeutic sol-gel derived AgBGs with promising ability to accelerate the healing process have been developed. Future work will investigate the effect on mammalian cells.

References:

1.Chernousova and Epple, Angew Chem Int Ed, 2013

2.Miguez-Pacheco, Acta Biomater, 2015

3.Lepry and Nazhat, Chem Mater, 2015

Notes

Plenary Session 2

Trainee Quick-shot Presentations

11:45 - 11:50am

Title: Development Of A Serum Free Medium Optimized For Human Epithelial Cell Culture

Sergio Cortez Ghio [1], Danielle Larouche [1], Alain Garnier [2] et Lucie Germain [1]

1. *Centre de recherche du CHU de Québec - Université Laval, centre de recherche en organogénèse expérimentale de l'Université Laval/LOEX, Département de Chirurgie, Faculté de médecine, Université Laval.*
2. *Département de génie chimique, Faculté des sciences de génie, Université Laval.*

The culture of epithelial cells (i.e. keratinocytes) has improved treatments for patients suffering from severe burns. To properly culture human keratinocytes in vitro, fetal bovine serum (FBS) must be added to the culture medium. However, FBS exact biological composition is undefined and is known for batch-to-batch variations. FBS is also associated with a risk of pathogen transmission. For these reasons, discarding FBS usage in clinical contexts would be desirable. Although serum-free media (also called defined media) are commercially available, they are not effective in culturing keratinocytes for more than a few passages. Therefore, our objective is to develop and test a defined medium optimized for keratinocyte growth in vitro. Four candidate molecular factors capable of substantially promoting keratinocyte growth were initially identified from an experimental screening. This led to the development of an effective defined medium for culturing keratinocytes (DMK). This medium was then optimized in terms of cost-effectiveness by testing multiple concentrations of these factors, which allowed the formulation of four DMK derivatives (α, β, γ and δ). DMK and its derivatives were then ranked on their ability to sustain keratinocyte culture quality by testing additional cell populations and using daily population doublings and cell size over as many passages as possible as proxies. We observed that keratinocytes cultured in DMKβ were smaller and could be grown over more passages than those cultured in DMK, other DMK derivatives (α, γ, and δ) or FBS-containing medium. In addition, keratinocyte population doubling rates were similar across all media. The morphology of keratinocytes cultured in DMKβ was also comparable to that of those cultured in FBS-containing medium. Although more analyses are needed to characterize the effects of DMKβ on cultured keratinocytes, results thus far show that this new medium is very promising.

Notes

Plenary Session 2

Trainee Quick-shot Presentations

11:50 - 11:55am

Title: A Surgical Device To Study The Efficacy Of Bioengineered Skin Substitutes In Mice Wound Healing Models

Datu AK[1], Jeschke MG[1,2] , Sadri AR[1] , Belo C[1] and Amini-Nik S[1,2,3]

1. Sunnybrook Health Sciences Center, Sunnybrook Research Institute, Toronto, ON.

2. Division of Plastic Surgery, Department of Surgery, University of Toronto, Toronto, ON.

3. Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

Due to the poor regenerative capacity of the adult mammalian skin, there is a need to develop effective skin substitutes for promoting skin regeneration after a severe wound. However, the complexity of skin biology has made it difficult to enable perfect regeneration of skin. Thus, animal models are used to test potential skin substitutes. Murine models are valuable but their healing process involves dermal contraction.

We have developed a device called a dome that is able to eliminate the contraction effect of rodent skin while simultaneously housing a bioengineered skin graft. The dome comes in two models, which enables researchers to evaluate the cells that contribute to wound healing from neighboring intact tissue during skin healing/regeneration. This protocol simplifies grafting of skin substitutes, eliminates the contraction effect of surrounding skin, and summarizes a simple method for animal surgery for wound healing and skin regeneration studies.

Notes

Plenary Session 3

Invited Lecture

1:00 - 1:30pm

Title: Role Of PARP1 In Solar UVB-Induced Non-Melanoma Skin Cancers

Girish M. Shah[1]

1 Université Laval and CHU de Québec Université Laval (CHUL campus), Laboratory for Skin Cancer Research, Quebec (QC)

Background: The non-melanoma skin cancers (NMSC), such as squamous and basal cell carcinoma account for ~40% of all the newly diagnosed cancers in Canada in 2015. Exposure to solar ultraviolet B radiations (UVB) is strongly linked to NMSC; and the cellular processes involved in various responses to UVB-exposure, such as DNA damage and its repair, immunosuppression, cell death and inflammation contribute to the development and progression of NMSC. In mammalian cells, a nuclear enzyme poly (ADP-ribose) polymerase 1 (PARP1) is activated in response to various types of DNA damages to transiently modify proteins with chains of poly (ADP-ribose) or PAR in the vicinity of DNA damage. The PARP1 and PARylation processes have been shown to participate in many of the processes that occur in response to DNA damage. Using cellular and animal models, we have observed that PARP1 is activated in skin cells after UVB-irradiation; and the global aim of our project is to understand its implication in the development of sunlight-induced skin cancers

Our studies have recently identified a protective role of PARP1 in removal of UV-induced DNA lesions from skin cells by the nucleotide excision repair pathway of DNA repair. We recently created albino hairless mouse strain in which PARP1 gene has been inactivated. Using these mice, we are currently examining the potential PARP1-targeted therapy for UVB-radiation induced NMSC skin cancers.

Notes

Plenary Session 3

Invited Lecture

1:30 - 1:45pm

Title: Building Innovative Wound Care Technology

Yunghan Au*

** Swift Medical, Montreal, QC.*

Our team, Swift Medical, has built an advanced, collaborative wound-care management system, bringing the accuracy of digital planimetrics to the ubiquitous smartphone, allowing clinicians to automatically image, measure, assess and document wounds at point of care and securely collaborate in real time. Both accuracy and inter-rater reliability were shown to be high (ICC = 0.99) and superior to that of the standard ruler method in a study with 124 patients with chronic wounds. Furthermore, infrared imaging was incorporated to detect local wound infection. Here, we discuss the challenges and opportunities to build innovative technologies that will enhance wound care management, reduce healthcare costs and ultimately improve patient outcomes.

Notes

Plenary Session 3

Trainee Quick-shot Presentation

1:45 - 1:50pm

Title: Exosomes In The Acellular Wharton's Jelly Of The Human Umbilical Cord Enhances Skin Wound Healing

Nazihah Bakhtyar [1], Marc Jeschke [1,2,3], Mohammad Ali Sheikholeslam [1,2], Yusef Yousuf [1,2], Elaine Herer[1,5] and Saeid Amini-Nik [1,3,4]

1. *Sunnybrook Research Institute,*
2. *Insitute of Medical Science, University of Toronto,*
3. *Department of Surgery, Division of Plastic and Reconstructive Surgery,*
4. *Department of Laboratory Medicine and Pathobiology (LMP),*
5. *Gynecology and Obstetrics Department, Sunnybrook Health Sciences Centre, University of Toronto, Canada*

Every year, burn injuries account for approximately 500,000 hospital emergency department visits in the United States. Burn injuries lead to dramatic physiological changes which include impaired wound healing. We recently reported that acellular gelatinous Wharton's jelly (AGWJ) from the human umbilical cord enhances wound healing in-vitro and in-vivo. However, the active ingredient(s) of AGWJ is not known.

Hypothesis: Native extracellular factors of the AGWJ contains factors(s) which are beneficial for wound healing. Methods: Isolated and fractionated acellular WJ. Mass spectrometry on AGWJ to identify proteins, then isolated exosomes from AGWJ. In-vivo, 6mm punch biopsies on the backs of BALb/c male mice were performed; wounds were treated with control matrigel, matrigel with AGWJ and matrigel with exosomes from AGWJ. Mice were sacrificed on day 7, histology was performed on wounds.

Results: AGWJ significantly enhanced fibroblast migration and changed morphology to a myofibroblastic phenotype, confirmed by upregulation of alpha smooth muscle actin (α SMA). In-vivo, a smaller wound length in the AGWJ treated mice were observed, with greater α SMA expression. Interestingly, the number of F4/80+ve macrophages were significantly higher in the AGWJ group compared to controls, suggesting that AGWJ enhances macrophage accumulation, leading to a faster upregulation of α SMA which causes faster contraction. Mass spectrometry on AGWJ revealed a protein characteristic of exosomes. In murines, wounds treated with only exosomes isolated from AGWJ were the smallest in length compared to total AGWJ and controls, suggesting that exosomes in AGWJ contains the main active ingredient that enhances wound healing. Western blot analysis revealed an enrichment of TGF- β protein in exosomes.

Conclusion: Data suggests that exosomes in AGWJ enhance wound healing through an increase in the number of myofibroblasts in granulation tissue, partly through activation of TGF- β pathway. AGWJ is biological, cost effective and globally available which makes it a highly promising wound healing remedy.

Notes

Plenary Session 3

Trainee Quick-shot Presentation

1:50 - 1:55pm

Title: Cellular Microrna Regulation By Fibrillin-1 And Fibronectin Is Mediated Through Integrins

Rongmo Zhang[1], Karina Zeyer[1], Heena Kumra[1] and Dieter P. Reinhardt[1,2]

1. *Faculty of Medicine and*
2. *Faculty of Dentistry, McGill University, Montreal, Canada*

Background and Aim: Fibrillin-1 interaction with cells via RGD-dependent integrins is essential for tissue integrity. Defects of fibrillin-1 has been linked to diseases that affect the skeletal, cardiovascular, and ocular systems, including Marfan syndrome, Weil-Marchesani syndrome, geleophysic and acromicric dysplasia. Fibronectin is an important regulator of the assembly of fibrillin-1 containing microfibrils. Fibrillin-1 contains one evolutionarily conserved integrin binding Arg-Gly-Asp (RGD) sequence in its fourth TB domain, and fibronectin possess a RGD sequence in the 10th type III domain. MicroRNAs (miRNAs) are small non-coding RNA molecules with critical functions in post-transcriptional regulation of gene expression. This study addresses how cell interaction of fibrillin-1 and fibronectin regulates gene expression through miRNAs.

Experiments and Results: Human skin fibroblasts (HSFs) attached differently to plates coated with the RGD wild-type fragments of fibrillin-1 and fibronectin in comparison to the RGA-containing mutants. The interaction of HSFs with the RGD sequence of both, fibrillin 1 and fibronectin, showed increased proliferation. Surprisingly, a microarray analysis displayed differential expression of many miRNAs and mRNAs after 24 h of HSFs grown on the fibrillin-1 wild-type and RGA fragments. Differential miRNA expression occurred as early as 2 hours of cell interaction. Pathway analysis indicated that the differentially expressed miRNAs act together in regulating cell adhesion, migration and growth factors. Among the differentially expressed miRNAs, miR-1208 expression was inhibited when HSFs were seeded on fibrillin-1 and fibronectin wild-type fragments. Moreover, miR-1208 showed higher expression in the HSFs interacting with wild-type fibrillin-1 compared to fibronectin. Inhibition of miR-1208 partially rescued the proliferation rate and the cell morphology of HSFs seeded on RGA-mutant fibrillin-1 and fibronectin. Among the predicted targets of miR-1208, extracellular signal-regulated kinase (Erk) was shown to be negatively correlated with miR-1208 expression. Overexpression and knockdown of miR-1208 inhibited and promoted Erk signaling, respectively. miR-1208 was further found to be necessary in fibroblast to myofibroblast differentiation.

In summary, our analyses systematically investigated the miRNA profile change triggered by HSFs' interaction with the RGD cell-binding sequence of fibrillin-1 and fibronectin, and reveal miRNA involvement in proliferation and differentiation. These results shed new lights on the outside-in signaling of matrix proteins by regulating miRNAs

Notes

Plenary Session 3

Trainee Quick-shot Presentation

1:55 - 2:00pm

Title: Fbln4 And Ltbp4 Cell Receptor Interactions

Hana Hakami[1], Amelie Pagliuzza[1], Jelena Djokic[1], Kungjun Lee[1], Chae Syng Lee[1] and Dieter P. Reinhardt[1,2]

1. *Faculty of Medicine and*
2. *Faculty of Dentistry, McGill University, Montreal, Canada*

Fibulin-4 (FBLN4) and latent transforming growth factor-β binding protein-4 (LTBP4) are important elastogenesis accessory proteins. Mutations in FBLN4 and LTBP4 cause autosomal recessive cutis laxa type 1B and type 1C, respectively, in human. FBLN4-/- and LTBP4-/- mice are characterized by high perinatal/neonatal mortality and severely affected elastic fibers, suggesting their essential functions in survival and elastogenesis. Previously, we have shown that FBLN4 interacts with primary smooth muscle cells and fibroblasts. However, cell interaction with LTBP4 has not been demonstrated. In this study, we show that fibroblasts bind strongly to LTBP4. We further demonstrate the functionality of FBLN4 multimerization in cell binding. FBLN4 multimers, but not monomers, interact with cells. Additionally, we have investigated potential cell receptor(s) for FBLN4 and LTBP4. Neither FBLN4 nor LTBP4 contains an arginine-glycine-aspartic acid (RGD)-integrin binding sequence. However, FBLN4 and LTBP4 have high affinity for heparin. This suggests heparan sulfate proteoglycans may mediate FBLN4 and LTBP4 cell interaction. We demonstrate that FBLN4 cell interaction is exclusively mediated by cell surface-located heparan sulfate. In the presence of heparin, cell binding to FBLN4, but not LTBP4, is entirely abolished. Our results exclude heparan-sulfate proteoglycans as LTBP4 cell binding receptors. These data establish a new paradigm for FBLN4 and LTBP4 role in elastogenesis. The determination of the FBLN4 and LTBP4 cell receptor(s) identity will reveal their significance in elastic fiber formation and homeostasis.

Notes

Plenary Session 3

Trainee Quick-shot Presentation

2:00 - 2:05pm

Title: Pullulan/Gelatin Scaffold: An Ideal Niche For Skin Regeneration

Nan Cheng[1,2], Marc Jeschke [1,2,3] and Saeid Amini-Nik[1,3,4]

1. *Sunnybrook Research Institute,*
2. *Institute of Medical Science, University of Toronto,*
3. *Department of Surgery, Division of Plastic and Reconstructive Surgery*
4. *Department of Laboratory Medicine and Pathobiology (LMP)*

The World Health Organization (WHO) estimates that every year over 300,000 deaths are due to burn injuries and millions more are suffering from burn-related physical and emotional consequences. Wound healing and its complications are the major underlying reason for morbidity and mortality of patients. Therefore, there is an urgent need to develop suitable skin substitutes to deliver cells to the wound bed and promote wound healing. Due to good biocompatibility, excellent support to cell growth and especially anti-oxidant property, scaffolds composed of pullulan and gelatin can service the purpose.

We developed our second generation of pullulan/gelatin scaffold (PG2) with physically cross-linked pullulan and chemically cross-linked gelatin by salt-leaching fabrication method and compared it to clinically used Integra® dermal regeneration template (Integra®) from aspects of material properties and in vitro cell study. Morphology, porosity, water retention, swelling behavior, mechanical strength, and anti-oxidant property of PG2 were evaluated. Its ability to support cell survival, proliferation, as well as penetration, was investigated by incorporation of human skin fibroblasts.

The results show that PG2 has heterogeneous interconnected round-shaped pores; the pore size is 20-200um; the porosity is around 74%. It has good water retention and low swelling in size. PG2 showed anti-oxidant property to protect incorporated cells from reactive oxidant species. In vitro cell study demonstrates that cells on PG2 have a comparable viability (86-90%), penetration capability (164-201um), and proliferation capacity (35%) to Integra®. Overall, the PG2 scaffold is a promising and affordable candidate as a cell-delivery substitute for skin regeneration.

Notes

Plenary Session 3

Trainee Quick-shot Presentation

2:05 - 2:10pm

Title: Targeting TGF-Beta Pathway In Squamous Cell Carcinoma By CRISPR/ Cas9-Mediated Genome Editing

Shufeng Zhou[1], Peter Siegel[2] and Anie Philip[1,2]

1 *McGill University*

Introduction: Cancer stem-like cells (CSCs) have been identified in squamous cell carcinoma (SCC) and implicated in cancer progression and metastasis. Epithelial-to-mesenchymal transition (EMT) is a highly conserved cellular process that is involved in normal embryogenesis and tissue repair, but it also contributes to tumor metastasis. In the context of advanced stage tumors, transforming growth factor-beta (TGF-β), a strong EMT inducer, can promote cancer cells to undergo EMT to generate CSCs, enhance tumor invasion and metastasis. CD109 is a TGF-b co-receptor that negatively regulates TGF-β function. However, the significance of CD109 in squamous cell carcinoma and its potential to regulate cancer progression and metastasis remain to be explored. To investigate CD109 overall influence in SCCs progression, CD109 was knocked out in the A431 cancer cell line using CRISPR/Cas9, a powerful genome editing tool.

Method: We sorted SCC cells into CD109high, CD109medium and CD109low sub-populations by FACs, then analysed the alterations in EMT and stem markers. Cellular migration and invasion were assessed as well as tumorigenicity. We also knocked out CD109 in A431 cells using CRISPR/Cas9 genome editing and then analyzed the same parameters as above in parental vs A431-CD109 KO cells.

Results: We showed that SCC cells express CD109 heterogeneously and cellular levels of CD109 are inversely correlated to the expression of TGF-b receptors and EMT markers, as well as to stemness, migration, invasion and tumorigenicity. Importantly, the CRISPR/Cas9-mediated knockout of CD109 caused profound morphologic and molecular changes indicative of enhanced EMT, stemness, increased invasive and tumorigenic potential.

Conclusion: Our findings implicate CD109 as an important regulator of EMT, migration, invasion and stemness in human SCCs. Additionally, as CD109-null A431 cells exhibit enhanced mesenchymal traits and pro-metastatic properties, CD109 may represent a potential target for therapeutic interventions in human SCC.

Notes

Plenary Session 4

Invited Lecture

2:30 - 2:45pm

Title: Wound Healing Clinical Cases and Basic Science Concept Application to Clinical cases

Lucie Lessard[1]

1 McGill University, Montreal, QC.

Abstract not available

Notes

Plenary Session 4

Invited Lecture

2:45 - 3:00pm

Title: Successful Treatment Of Atrophic Facial Leishmaniasis Scars By CO2 Fractional Laser

Huma K[1], M.D. Khalid Alghamdi

1 Dermatology Department, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Background: A permanent unpleasant atrophic leishmaniasis scar is a potentially disfiguring condition causing social stigma with limited treatment choices. Fractionated carbon dioxide (CO2) laser resurfacing is expected to be a safe and an effective treatment for leishmaniasis scars. Objective: To assess the safety and efficacy of ablative fractional resurfacing (AFR) with CO2 laser for facial leishmaniasis atrophic scar.

Methods: Eleven patients (male 5, aged 18-47 years) underwent the fractional CO2 laser procedure. Mean duration for scar was 18.3 years. Three to five sessions of fractional CO2 laser were done for each patient, at 2 months interval under topical anesthesia. Two passes with tip type 120, density 150 spots/cm2 in static mode, and peak power of 30 Watt were applied to each leishmaniasis scar. Pulse energies ranged between 100-140 mJ. Post-treatment improvements in texture, atrophy, and overall satisfaction with appearance were graded on a quartile scale by patients and investigators one month after the second session and three months after the final session. Improvement of scar was graded by using a 4-point score with a maximum score of 20.

Results: At the 3-month post-treatment follow-up, all subjects were rated as having at least 50% improvement in texture, atrophy, borders and overall appearance of scars. The median score of improvement was 18/20 (range 11-19). Mild post inflammatory hyperpigmentation was the only adverse effect observed in 18% (2/11)of the subjects. After the procedure, moderate to severe erythema and edema typically resolved within 24 to 48 hours. No additional adverse effects were observed.

Conclusion: Carbon-dioxide fractional resurfacing represents a safe, effective and well tolerated potential treatment for atrophic facial leishmaniasis scars in ethnic skin.

Notes

POSTER PRESENTATION ABSTRACTS

PO1: The Key Role Of Fibronectin In The Maturation Of Tissue Engineered Blood Vessels

Daniele Pezzoli[1], **Joseph Di Paolo**[2], Heena Kumra[2], Gabriele Candiani[3], Dieter P. Reinhardt[2,4] and Diego Mantovani[1]

1. Laboratory for Biomaterials and Bioengineering, Department of Mining, Metallurgical and Materials Engineering and CHU de Québec Research Centre, Université Laval, Quebec City, QC, Canada

2. Faculty of Medicine and 4Faculty of Dentistry, McGill University, Montreal, Canada

3. Department of Chemistry, Materials and Chemical Engineering, Politecnico di Milano, Milan, Italy

Background and Rationale: In the western world, coronary artery disease is responsible for more than half of all cardiovascular disease-related deaths. One of the most pressing clinical problems of the field is the need for small diameter vascular grafts for coronary bypass surgery. Tissue engineered blood vessels (TEBVs) have been proposed as arterial substitutes but, despite the many advancement in the field, further work is required to address the biggest issue toward their clinical application, the lack of strength and elasticity caused by limited elastic fiber formation.

Methods and Results: In this study, TEBVs were prepared using collagen gels cellularized with porcine aortic smooth muscle cells (SMCs) and supplemented with human plasma fibronectin (FN), a known master organizer of the extracellular matrix (ECM) that could promote cell adhesion and a synthetic phenotype in SMCs. The maturation of the constructs over time was investigated in terms of matrix contraction, mechanical properties (stress-relaxation tests), expression and deposition of ECM proteins (immunohistochemistry and quantitative PCR). Results showed a time-dependent increase in SMC-mediated gel contraction and mechanical properties and, in FN supplemented constructs, tensile elastic modulus was more than twice higher than in control gels ($p < 0.05$), reaching the relevant value of 0.12 ± 0.02 MPa after 7 days of maturation. In addition, supplementation with FN increased the production by SMCs and deposition in the construct of elastic fiber-related proteins such as fibrillin-1 and tropoelastin, and influenced the expression profile of several ECM-related genes.

Conclusions: Altogether, this study demonstrates the pivotal role of FN in directing the maturation and remodeling of collagen gel-based scaffolds by SMCs toward the production of physiological-like, elastic fiber-containing TEBVs with superior mechanical properties and its use should be taken into account in tissue engineering approaches to promote the cell-guided generation of mature tissues with an organized ECM.

PO2: Tissue-Engineered Skin Model Derived From Neurofibromatosis Type 1 Patients To Study Tumor Genesis And To Predict Response To Therapy

Vincent Roy[1,4], Édouard Marques[1,4], Lydia Touzel-Deschênes[1,4], Peter Kannu[2], Nicolas Dupré[3,4], Hélène T. Khuong[1,4] et François Gros-Louis[1,4]

1. *Departement of Surgery, Faculty of medecine, Laval University;*
2. *Departement of paediatrics, Faculty of medecine, University of Toronto;*
3. *Departement of neurological sciences, Faculty of medecine, Laval University;*
4. *Regenerative medecine, Centre de Recherche du CHU de Québec-Laval University, LOEX/HEJ, CHU de Québec-Laval University.*

Background: Neurofibromatosis type 1 (NF1) is an autosomal dominant multisystemic disorder caused by aberrations in the neurofibromin gene. The population incidence is approximately 1 per 3000. Typically, patients develop multiple cutaneous tumours that grown from axon of peripheral nerve, called neurofibromas. These benign tumours are generally composed of Schwann cells (SC) and fibroblasts, but others cells type can also be found. Highly variable clinical manifestations between NF1 patients are observed. Actually, there is no specific treatment for this stigmatizing disease.

Objective: The purpose of this study is to develop a tissue engineered human skin model derived from NF1 patients to characterized and understand the formation of neurofibromas.

Methods: The auto-assembly model was used to generate tissue-engineered skin (TES) in vitro with fibroblasts and keratinocytes isolated from NF1 patients (n=3). We used spheroid suspension culture to generated neurofibroma-like tumours; one composed of immortalized SC and another with an equal number of SC and fibroblasts. Then, spheroids were added on the dermis 10 days before keratinocytes seeding.

Results: We first determined the best conditions for the formation of spheroids. Densification area was significantly increased already at day 3 and continued until day 10. Spheroids growth was significantly faster than control cells. Immunofluorescence revealed that spheroids/neurofibromas-like, seeded with NF1-TES, are in a proliferative state. Furthermore, non-apparent activation of apoptosis within spheroid is detected. Neurofibroma-like tumours composed of SC seem to affect the proper formation of the epidermis.

Conclusion: Our NF1 skin model could become a unique tool to better characterize the mechanism of action of a new drug on NF1 tumor shape and growth as well as to assess tumorigenic properties of each of the tested NF1 gene mutation, and ultimately provide better tools to develop new therapies for patients through development of precision/personalized medicine strategies.

PO3: Sox9: A Master Regulator Or An Innocent Bystander In Skin Fibrosis?

Yusef Yousuf[1,2], Nazihah Bakhtyar[1], Marc Jeschke[1,2,3] and Saeid Amini Nik[1,3]

1. *Sunnybrook Research Institute,*
2. *Sunnybrook Hospital, University of Toronto Institute of Medical Science,*
3. *University of Toronto Department of Surgery, Division of Plastic Surgery, Toronto, Ontario, M4N 3M5*

Background: Skin fibrosis can lead to the development of debilitating pathologies such as keloid and hypertrophic scarring (HTS). This pathology arises from the excessive deposition of extracellular matrix (ECM) by myofibroblasts leading to scarring and organ failure. During chondrogenesis, Sox9 regulates ECM deposition and is a downstream target of TGF-β1. In skin, however, Sox9 is a stem cell transcriptional regulator of the hair-follicle stem cell nice and is crucial for their maintenance both in vivo and in vitro. Considering that Sox9 is expressing in mesenchymal lineage cells, it is plausible that Sox9 may play a role in skin fibrosis. The purpose of this project was to examine the role of Sox9 in wound healing and skin fibrosis.

Methods & Results: We collected normal, keloid, and HTS human skin from the Ross Tilley Burn Centre and performed immunohistochemistry for Sox9. We found a significant increase in the number of Sox9+ cells in the dermal layer of the skin in keloid and HTS patients. To recapitulate some of the aspects of fibrosis, we treated human normal, keloid and HTS fibroblast with TGF-β1 to enhance the myofibroblastic phenotype. Western blotting revealed an increase in Sox9 protein level in fibroblasts treated with TGF-β1. Lastly, we performed 4 mm punch biopsy in young (8 weeks) C57BL/6 mice to evaluate Sox9 expression during wound healing. We found that the number of Sox9+ cells increased significantly at 5 days' post-injury during the height of the proliferative phase of wound healing.

Conclusion: Results thus far suggest that Sox9 is highly expressed in the skin of keloid and HTS patients who have active proliferation. In mice, Sox9+ cells are mainly present during the proliferative phase of wound healing in the dermal component. Pharmacological inhibition of Sox9 could potentially be a therapeutic intervention that attenuates skin fibrosis.

PO4: Therapeutic Potential Of Osteoclast Inhibitory Fibrillin-1 Fragments

Muthu Lakshmi Muthu [1,3], Kerstin Tiedemann [1,2], Svetlana Komarova [1,2] and Dieter P. Reinhardt [2,3]

1. *Shriners Hospital for Children and*
2. *Faculty of Dentistry, McGill University, Montreal, Canada 3 Faculty of Medicine, McGill University, Montreal, Canada*

Marfan syndrome due to mutations in fibrillin-1 gene is the most common type-I fibrillinopathy characterized by severe skeletal complications, including osteopenia, stiff skin syndrome, long bone overgrowth, and kyphosis. However, how fibrillin-1 mutations lead to the skeletal problems is poorly understood. The sub-fragment of fibrillin-1 rF31 (32 kDa) were recently identified as strong inhibitor of osteoclastogenesis in vitro and in vivo in healthy animals. To identify the most potent osteoclast inhibitory sub-fragments of fibrillin-1, we produced recombinant half fragments of rF31 and four different fibrillin-1 fragments spanning rF31 in the HEK293 system. The purified proteins were tested for their effect on osteoclastogenesis using primary osteoclasts. We observed reduced number and size of the differentiated osteoclasts. Next, we plan to examine if fibrillin-1 fragments exhibit sufficient anti-resorptive activity in a Marfan syndrome mouse model Fbn1mgR/mgR. To understand the baseline bone parameters as well as identify the therapeutic window in this mouse model, we analyzed bones of Fbn1mgR/mgR 4, 8, 12 and 15 weeks after birth. Fbn1mgR/mgR mice have increased length of long bones and increased body lengths at all time points compared to wild type littermates (WT). Using DEXA we found a trend of decreased BMD in young Fbn1mgR/mgR mice compared to WT, which became significant at 15 weeks of age. Primary osteoclast cultures were derived and differentiated from the bone marrow cells. We found no significant difference in osteoclast number between the WT and the Fbn1mgR/mgR mice. The expression of RANKL and OPG was increased in Fbn1mgR/mgR mice of both sexes, however RANKL/OPG ratio was affected differently – it was higher in Fbn1mgR/mgR males compared to wild type, but lower in females. In conclusion, we have identified smaller fragments of rF23 that exhibit osteoclast-inhibitory activity. Bone phenotype development in Fbn1mgR/mgR mice suggest that treatment can be started at 4-week-old animals.

PO5: Impacts Of Diabetes On Wound Healing

De Serres-Bérard, Thiéry, Thouin, Kiefer, Bellenfant, Sabrina and François Berthod
LOEX, Centre de recherche du CHU de Québec; Département de Chirurgie, Faculté de Médecine, Université Laval

Skin wound healing is severely compromised in patients with diabetes and can lead to ulcer formation requiring lower limb amputation. Hyperglycemia promotes the formation of advanced glycation end-products (AGEs). AGEs are toxic for cells and have deleterious effects on wound healing. It was found recently that AGEs could inhibit reepithelialization by a direct effect on keratinocytes. Ulcer formation often originates in lower limb from neuropathy-induced loss of pain and tactile sense. Skin denervation induced by AGEs may compromise wound healing by reducing neurogenic inflammation. Since neuropeptides released during neurogenic inflammation can enhance keratinocytes proliferation and migration, neuropathy can also directly impair epidermal repair.

Hypothesis and objectives: We believe that the combination of the deleterious effects of AGEs on epidermal self-repair capacity and the lack of neuropeptides in the skin induced by neuropathy contribute to the formation of persistent ulcers in diabetic patients. The aim of our project is to assess in vitro the influence of both AGEs and a treatment with AGEs inhibitor and neuropeptides on the reepithelialization process by keratinocytes.

Method: We developed an endothelialized tissue-engineered skin model in which we performed an 8mm diameter wound to follow the reepithelialization process. To determine the effects of glycation on wound healing, we treated the reconstructed skin with glyoxal, which promote quickly AGEs formation. Then, we attempted to enhance glycated-wound healing by treating the model with an anti-AGE molecule like aminoguanidine or an AGE-breaker like alagebrium. We also treated the model with neuropeptides secreted during neurogenic inflammation like the calcitonine-gene related peptide (CGRP) and substance P.

Results and conclusion: Results suggest that a treatment with aminoguanidine, substance P and CGRP can prevent the deleterious effects of AGEs on skin and enhance wound healing.Therefore, their topical application on ulcers could be a valuable approach to improve wound healing in diabetic patients.

PO6: Modélisation Par Génie Tissulaire De L'impact De L'innervation Cutanée Dans Le Psoriasis

Josy Naud[1,2], Francois Berthod[1,2], Roxane Pouliot[1,3]

1. *LOEX, centre de recherche du CHU de Québec-UL*
2. *Département de chirurgie, Faculté de Médecine, Université Laval*
3. *Faculté de Pharmacie, Université Laval*

Le psoriasis se caractérise par la prolifération anormale des kératinocytes et par des altérations dans leur différenciation, étape décisive pour la formation d'un épiderme fonctionnel. Les lésions psoriasiques apparaissent sur la peau sous la forme de plaques squameuses. Sur ces sites, on retrouve un plus grand nombre de nerfs sensoriels, qui sécrètent des neuropeptides induisant la sécrétion par les kératinocytes de facteurs de croissance neuronaux. Ces neurotrophines ont un rôle chimiotactique et prolifératif sur les neurones et sur les kératinocytes eux-mêmes.

OBJECTIF Reproduire le profil psoriasique avec un modèle de peau innervée produite avec des cellules de patient afin d'évaluer le rôle de l'innervation dans la maladie.

MATERIEL ET MÉTHODES 1) Construction d'un modèle de peau psoriasique innervée avec des kératinocytes de patient sur une matrice composée de collagène et chitosane. L'analyse du profil psoriasique sera faite par immunohistochimie et microscopie confocale en utilisant des anticorps contre les marqueurs de prolifération et de différenciation des kératinocytes. 2)Évaluation de l'expression et de la sécrétion des facteurs neurotrophiques par les kératinocytes en monochouche et en 3D suite à l'induction par des neuropeptides. Les analyses seront faites par qPCR, immunobuvardage et ELISA.

RÉSULTATS Notre modèle de peau reconstruite innervée secrète le neuropeptide SP et l'épiderme du modèle psoriasique est plus épais par rapport à celui reconstruit avec des kératinocytes normaux, cette augmentation étant plus accentuée lorsque la peau reconstruite est innervée. On a confirmé que les kératinocytes lésionnels produisent plus de NGF par rapport aux kératinocytes normaux.

CONCLUSION L'innervation sensorielle semble jouer un rôle important dans le développement des plaques psoriasiques, dont les neuropeptides et le NGF pourraient être les acteurs principaux. Si cet effet est confirmé par nos prochains travaux, cela pourra nous faire envisager l'utilisation des antagonistes des récepteurs neurotrophiques ou des agents modulateurs de neuropeptides comme cible thérapeutique.

PO7: Simple Method For Accurate Measurement Of Non Melanoma Skin Cancer Burden In Mice Using Photography Images

Marc Bazin, Nupur K. Purohit, and Girish M. Shah

The vernier caliper is a manual measuring device that has been used as a gold standard to measure the length, width and height of skin tumors to calculate their area and volume. This method works very well for collecting data on a few tumors at a time, but it becomes tedious, time-consuming and stressful for the animals and the operator when used for measuring multiple tumors in a large number of animals in protocols such as UVB-induced non-melanoma skin cancer in SKH-1 mice. Here, we show that photographs of these mice taken within a few minutes under optimized conditions can be subjected to computerized analyses to determine tumor volume and area as accurately as the caliper method. Unlike the caliper method, the photographic method also records the incidence and multiplicity of tumors, thus permitting comprehensive measurement of tumor burden in the animal. The serial photographic images of mice taken over the entire period of the protocol permits an accurate identification and follow-up of each tumor from its early stages to late phases of cancer. The simplicity and ease of our photographic method will permit more frequent monitoring of tumor burden in long protocols, resulting in the creation of additional data about dynamic changes in progression of cancer or the efficacy of therapeutic intervention. The photographic method can also broadly substitute the caliper method for quantifying other skin pathologies.

PO8: An Evaluation Of The Quality Of Life, Treatments, And Resources Available For Patients With Psoriasis In Canada: A Comparison Of Biologic And Non-Biologic Users

Arvin Ighani [1], Morris F. Manolson [2,3]

1. *Faculty of Medicine, University of Toronto, Toronto, ON*
2. *University of Toronto, Toronto, ON*
3. *Canadian Association of Psoriasis Patients, Ottawa, ON*

Intro: There is a need to update population studies analyzing Canadians with psoriasis given the introduction of new biologic treatments. Here we evaluate the quality of life, treatments, and resources available for psoriasis patients using biologics or non-biologics as treatment modalities.

Methods: An online survey, conducted from July to September 2016, used the following inclusion criteria: Patients with moderate-to-severe psoriasis on one of the following treatments: biologic, biosimilar, methotrexate, cyclosporine, apremilast, or phototherapy. Additional criteria for non-biologic users included psoriasis covering ≥10% of body or psoriasis on the feet, hands, face, or genitals. 343 patients (218 biologic users/125 non-biologic users) were included.

Treatment results: 84% of non-biologic users were aware of biologics, and when evaluating various blinded biologic treatments, 45% of non-biologic users selected blinded Stelara as their preferred treatment. More biologic users were satisfied with their treatment (80%) compared to non-biologic users (48%).

Quality of life results: 41% of biologic users stated they felt their best when it came to their psoriasis compared to 25% of non-biologic users. More Stelara users (70%) than Humira users (28%) say they felt their best regarding their psoriasis, although Humira was more widely used.

Patient resource results: 57% of patients used resources to manage their psoriasis. 77% of patients selected websites and 73% selected in-person information as one of their top five preferred resources. Facebook and Twitter were least preferred. 28% of biologic users compared to 13% of non-biologic users mentioned health-care professional advice as a resource. Non-biologic users preferred websites, online forums, and Facebook compared to biologic users.

Conclusion: Biologic users were more satisfied with their treatment and experienced a more positive life impact compared to non-biologic users. Of the available biologics, blinded Stelara was most preferred. Patients preferred websites and in-person information over social media (Facebook/Twitter) as resources for psoriasis information.

CONFERENCE INFORMATION

Conference Venue:

McGill New Residence Hall

3625 Avenue du Parc, Montréal, QC, H2X 3P8

On-site Registration:

Limited onsite registration available.

Wireless Network:

Login Information provided along with registration package.

For dual participants (SRGs and CCTC), we request to keep the same login information.

Location of Sessions:

McGill New Residence Hall Ball Room - Prince Arthur B

Location of Poster Sessions:

NRH Salle Du Parc / NRH Salle Des Pins

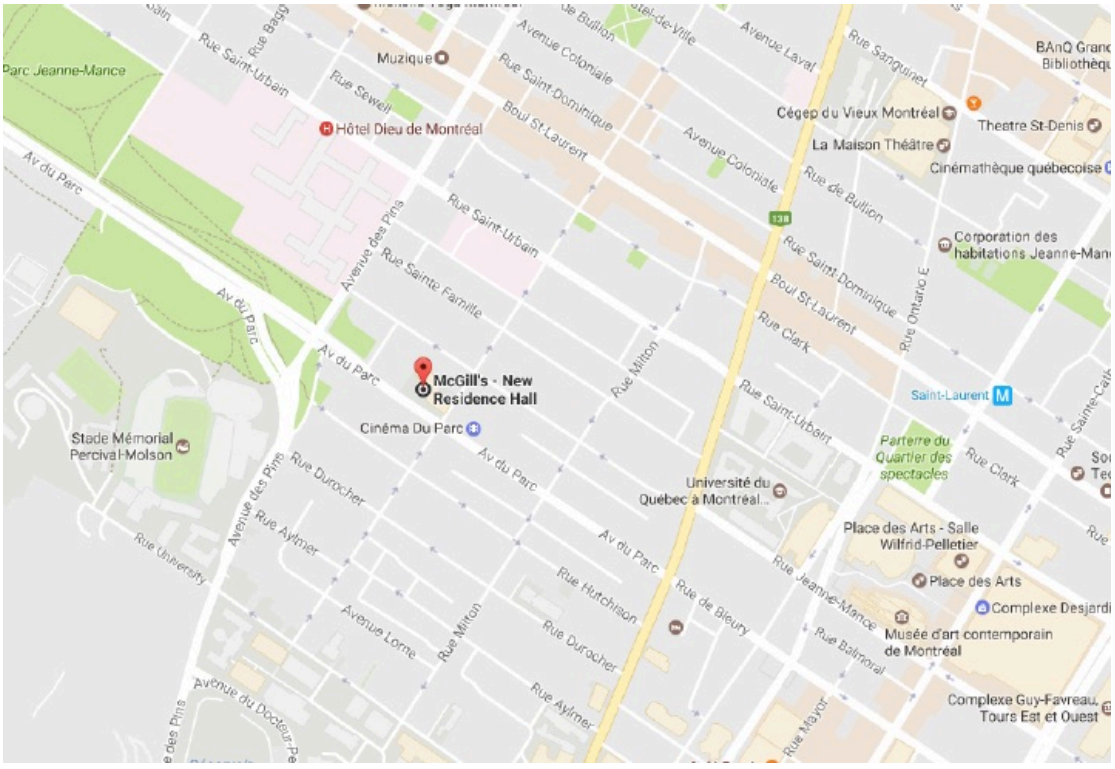
Reception and Cocktails:

Wednesday, May 17

From 6 - 7PM

McGill New Residence Hall C Foyer

Venue Map



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