Skin Research Group *of* Canada

8th Annual Conference

November 11 – 13, 2021

Le Westin

Montreal, Quebec

PROGRAM & ABSTRACTS

Skin Research Group *of* Canada 2021

Dear Colleagues and Friends,

It is my great pleasure to welcome you to the 8th Annual Skin Research Group of Canada (SRGC) Conference. The SRGC annual meeting is the premier national conference focused on skin research in Canada and has been held since 2014 after its inception in 2013. The SRGC conference represents a great platform and a highlight for skin researchers in Canada to come together to advance skin science, promote collaboration, interact with skin disease patients and support the next generation of skin scientists.

The SRGC 2021 conference is held in a hybrid format of in-person and virtual. We have a greater than usual attendance this year. The continued growth of our meeting is an indication of its high quality and impact. This year's meeting is co-chaired by Dr. Jeff Biernaskie from the University of Calgary and Dr. Josh Vorstenbosch of McGill University. We will have more than 140 attendees including researchers, clinicians and trainees from across Canada and a few international participants. The organizers have recruited a roster of distinguished thought leaders as keynote speakers, including Dr. Michael Longaker of Stanford University, Dr. Robert Gniadecki from the University of Alberta, and Dr. Sarvesh Logsetty, University of Manitoba.

The SRGC conference was established primarily as a liaison to bridge the gaps in basic and clinical skin research. A major focus of the conference is to encourage and motivate the next generation of young Canadian skin scientists by giving them the opportunity to showcase their research, as well as to interact with leading scientists in the field. Promising young basic- and clinician-scientists are recognized by providing best presentation awards, travel awards, and other engagement awards.

The objectives and anticipated impact of the conference is:

- *To improve the skin health of Canadians by stimulating knowledge exchange*
- *To facilitate the interaction of basic- and clinician-scientists*
- *To enhance the interaction between scientists and skin patient groups and industry partners.*

Again, welcome to SRGC 2021. I hope you will find the meeting to be both stimulating and rewarding. Thank you.

President, Skin Research Group of Canada
Anie Philip, Ph.D.
Professor, McGill University

Skin Research Group *of* Canada 2021

On behalf of the Scientific Organizing Committee, we would like to welcome you to the 2021 Skin Research Group of Canada Annual Scientific Meeting. As in years past, SRGC2021 will serve to showcase the very best in Canadian basic science, translational and clinical skin research.

We are particularly excited about this year's conference. The quality of abstracts across the wound healing & regeneration, clinical skin research, inflammatory skin diseases, skin cancer, and basic science domains impressed all the reviewers, leaving us confident that SRGC2021 will be our best yet.

We think that the breadth of our content will appeal to basic scientists, clinicians, and industry partners alike. And that by bringing together skin researchers from across Canada, we hope to further promote multi-disciplinary discussion and forging of new collaborations that will ultimately propel Canadian skin research even further forward.

This year SRGC2021 will be strategically held in parallel with DermUpdate, which will provide attendees with additional opportunities to learn about recent advances in understanding pathogenesis or novel therapeutics related to psoriasis, eczema, acne, skin cancer, autoimmune diseases, wound healing and many other topics.

Along with presentations from outstanding faculty and trainees from across Canada, we have an incredible slate of invited keynote speakers who will provide state-of-the-art lectures in pertaining to different aspects of skin disease and innovative therapeutics.

*We are extremely fortunate to have **Dr. Michael Longaker** from Stanford University, who will share his pioneering work into fibroblast biology and the influence of tissue biomechanics in determining wound healing outcomes. **Dr. Robert Gniadecki** from the University of Alberta will share new insights from his laboratory into the origins of cutaneous lymphoma. **Dr. Sarvesh Logsetty** from the University of Manitoba will discuss emerging innovations in clinical management of burn injury. Our final keynote lecture will be delivered by an SRGC founding member and a tireless advocate for interdisciplinary and translational skin research, **Dr. Anie Philip** of McGill University.*

Again, we are very excited about this year's program. SRGC 2021 will be offered in a hybrid format; both in-person at the Le Westin Hotel in Montreal and virtually in order to maximize our engagement across the skin research community. We look forward to sharing our programming with you as we celebrate cutting-edge skin research here in Canada.

Sincerely,
SRGC2021 Scientific Organizing Committee Co-chairs

Jeff Biernaskie, PhD ***Joshua Vorstenbosch, MD PhD FRSCS***

SKIN RESEARCH GROUP *OF* CANADA 2021

SRGC2021 Scientific Organizing Committee Co-chairs

Jeff Biernaskie, PhD
Dept. of Comparative Biology and Experimental Medicine
Faculty of Veterinary Medicine
University of Calgary

Joshua Vorstenbosch, MD PhD FRSCS
Plastic and Reconstructive Surgeon
Assistant Professor of Surgery
McGill University
Royal Victoria Hospital

Skin Research Group *of* Canada 2021

Scientific review committee

Andrew Leask, BSc, PhD
University of Saskatchewan

Anie Philip, PhD
McGill University

Aziz Ghahary, MSc, PhD, PDF
University of British Columbia

Dieter Reinhardt, MSc, PhD
McGill University

Ivan V Litvinov, MD, PhD, FRCPC
McGill University Health Centre

Jeff Biernaskie, PhD
University of Calgary

Joshua Vorstenbosch, MD, PhD, FRCSC
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Julie Fradette, PhD
LOEX/ Université Laval

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McGill University; Lady Davis Institute

Rachel Asiniwasis, MD, FRCPC, DABD
Origins Dermatology Centre, University of Saskatchewan, Department of Dermatology

Stéphane Roy, PhD
University of Montreal

Veronique Moulin, PhD
LOEX/ Université Laval

Skin Research Group *of* Canada 2021

Volunteers

Amelia Martínez Villarreal
Research Institute - McGill University Health Centre
Experimental Medicine | McGill University

Carla Spina
Exciton Pharma

François Lagacé
McGill University

Ilya Mukovozov
University of British Columbia

Jennifer Gantchev
Research Institute - McGill University Health Centre
Experimental Medicine | Cancer Research Program

Katlyn Richardson
Department of Pathology and Laboratory Medicine | University of British Columbia

Megan Pawluk
Department of Pathology and Laboratory Medicine | University of British Columbia

Nadia Kashetsky
Faculty of Medicine | Memorial University of Newfoundland

Neha Dinesh
Department of Anatomy and Cell Biology | McGill University

Nickoo Merati
McGill University

Rong-Mo Zhang
Department of Anatomy and Cell Biology | McGill University

Santina Conte
Faculty of Medicine | McGill University

Sara Mirali
University of Toronto

Sarthak Sinha
University of Calgary

Serena Mandla
University of Toronto

Thank you

SRGC 2021 Program November 11 – 13

THURSDAY, 11 NOVEMBER		
8:00 - 9:00am	**Registration & Poster Set Up**	
9:00 - 10:20am	**Plenary Session I**	**Wound Healing and Regeneration**
	Moderators: Katlyn Richardson & Ivan V Litvinov	
9:00am	**"Dynamic Interactions Between Host and Device at the Tissue-Implant Interface"** *Joshua Vorstenbosch, McGill University*	
9:20am	**"Quantifying hypertrophic scar and donor scar following burn injury"** *Zoë Edger-Lacoursière, McGill University*	
9:30am	**"Functional Roles of Fibulin-4 and Latent Transforming Growth Factor-β Binding Protein-4 in Skin Elastogenesis"** *Neha Dinesh, McGill University*	
9:40am	"**Filling the wound gap: Clinical translation of an instructional peptide-modified hydrogel in xenografted human skin wounds"** *Serena Mandla, University of Toronto*	
9:50am	**"Single-cell multi-omics reveals skin regeneration is enabled in the absence of fibroblast inflammatory priming"** *Sarthak Sinha, University of Calgary*	
10:00am	**"A shift in fibroblast heterogeneity in aging mice inhibits wound induced hair neogenesis (WIHN)"** *Wisoo Shin, University of Calgary*	
10:10am	**"Hypervalent Complexes in Wound Infection and Healing"** *Carla Spina, Exciton Pharma Corp.*	
10:20 - 12:00pm	**Come See My Poster (Moderated Poster Walks)** **Visit Our Sponsor Booths**	
12:00-1:00pm	*SRGC State-of-the-art Lecture* **Michael T. Longaker, MD, MBA, DSc (hon) FACS** **"Wound Repair, Fibroblast Heterogeneity and Fibrosis"** *Moderator: Anie Philip*	

1:00 - 2:50pm	**SRGC/ SkIN Canada Workshop – Industry career path** **Come See My Poster/ Visit Our Sponsor Booths**	
3:00 - 3:50pm	**Plenary Session II**	**Clinical Skin Research**
	Moderators: Anie Philip & Sarthak Sinha	
3:00pm	**"Prevalence of Contact Allergy to Nickel: A Retrospective Chart Review"** *Ilya Mukovozov, University of British Columbia*	
3:10pm	**"Extracellular Granzyme B in cutaneous leishmaniasis"** *Layla Nabai, University of British Columbia*	
3:20pm	**"Cosmesis and Viability of Right Angle Paramedian Forehead Flaps: A Retrospective Chart Review"** *Ilya Mukovozov, University of British Columbia*	
3:30pm	**"Ex vivo gene therapy of skin cells and autologous bilayered skin susbtitutes as a potential treatment for Recessive Dystrophic Epidermolysis Bullosa skin wounds"** *Martin Barbier, LOEX*	
3:40pm	**"Light and Laser-based Treatments for Granuloma Annulare: A Systematic Review"** *Nadia Kashetsky, Memorial University of Newfoundland*	
4:00 – 5:00pm	*SRGC State-of-the-art Lecture* **Robert Gniadecki, MD, PhD, DMSci** **"Systemic origin of the primary cutaneous lymphomas"** *Moderator: Joshua Vorstenbosch*	
5:00 - 6:00pm	**Reception TBA** **(Social distancing enforced, if permitted by public health officials)**	
	END OF DAY ONE	

FRIDAY, 12 NOVEMBER		
9:00 - 10:30am	**Plenary Session III**	**Inflammatory Skin Diseases**
	Moderators: Ilya Mukovozov & Carla Spina	
9:00am	**"Targeting the tumor stroma in checkpoint inhibitor-resistant melanoma"** *Andrew Leask, University of Saskatchewan*	
9:20am	**"Granzyme K: A Novel Therapeutic Target for Psoriasis"** *Katlyn Richardson, University of British Columbia*	

9:30am	**"Granzyme B Contributes to Radiation Dermatitis through E-Cadherin Cleavage and Loss of Epithelial Barrier Function"** *Megan Pawluk, University of British Columbia*
9:40am	**"Study of the role of pathological keratinocytes and their communication with T cells using tissue engineered psoriatic skin"** *Geneviève Rioux, Université Laval*
9:50am	**"Light and Laser-based Treatments for Hidradenitis Suppurativa: a Systematic Review"** *Sara Mirali, University of Toronto*
10:00am	**"Dermatological Conditions in Rural and Remote Indigenous Communities of North America: A Systematic Review"** *Jordanna Roesler, University of British Columbia*
10:10am	**"Investigation of the influence of alpha-linolenic acid in a 3-D engineered immunocompetent psoriatic skin model"** *Sophie Morin, Université Laval*
10:20am	**"Regulation of pulmonary fibrosis by cd109 in a murine model"** *Maha Alsharqi, McGill University*
10:30 - 12:00pm	**Come See My Poster: Virtual poster session**
12:00 - 1:00pm	*SRGC State-of-the-art Lecture* **Sarvesh Logsetty, MD, FRCPS, FRCS** **"Strength through Collaboration. Answering bedside questions with bench side science!"** *Moderator: Joshua Vorstenbosch* (Virtual presentation)
1:00 - 2:50pm	**SRGC/ SKiN Canada Workshop – Patient Engagement in Research** **"PATIENT ENGAGEMENT IN RESEARCH: TOP TIPS FOR WORKING WITH PATIENT ORGANIZATIONS"** *Rachael Manion, Executive Director; Canadian Skin Patient Alliance, Canadian Association of Psoriasis Patients* *Co-director; Skin Investigation Network of Canada* **"CLINICAL TRIALS ONTARIO - PATIENT DECISION AID"** *Dawn Richards, David Wells and Monica Parry* *Clinical Trials Ontario*
3:00 - 4:20pm	**Plenary Session IV** | **Skin Cancer** Moderators: *Joshua Vorstenbosch & Rong-Mo Zhang*
3:00pm	**"The transcriptional landscape analysis of basal cell carcinomas reveals novel signaling pathways and actionable targets"** *Philippe Lefrançois, Lady Davis Institute; Jewish General Hospital Division of Dermatology*

3:20pm	**"Unraveling the contribution of ACTL6A, a chromatin remodeling factor, to immune evasion in head and neck squamous cell carcinoma"** *Shu Feng Zhou, Harvard medical school*
3:30pm	**"Targeting the CD109-IL6 pathway in Squamous Cell Carcinoma"** *Amani Hassan, McGill University*
3:40pm	**"Therapeutic Targeting of Oncogenic EGFR Signaling using a CD109-based Peptide"** *Tenzin Kungyal, McGill University*
3:50pm	**"Intralesional rituximab in the treatment of indolent primary cutaneous B-cell lymphoma"** *Meagan-Helen Henderson Berg, McGill University*
4:00pm	**"How the Meiosis Gene HORMAD1 Contributes to the Development of Squamous Cell Carcinomas in Melanoma Patients"** *Jennifer Gantchev, McGill University*
4:10pm	**"PRAME Enhances Proliferation and Attenuates Retinoid Response in Keratinocyte Carcinoma and in Head and Neck Squamous Cell Carcinoma"** *Brandon Ramchatesingh, RI-McGill University Health Center*
4:30 -5:50pm	**Virtual Plenary Session** Moderators: Jeff Biernaskie & Julie Fradette
4:30pm	**"Application of a liquid dermal scaffold promotes wound healing in a mouse model"** *Aziz Ghahary, University of British Columbia*
4:50pm	**"Preferential recruitment of immature neutrophils enables robust skin regeneration"** *Elodie Labit, University of Calgary*
5:00pm	**"Investigating the Effects of CSF1R Inhibition on Skin Regeneration"** *Eren Kutluberk, University of Calgary*
5:10pm	**"Mental Health Prior to and Longitudinally During COVID-19: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study"** *Richard Henry, McGill University*
5:20pm	**"The PGC-1 coactivators control inflammation and immunosuppression in melanoma"** *Simon-Pierre Gravel, Université de Montréal*
5:30pm	**"Loss of Kindlin-1 causes actin cytoskeleton dysregulation and impaired keratinocyte cellular function"** *Samar Sayedyahossein, University of Western Ontario*
5:40pm	**"Transcriptomic Changes During Stage Progression of Mycosis Fungoides"** *Maggie Xiao, University of Alberta*
	END OF DAY TWO

SATURDAY, 13 NOVEMBER		
12:00-1:50pm	**SRGC/ SKiN Canada Workshop - Academic career path** **'Career Path of a University Professor in a Life Sciences Department: Challenges and Rewards'** *John H. White, McGill University* **'Career Path of an Academic Clinician-Scientist: Challenges and Rewards"** *Robert Gniadecki, University of Alberta* **'Academic Career Path from the Perspective of an Early Career Investigator'** *Holly Sparks, University of Calgary*	
2:00 - 3:00pm	*SRGC Keynote lecture* **Anie Philip, PhD** **"Role and Impact of SRGC in Advancing Skin Research in Canada"** *Moderators: Joshua Vorstenbosch & Ivan V Litvinov*	
3:00 - 4:10pm	**Plenary Session V**	**Basic Sciences**
	Moderators: Dieter Reinhardt & Amelia Martínez Villarreal	
3:00pm	**"Sex specific role of fibrillin-1 in adipose tissue development and function"** *Muthu Lakshmi Muthu, McGill University*	
3:10pm	**"Role of N-linked glycans in Fibulin-5 and LTBP-4S mediated matrix assembly and function"** *Valentin Nelea, McGill University*	
3:20pm	**"Exploring the role of autophagy in skin pigmentation"** *Brice Magne, Université Laval*	
3:30pm	**"Immunocompetent, vascularized, autologous 3D skin model reconstructed by tissue engineering for wound healing studies"** *Emilie Attiogbe, LOEX*	
3:40pm	**"Differential interaction of LOXL1 variants linked to pseudoexfoliation syndrome with fibulin-4, fibulin-5 and tropoelastin"** *Valentin Nelea, McGill University*	
3:50pm	**"Using physiological factors to improve self-assembled skin substitutes pigmentation"** *Karel Ferland, LOEX*	
4:00pm	**"Deciphering the functions of FGD RhoGEFs during skin development"** *Melanie Laurin, Université Laval*	
4:30 - 5:00pm	**AWARD CEREMONY/ INTRODUCTION OF NEW SRGC PRESIDENT**	
5:00 - 6:00pm	**PRESIDENT RECEPTION (TBD)**	

SRGC
State-of-the-art Lecture

Thursday
November 11, 2021
(12:00 – 1:00 PM)

"Wound Repair, Fibroblast Heterogeneity and Fibrosis"

Michael T. Longaker, MD, MBA, DSc (hon) FACS
Deane P. and Louise Mitchell Professor and Vice Chair
Co Director, Stanford Institute for Stem Cell Biology and Regenerative Medicine
Director, Children's Surgical Research
Director, Program in Regenerative Medicine
Professor, by Courtesy, of Bioengineering
Professor, by Courtesy, Department of Materials Science and Engineering
Director, Human Health Initiative
Stanford University School of Medicine
Lucile Salter Packard Children's Hospital

Wound healing represents an acute form of fibrosis, in contrast to chronic forms of fibrosis seen in radiation skin injury, adhesions, pulmonary fibrosis, foreign body response, and the desmoplastic /scar reaction that occurs around tumors. There are 100 approximately 100 million new scars per year in the United States between surgery and injuries and this number is 4 to 5 times higher but when taking it worldwide. This talk will review how inhibiting mechanotransduction reduces fibrosis during wound repair. I will review YAP inhibition during wound healing resulting in regeneration rather than scarring. A novel artificial intelligence extra cellular matrix ultrastructure method will be discussed. Lastly, I will be presenting unpublished data using an integrated spatial multi-omics strategy to reveal fibroblast fate during wound repair.

Michael T. Longaker earned his undergraduate degree at Michigan State University, (where he played varsity basketball and was a member of the 1979 NCAA Men's Basketball Championship Team) and his medical degree at Harvard Medical School. He completed his surgical residency at the University of California, San Francisco, a residency in Plastic Surgery at NYU and a craniofacial fellowship at UCLA. The majority of his research training took place while he was a Post Doctoral Research Fellow in the Fetal Treatment Program under Dr. Michael Harrison and in the laboratory of Dr. Michael Banda in Radiobiology, both at UCSF. In December 2003, Dr. Longaker earned his M.B.A. from University of California – Berkeley and Columbia University, in the inaugural class of their combined program. He was elected into Beta Gamma Sigma at Columbia Business School, which is the analogous to Phi Beta Kappa for business programs

Dr. Longaker joined the Stanford University School of Medicine on September 1, 2000, as Director of Children's Surgical Research in the Department of Surgery, Division of Plastic and Reconstructive Surgery and the Lucile Salter Packard Children's Hospital. In 2003, he was named the Deane P. and Louise Mitchell Professor. As Director of Children's Surgical Research, Dr. Longaker has the responsibility to develop a children's surgical research program in the broad areas of developmental biology, epithelial biology and tissue repair, and tissue engineering. Dr. Longaker is the Co- Director of the Stanford Institute of Stem Cell Biology & Regenerative Medicine, as well as the Director of the Program in Regenerative Medicine, Director of Research in the Division of Plastic and Reconstructive Surgery, and has been name Professor, by Courtesy, in the Department of Bioengineering, and Professor, by Courtesy, Department of Materials Science and Engineering. Dr. Longaker is Vice Chair of the Department of Surgery.

Michael Longaker's extensive research experience includes the cellular and molecular biology of extracellular matrix with specific applications to the differences between fetal and post-natal wound healing, the biology of keloids and hypertrophic scars and the cellular and molecular events that surround distraction osteogenesis with respect to craniofacial development. Most recently he has identified a scar culprit on the dorsum of mice and has blocked mechanotransduction to yield wound regeneration without scarring.

Dr. Longaker is a member of all the major academic surgery societies and was president of both the Society of University Surgeons (2007-08) and the Plastic Surgery Research Council (2006-07). He is one of a handful of surgeons elected into the American Society for Clinical Investigation, Association of Physicians, and National Academy of Medicine. To date, he has over 1300 publications and multiple federal grants to support his research.

SKIN RESEARCH GROUP *of* CANADA

8th Annual Conference

SRGC
State-of-the-art Lecture

Thursday
November 11, 2021
(4:00 – 5:00 PM)

"Systemic origin of the primary cutaneous lymphomas"

Robert Gniadecki, MD, PhD, DMSci
Director & Professor
Faculty of Medicine & Dentistry - Medicine
Dept Dermatology
University of Alberta

Dr. Robert Gniadecki received his MD degree from Warsaw Medical School (Poland) in 1991 and three years later he obtained his PhD from the Faculty of Health Sciences at Copenhagen University (Denmark) and became a specialist in dermatology in 2001 (certified in Denmark and Canada). In 2010 he was appointed as a full clinical professor at the University of Copenhagen and in 2015 at the University of Alberta, Canada. Dr. Gniadecki has served as a president of the Danish Dermatological Society, treasurer of the Canadian Dermatology Foundation and board members of the ESDR (European Society of Dermatological Research) and ISCL (International Society of Cutaneous Lymphomas). Among major clinical and scientific accomplishments are: development of the low-dose protocol of total skin irradiation for patients with cutaneous lymphomas, the discovery of lymphoma stem cells and introduction of photophoresis and Mohs surgery to dermatology in Denmark. His current scientific activities focus on genomics the experimental therapeutics of cutaneous lymphoma and autoimmune skin diseases and the clinical aspects of the biological treatment of psoriasis.

SKIN RESEARCH GROUP *of* CANADA

8th Annual Conference

SRGC
State-of-the-art Lecture

Friday
November 12, 2021
(12:00 – 1:00 PM)

"Strength through Collaboration. Answering bedside questions with bench side science!"

Sarvesh Logsetty, MD, FRCPS, FRCS
Director Manitoba Firefighters Burn Unit
Professor Departments of Surgery, Psychiatry, Children's Health
Rady Faculty of Health Sciences
University of Manitoba

After graduating from the University of Alberta with a Bachelor of Science and M.D in 1990, Dr. Logsetty obtained his Diploma in Clinical Epidemiology from the University of Toronto in 1996. Dr. Logsetty completed the Surgical-Scientist Program at University of Toronto in 1994-1996. He continued his training in fellowships in Acute Burn Care & Reconstructive Surgery at Ross Tilley Burn Centre in Wellesley Hospital in Toronto, Ontario (1996-1998) and in Critical Care of Burns at Harborview Medical Centre in Seattle, Washington (1998-1999). Dr. Logsetty holds certifications with The Royal College of Physicians and Surgeons and the American Board of Surgery.

Dr. Logsetty was Associate Director of the Firefighters Burn Treatment Unit at the University of Alberta Hospital from 1999-2007. In 2007 he was recruited by the University of Manitoba and the Health Sciences Centre to be Provincial Director of the Burn program located at Health Sciences Centre in Winnipeg. He is a Professor of Surgery at the University of Manitoba with cross-appointments to Psychiatry and Pediatrics.

He has dedicated his career to building a strong clinical program and creating a multi-disciplinary program of research specializing in burn and traumatic injury in order to improve patient care. Over his thirty-year career, his goal has been to improve healthcare and healthcare access.

Dr. Logsetty has taught multidisciplinary healthcare students at all levels of education from undergraduates, to established practitioners. Additionally, he has participated in the creation of new and innovative means of delivering educational content. As a result of his success he has been nominated for teaching awards, winning the Top Clinician Award and Patient Advocacy awards. A significant outcome of his teaching is the creation of evidence based standardized care for burn patients for Manitoba. This standardization facilitates referrals, inter-region transfer, and improved overall patient care.

He has rewritten the Burn chapter for the current edition of ATLS, aligning it with ABLS and participated in the conversion to the ATLS mobile learning platform. In January 2016, he recorded the 'Voice of Experience' for the Burn chapter of the ATLS mobile edition. Striving to improve burn care throughout the world, he is the lead author of the Essential Burn Management course for Low- and Middle-Income countries. This course has been developed through a grant from CIDA and published under the Canadian Network for International Surgery.

Research based on patient needs is the foundation for his success. All his research questions start with: 'What is important for the patient?'. He has developed multidisciplinary collaborations with experts in various fields to address these needs. Experts include biomaterials engineers, medical microbiology and infectious disease specialists, administrative data and epidemiology researchers, stem cell and regenerative medicine researchers and community members. By breaking down silos of knowledge, he has developed a robust cross platform program of research that addresses bedside needs with advanced bench side techniques leading to innovations in research approaches, novel strategies and products, and a successful and fruitful learning environment for students. He is widely published in many topics, with over 80 publications and book chapters. Scopus identifies over 1000 citations of his work with an H-index of 18. He holds over $2 million dollars of peer reviewed funding at the Tri-council level as PI, and is a co-investigator on numerous other grants.

Dr. Logsetty has also led the Canadian burn community to a successful CIHR Network catalyst grant application. This funded network has created an annual Canadian Burn symposium, a website for patients and providers alike, a national burn registry organization, is developing a disaster plan for Burn care for Canada, and triggered the formation of a multidisciplinary Canadian Burn Association. The network has coalesced burn care from isolated silos of excellence to a national group that is poised to standardize burn care in the nation and embark on multicenter trials to improve care for Canadians.

More recently Dr. Logsetty has built on his clinical observations that injury disproportionately affects some socioeconomic groups, to investigate social determinants of health. His work on pediatric burn injury and social determinants won the top pediatric burn award at the American Burn Association meeting in 2020. This information will be used to create prevention plans to reduce burn injury in children.

SKIN RESEARCH GROUP *of* CANADA

8th Annual Conference

SRGC keynote Lecture

Saturday
November 13, 2021
(2:00 – 3:00 PM)

"The Role and Impact of SRGC in Advancing Skin Research in Canada"

Anie Philip, PhD

Professor, McGill University
Director, Plastic Surgery Research
Department of Surgery, McGill University
President, Skin Research Group of Canada
Associate Director, Skin Investigation Network of Canada

The talk will discuss the origin and history of the Skin Research Group of Canada (SRGC) and its evolution into the SRGC of today. It will also examine SRGC's core values, strengths, and opportunities for growth as well as future challenges. In addition, the talk will review SRGC's commitment to improving the skin health of Canadians by advancing skin research and stimulating knowledge exchange. We will discuss how SRGC's success is dependent on factors such as strong interactions between basic- and clinician-scientists, between scientists and skin patient groups and industry partners, and fostering of the next generation of skin scientists.

Anie Philip (PhD) is a full professor at McGill University and a Senior Scientist at the Research Institute of the McGill University Health Center (RI-MUHC).

Dr. Philip's research is centered on understanding the cellular mechanisms underlying the differential regulation of transforming growth factor-beta (TGF-β) signaling pathways and their role in diseases such as organ fibrosis, osteoarthritis, and squamous cell carcinoma. Her team uses a combination of molecular and genetic approaches employing in vitro, in vivo and ex vivo models to study the dysregulation of distinct TGF-β signaling pathways, ad their cross-talk with other signaling pathways and networks, in the context of diseases mentioned above.

Dr. Philip's research is supported by several granting agencies including CIHR Project Grants, CIHR Network grant, NSERC Discovery grant, and an FRQS grant. Her laboratory has trained a large number of PhD and MSc students, post-doctoral Fellows/surgical residents, and undergraduate/ medical students. Dr. Philip has served as the Graduate Program Director for the Department of Surgery from 2013-2020. Dr. Philip is a founding member and is currently the President of 'Skin Research Group of Canada'. She is also a founding member and Associate Director of the 'Skin Investigators Network of Canada (SkIN Canada)'.

Oral Presentation Abstracts

Thursday, 11 November **Plenary Session I Wound Healing and Regeneration** **9:00 - 10:20am**	
Joshua Vorstenbosch	**9:00 – 9:20am**
Dynamic Interactions Between Host and Device at the Tissue-Implant Interface	
Joshua Vorstenbosch **McGill University**	
Abstract not available	

Zoë Edger-Lacoursière	**9:20 – 9:30am**

Quantifying Hypertrophic Scar and Donor Scar Following Burn Injury

Zoë Edger-Lacoursière, MSc OT 1, Elisabeth Marois-Pagé MD 2, Ana de Oliveira, BScb, 3, Marie-Andrée Couture MRéad, BSc OT 2, V. Calva BSc OT 2, José A. Correa, PhD 4, Bernadette Nedelec, BSc OT, PhD 1,2,3

Introduction: Very few objective scar evaluations have been conducted with the burn survivor population, which limits our knowledge of the clinical recovery profile of hypertrophic scars (HSc) and donor site scars (D). **The study purpose was to prospectively quantify skin characteristics of post-burn HSc in different anatomical locations, donor (D) and normal skin (N) using objective instrumentation.**

Methods: Skin characteristics of HSc, D and N in 44 burn survivors were measured at 2, 3, 4, 5, 6- and 7-months post-burn using validated instrumentation: high-frequency ultrasound for thickness, Cutometer® to measure pliability and Mexameter® to measure erythema and pigmentation. Up to five sites were assessed on the same participant if their scar was located on the upper extremity (UE), lower extremity (LE) and trunk. A mixed model two-way analysis of variance was used to investigate the differences in means between sites at each time point and between time points at each site.

Results: The results revealed that HSc sites were thicker than D and N at all time points and UE and trunk HSc were thicker than LE HSc at 7 months post-burn, pliability of trunk HSc did not improve over time, and UE HSc was more erythematous at 7 months compared to other anatomical sites whereas D erythema decreases from 2 to 7 months.

Conclusions: Scar management treatments should prioritize the UE and trunk sites which developed HSc during the first two months post-burn and continues to vary significantly from normal scar and normal skin at 7 months. Furthermore, these results provide preliminary evidence that the recovery profile of HSc varies at different anatomical sites and that thickness is the characteristic that distinguishes HSc from normal scar and normal skin.

Learning objectives:

- Distinguish the recovery profile of HSc and donor site scar following burn injury
- Justify the scar management treatment priorities according to anatomical location
- Describe the different objective instrumentation used to characterize HSc

Takeaway Message: Clinicians have prioritized UE treatments due to their functional importance; this study provides objective measurements to further support this practice and encourages clinicians to also prioritize trunk HSc treatments after burn injury.

Neha Dinesh	9:30 – 9:40am

Functional Roles of Fibulin-4 and Latent Transforming Growth Factor-β Binding Protein-4 in Skin Elastogenesis

Hakami. H*1; Dinesh. N*1; Nelea V*1,2; Zhao Y*1; Zhang. R*1; Vane. NL*1; Blum. SR*3; Reinhardt. DP*1,2

1.Faculty of Medicine, Department of Anatomy and Cell Biology, McGill University, Montreal, QC H3A 0C7, Canada;

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3.Institute of Molecular and Supramolecular Chemistry and Biochemistry, UMR 5246, Villeurbanne, France.

Introduction: Elastic fibers provide elasticity as well as a growth factor repository to skin and blood vessels. Elastogenesis is a hierarchical process, involving several key matrix proteins such as fibulin-4 (FBLN4) and latent TGF-β binding protein-4 (LTBP4). It is known that cells interact with FBLN4 and LTBP4, however the cell receptors involved remains unidentified. Therefore, identification of the target cell receptors and understanding the associated molecular mechanism, are the subjects of the present study.

Methods: Normal skin fibroblasts (NSF) and vascular smooth muscle cells (SMC) were employed as the cell culture model. Cell interaction and binding to recombinant FBLN4 and LTBP4 was analyzed through cell binding and solid phase assay. siRNA knockdown experiments were performed to identify the target cell receptors. The effect of FBLN4 and LTBP4 on cell contraction was explored using collagen-gel contraction assays.

Results: NSFs and SMCs bind strongly to FBLN4 and LTBP4. FBLN4 exclusively interacted as multimers and the multimerization sites were mapped to cbEGF4-5 and the C-terminal domain. We identified two cell interaction epitopes on FBLN4, located in cbEGF2-3 and the C-terminal domain. New cell interaction site in LTBP4 were mapped to the N-terminal half. Cell interactions with FBLN4 and LTBP4 significantly enhanced focal adhesion formation (FA) and reduced cell contraction, with a significant increase of Erk1/2 protein levels and RhoA GTP. Cell binding to FBLN4 and LTBP4 was absent in the presence of heparin and was significantly reduced upon heparan sulphate or heparinase treatment. siRNA knockdown of syndecan (SDC)-2 or -3 abolished NSF interaction with FBLN4, whereas only SDC-3 knockdown abolished the interaction with LTBP4. Direct interactions between FBLN4 and either SDC-2 or -3, and between LTBP4 and SDC-3 were determined. Knockdown of SDC-2 or -3 in NSFs also resulted in compromised elastic fibers.

Conclusions: The results suggest that FBLN4 and LTBP4 cell interactions via (SDC)-2 or -3, promote elastogenesis by enhancing FA formation, leading to cell contractility through Erk1/2 and RhoA activation. The identified mechanism is essential for proper elastic fiber formation in skin.

Learning objectives:

- To analyze cell interactions with elastogenic proteins FBLN4 and LTBP4 and map the interaction sites on these molecules.
- To identify the cell receptors involved in FBLN4 and LTBP4 cell interactions.
- To determine the functional consequence of the FBLN4 and LTBP4 cell receptor interaction on elastogenesis.

Takeaway Message: Elastogenic skin cells interact with FBLN4 and LTBP4 through receptors (SDC)-2 or -3, to promote elastogenesis by enhancing focal adhesion formation and cell contractility. Inhibition of the identified mechanism leads to compromised elastic fibers. FBLN4 and LTBP4 mediated cell interactions are therefore essential for proper elastogenesis in skin.

Serena Mandla	9:40 – 9:50am

Filling the Wound Gap: Clinical Translation of An Instructional Peptide-Modified Hydrogel in Xenografted Human Skin Wounds

Serena Mandla*2-3+, Holly D. Sparks1+, Katrina Vizely2-4, Nicole Rosin1, Jeff Biernaskie1,3,4*, and Milica Radisic2-4

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Introduction: Poor quality (eg. excessive scarring) or delayed closure of skin wounds can have profound physical and pyschosocial effects on patients as well as pose an enormous economic burden on the healthcare system. Despite wound care being a multi-billion-dollar industry, effective treatments aimed at rapidly restoring the skin barrier function or mitigating the severity of fibrotic scar remain elusive. There is a great need in the clinic for instructional biomaterials, which can provide healing cues to accelerate wound closure.

Methods: Previously, a conjugated angiopoietin-1 derived peptide (QHREDGS; Q-peptide) was shown to increase keratinocyte migration and improve wound healing in diabetic mice and equine lower limb wounds. Here, we evaluated the effect of this Q-Peptide Hydrogel on adult human skin wound healing using a mouse xenograft model.

Results: Q-Peptide Hydrogel treatment enhanced wound re-epithelialization via increased keratinocyte migration and survival, rather than proliferation. Through ELISA analysis, we observed an increase in several key cytokines that are known to positively impact wound healing when keratinocytes were grown on the Q-Peptide hydrogel, demonstrating a possible pro-healing phenotype shift. Moreover, we also observed an increase in neovascularization and new fibrillar collagen deposition within wound neodermis, indicating that Q-peptide positively influences both epidermal regeneration and dermal fibroblast behavior during wound healing.

Conclusions: These data provide strong evidence that the single topical application of QHREDGS peptide-modified hydrogels result in accelerated closure and superior quality of wound healing that may lead to improved outcomes for patients.

Learning objectives:

- Development and characterization of an instructional biomaterial for wound healing applications.
- The use of a human skin xenograft model as an early predictor for human clinical data.
- The QHREDGS peptide is effective at accelerating healing, and is ready for future use on humans' wounds.

Takeaway Message: The wound healing space is in desperate need of a novel, instructional biomaterial. Safety and efficacy data on the Q-Peptide Hydrogel supports accelerated healing in animal models, and clinical translation into humans.

Sarthak Sinha	9:50 – 10:00am

Single-Cell Multi-Omics Reveals Skin Regeneration Is Enabled in The Absence of Fibroblast Inflammatory Priming

Sarthak Sinha (1), Holly D. Sparks (1), Hayley Robbins (1), Kevin Gowing (1), Arzina Jaffer (1), Rohit Arora (1), Micha Sam Brickman Raredon (6,7), Leslie Cao (1), Scott Swanson (8), Peng Jiang (8), Olivia Hee (1), Hanna Pope (1), Elodie Labit (1), Matt Workentine (1), Laura Niklason (6,7), Nicole L. Rosin (1), Greg Muench (1), Ron Stewart (8), John Matyas (1,5), Robert McCorkel (l1), Jeff Biernaskie (1,2,3,4)

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Introduction: In adult mammals, skin wound healing has evolved to favor rapid repair through formation of fibrotic scar, leading to chronic impairment. Mechanisms that drive fibrosis and prevent tissue regeneration remain unknown. We show that adult reindeer (*Rangifer tarandus*) antler velvet exhibits regenerative wound healing, whereas identical full-thickness injury in back skin forms fibrotic scar. This remarkable regenerative capacity is retained even following ectopic transplantation of velvet to a scar-forming site.

Methods: Single-cell mRNA and ATAC-Sequencing was performed at four wound stages to reconstruct spatiotemporal dynamics of fibroblasts and immune cells during regenerative and fibrotic healing. Candidates identified were validated using RNAScope and by pharmacologic manipulation of signalling pathways via peri-wound intra-dermal injections.

Results: Single-cell RNA- and ATAC-Seq of uninjured skin revealed a marked divergence in resting fibroblast states and immunomodulatory function. Uninjured velvet fibroblasts shared a striking similarity to human fetal fibroblasts (marked by enrichment of *MDK, CRABP1, TPM1*) whereas back skin fibroblasts were enriched for pro-inflammatory genes resembling adult human fibroblasts (*IL6, PTGES, PTGDS, CCL2, CXCL3, CSF1*). Injury resulted in site-specific fibroblast polarization; back skin fibroblasts amplified the inflammatory response, whereas velvet fibroblasts adopted an immunosuppressive state leading to an accelerated adoption of anti-inflammatory and immature immune states followed by expedited resolution of immune response. Consequently, velvet fibroblasts underwent fate reversion to readopt their native regeneration-competent ground state. Pharmacologic recapitulation of back skin fibroblast immunostimulatory secretome (PLAU, PDG, or a combination of PLAU, CSF1, CXCL3 and CCL2) or inhibition of velvet fibroblast regenerative secretome (MDK) attenuated velvet regenerative potential and promoted scarring.

Conclusions: Purposeful decoupling of stroma-immune crosstalk and reinforcement of fibroblast regenerative programming represent important therapeutic avenues to mitigate scarring and improve regenerative healing. Our online companion *Reindeer Atlas* (www.biernaskielab.ca/reindeer_atlas) provides an accessible conduit to further explore the molecular programs underlying skin regeneration versus fibrosis and to spur further discovery.

Learning objectives:

- Single-cell mRNA-Sequencing allows dissection of transcriptional dynamics at single-cell resolution to study cellular heterogeneity and function during health, healing, and disease.
- Single-cell Assay for Transposase-Accessible Chromatin with sequencing (scATAC-Seq) allows examination of epigenetic states by measuring genome-wide chromatin accessibility and asking how chromatin configuration and other factors (e.g., transcription factor binding motif accessibility) impact transcription.
- Fibroblast secretome refers to the set of proteins fibroblasts secrete into the extracellular space during hemostatic or healing skin.
- Similar to immunopathologies seen during lung infection (Boyd et al. *Nature* 2020) or autoimmune skin lesions (Reynolds et al. *Science* 2021), our findings suggest that pathologic healing in reindeer back skin is driven by fibroblast-potentiated inflammatory signals that amplify effector immune programs at the expense of tissue function.

Takeaway Message:

1. The adult reindeer represents a powerful mammalian model to directly compare skin regeneration and fibrosis within the same animal.
2. Mammalian skin regeneration may be the intrinsic reparative response, but its realization is pre-empted by exuberant inflammation incited by fibroblast ground-state priming.

Wisoo Shin	10:00 – 10:10am

A Shift in Fibroblast Heterogeneity in Aging Mice Inhibits Wound Induced Hair Neogenesis (WIHN)

Wisoo Shin1,2, Elodie Labit1, Sarthak Sinha1, Sepideh Abbasi1, Eren Kutluberk1, Leslie Cao1 and Jeff Biernaskie1,3,4

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Introduction: Aging animals accumulate tissue-specific impairments throughout life. One example is a reduced capacity to heal and regenerate the aged skin after injury. Recent work has highlighted the impact of advanced age on fibroblast biology and ultimately how aging fibroblasts affect normal dermal function and wound healing. Yet, how aging affects the processes involved in mammalian tissue regeneration remains largely in question. Here, we utilize a unique mammalian regenerative phenotype known as wound induced hair neogenesis (WIHN) to investigate the impact of aging fibroblasts on skin regeneration after wounding.

Methods: To first characterize the fibroblast transcriptional response to injury in young versus aged animals, wound samples were collected for single cell RNA sequencing (scRNAseq) from wound-age matched 2mo (young, 14dpw) and 18mo (aged, 21 dpw) Hic1CreERT2:RosaTDTomato mice (n = 2). Further analysis of dermal progenitor response to injury was completed by isolating dermal progenitors prior to injury (control) and 14dpw (wound) from 2mo and 18mo Hic1CreERT2:RosaTDTomato mice (n=2) for scRNAseq analysis.

Results: Aged mice fail to undergo WIHN and do not regenerate appendages such as hair follicles and sebaceous glands after injury. Our scRNAseq data uncovers a profound shift in fibroblast heterogeneity and their response during wound healing. Aged wounds are dominated by fibroblasts possessing "senescent-like" characteristics and these fibroblasts persist into late stages of wound healing, which may interfere with the typical regenerative response. Further scRNAseq analysis also revealed that aged, but not young, fibroblasts exhibit "senescent-like" characteristics after an injury, suggesting aged fibroblasts possess a preferential bias to adopt a senescence state. Indeed, the altered fibroblast phenotypes within the aged wound bed create an unorthodox paracrine microenvironment that suppresses WIHN in aged mice.

Conclusions: Progressive dysfunction within wound-responsive dermal fibroblast progenitors and consequent deviation in fibroblast heterogeneity in the aged wound bed contribute to the age-related loss of regenerative capacity.

Learning objectives:

- To describe the impact of aging on fibroblast transcriptional profiles.
- Provide an overview of how to interpret data generated using single cell RNA sequencing
- To describe the impact of advanced age on fibroblast response to injury and to specifically examine the impact on known pro-regenerative programs

Takeaway Message: Aging alters dermal fibroblasts ground state, which predisposes their adoption of a senescent state in response to injury and this prevents engagement of transcriptional programs necessary for regeneration.

Carla Spina	10:10 – 10:20am

Hypervalent Complexes in Wound Infection and Healing

Carla Jehan Spina(a)*, Vida Maksimoska(b), Carlie Goodall(c), Johanny Notarandrea-Alfonzo(a), Danae Guerra López(d), Cezar M. Khursigara(c), D. Scott Bohle(d), Katalin Szaszi(b), Rod Precht(a)

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Introduction: Wound healing is a complex process, further complicated by infection. This study investigates *in-vitro antimicrobial and cytotoxic and healing* response to a dual hypervalent chelate complex.

Methods: Tripotassium silver bisperiodate of the general formula K3AgBP (BP = [IO4(OH)2]2)(H2O)4) was prepared via chemical oxidation. Antibacterial susceptibility to K3AgBP and a β-lactam antibiotic were evaluated against clinical isolates of methicillin-susceptible and resistant *Staphylococcus aureus* (USA-300 MSSA & MRSA). Experimental evolution of resistance against MSSA was profiled over 20 days sub-MIC exposure to K3AgBP and oxacillin. Antibiofilm efficacy of the K3AgBP complex was determined against established *S. aureus* (ATCC 6538) biofilm. Keratinocyte (HaCaT) 2hr *in-vitro* cytotoxicity and mobility was investigated via MTT assay and gap migration, respectively.

Results: Spectroscopic and solid-state studies confirm stable hypervalent states of Ag(III) and I(VII) within the chelate complex. MRSA and MSSA isolates are susceptible to K3AgBP. K3AgBP exhibited significantly greater ($p < 0.001$) efficacy versus oxacillin against MRSA. No acquired resistance was observed for K3AgBP over 20-day sub-MIC exposure, versus a 12-fold increase in MIC for oxacillin. Within this K3AgBP concentration range, >75% keratinocyte metabolic activity was maintained versus control without delaying cell migration. Established *S. aureus* biofilm were readily disrupted and eradicated, >6 log reduction, within 6 hours of K3AgBP treatment.

Conclusions: Stabilized in a distorted square planar bis-chelate complex, containing silver, Ag(III), and iodine I(VII) in hypervalent states, K3AgBP exhibits antimicrobial efficacy against drug-resistant bacteria inclusive of biofilm without impairing keratinocyte migration.

Learning objectives:

- K3AgBP is an effective antimicrobial against MRSA/MSSA.
- MSSA more readily acquires resistance to β-lactam antibiotic oxacillin.
- K3AgBP effectively disrupts *S. aureus* biofilm.
- K3AgBP does not impair keratinocyte cell migration.

Takeaway Message: K3AgBP may be a viable antimicrobial agent for the topical management of skin and wound infection. Further in-vivo studies are needed to verify in-vitro findings.

Thursday, 11 November
Plenary Session II Clinical Skin Research
3:00 - 3:50pm

Ilya Mukovozov	**3:00 – 3:10pm**

Prevalence of Contact Allergy to Nickel: A Retrospective Chart Review

Ilya M. Mukovozov1*, Nadia Kashetsky2* and Gillian de Gannes1,3
**** Equal contribution***
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Introduction: Nickel allergy is currently the most common cause of contact dermatitis in the industrial world, however, there are no studies reporting the prevalence of contact allergy to nickel in Canadians.

Methods: Retrospective chart review of 3263 patients patch tested for nickel sensitivity at the Contact Dermatitis Clinic at St. Paul's Hospital in Vancouver, Canada, from January 1, 2008 to April 14, 2020. Nickel sensitivity was defined as a positive patch test to nickel. Descriptive statistics, chi-square tests and the chi-square test of trend were used for statistical analysis.

Results: In total, 24.3% (n=792/3263) of patients were sensitive to nickel. There was a significant increase in nickel sensitivity over time occurred from 24.3% (n=388/1597) in 2008 to 2012, to 27.9% (n=282/1010) in 2016 to 2020. Patients with nickel sensitivity were significantly more likely to be female ($p < 0.001$; relative risk [RR]: 1.83; 95% confidence interval [CI]: 1.52-2.19), between the ages of 19 and 64 ($p = 0.010$; RR: 1.29; 95% CI: 1.05-1.53), and have dermatitis affecting the face ($p = 0.001$; RR: 1.23; 95% CI: 1.09-1.39) and hands ($p = 0.001$; RR: 0.79; 95% CI: 0.68-0.91). Nickel sensitive patients were significantly less likely to be 65 or older ($p = 0.001$; RR: 0.71; 95% CI: 0.57-0.88) and have dermatitis affecting the legs ($p = 0.002$; RR: 0.63; 95% CI: 0.47-0.86). There was no statistical difference in the frequency of nickel sensitivity by presence or type of atopic history.

Conclusions: Approximately one quarter of patients were sensitive to nickel and frequency of nickel sensitivity significantly increased over time. Nickel sensitive patients were more likely to be female, age 19 to 64, and have dermatitis affecting the face and hands; and less likely over age 64 and have dermatitis affecting the legs. As detailed analysis of trends in nickel sensitivity in Canada are lacking, we encourage other Canadian sites to share their nickel sensitivity results.

Learning objectives:

- Clinicians should be aware of a significant increase in nickel sensitivity over time in Canada from 24.3% to 27.9% from 2008 to 2020.
- Nickel sensitive patients were significantly more likely to be female, between the ages of 19 and 64, and have dermatitis affecting the face, and hands; and significantly less likely to be 65 or older and have dermatitis affecting the legs.
- Approximately half of nickel sensitive reactions were new positive reactions at the second reading, reinforcing the importance of delayed readings in determining nickel sensitivity.

Takeaway Message: Approximately one quarter of patients were sensitive to nickel and frequency of nickel sensitivity significantly increased over time. Nickel sensitive patients were more likely to be female, age 19 to 64, and have dermatitis affecting the face and hands.

Layla Nabai	3:10 – 3:20pm

Extracellular Granzyme B in Cutaneous Leishmaniasis

Layla Nabai1, Yasaman Kaviani1, Karen Jung1, Reza Yaghoobi2, Farhad Handjani3, Nastaran Ranjbari4, Fatemeh Sari Aslani3, Nader pazyar2, Mohammad Mahdi Parvizi3, Nicholas Carr5 , Hongyan Zhao1, W. Robert McMaster6 , David Granville1

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Introduction: Cutaneous leishmaniasis (CL) is an infectious disease caused by leishmania parasite and affects up to 1 million new cases worldwide annually. The inflammatory reaction towards elimination of the parasite commonly results in severe scarring and disfigurement with significant psychosocial sequelae. Granzyme B (GzmB) is a serine protease classically known to be secreted by cytotoxic lymphocytes through synapses to targeted cells to mediate intracellular apoptosis. It is now established that GzmB is also active in the extracellular milieu in chronic inflammatory conditions as a result of synapse leakage and release by immune and non-immune cells. A considerable body of evidence has shown a significant increase in granzyme B expression and activity in CL lesions. Although the cytotoxic role of intracellular GzmB in parasite killing and targeted apoptosis in CL is well known, the contribution of extracellular GzmB to chronic inflammation, tissue damage, and scarring seen in CL has not been elucidated yet. Here we investigated the cellular sources of extracellular granzyme B and its association with pathological changes seen in human CL.

Methods: Paraffin-embedded human skin biopsy specimens with confirmed diagnosis of cutaneous leishmaniasis were included in this study. Sections were subjected to the histological analysis using Hematoxylin& Eosin, Immunohistochemistry, sequential and double immunofluorescent staining for GzmB and cellular markers for different immune cells and GzmB substrates in epidermis and dermis.

Results: Our results showed significantly high expression of GzmB by immune cells and a close correlation between the GzmB expression and degradation of its substrates such as E cadherin, collagen VII, and collagen XVII in human CL lesional skin biopsy specimens.

Conclusions: Our findings suggest that extracellular GzmB contributes to the tissue damage, delayed wound healing, and scarring in CL by cleaving cell-cell junction, cell-basement membrane junction, and matrix proteins.

Learning objectives: At the end of this presentation the audience will learn about:

- Leishmania parasite, route of transmission, and clinical presentation of cutaneous leishmaniasis
- Hallmarks of the histological findings in cutaneous leishmaniasis
- Granzyme B and its role in infection and inflammation
- Main sources of granzyme B expression in cutaneous leishmaniasis
- Substrates cleaved by granzyme B in skin

Takeaway Message: Extracellular granzyme B, produced by a variety of immune cells in cutaneous leishmaniasis and contributing to the tissue damage and scarring, might be a potential target for development of novel treatment for the WHO top neglected tropical disease.

Ilya Mukovozov	3:20 – 3:30pm

Cosmesis and Viability of Right Angle Paramedian Forehead Flaps: A Retrospective Chart Review

Ilya M. Mukovozov1, Alexandre Laroche1, Aaron Wong1, and David Zloty1.

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Introduction: Paramedian forehead flaps (PMFF) are commonly used for reconstruction of nasal defects. The classic PMFF is vertically oriented, from the eyebrow to the frontal hairline, while the modified PMFF is designed with a 90-degree angle to avoid transposing hair from the scalp to the nose. No study has compared outcomes between the two flap designs.

Methods: Retrospective chart review of 70 consecutive patients with vertical or 90-degree angle PMFF designs for nasal repairs following Mohs micrographic surgery (MMS). Cosmesis was assessed on a 10 cm, 100-point, visual analog scale (VAS) by an independent observer using standardized 3-month post-operative photographs. Flap viability was assessed using standardized 3-week post-operative photographs, and degree of necrosis expressed as a percentage of necrotic area compared to the original defect size. Descriptive statistics, t-test and Mann Whitney test were used for statistical analysis.

Results: Forty-eight patients were repaired with a vertical PMFF and 22 using the 90-degree design. There was no significant difference in cosmetic outcome (75.9 ± 9.4 vs 72.9 ± 7.2, $p=0.19$), or flap viability ($20.4\% \pm 20.4$ vs $14.5\% \pm 14.5$, $p=0.62$) between vertical and 90-degree designs respectively.

Conclusions: Vertical and 90-degree PMFF designs for nasal repairs following MMS are equivalent in cosmesis and viability.

Learning objectives:

- Describe vertical and 90-degree angle paramedian forehead flaps (PMFF) designs for repairs of nasal defects following Mohs micrographic surgery
- Compare flap cosmesis between vertical and 90-degree angle PMFF designs
- Compare flap viability between vertical and 90-degree angle PMFF designs
- Enumerate complications and procedures received at follow-up between vertical and 90-degree angle PMFF designs

Takeaway Message:

Vertical and 90-degree PMFF designs for nasal repairs following MMS are equivalent in cosmesis and viability.

Martin Barbier	**3:30 – 3:40pm**

Ex Vivo Gene Therapy of Skin Cells and Autologous Bilayered Skin Susbtitutes As A Potential Treatment for Recessive Dystrophic Epidermolysis Bullosa Skin Wounds

Martin Barbier, Angela Dakiw Piaceski, Amélie Morissette, Alex Larose, Andréanne Cartier, Sarah Villeneuve, Danielle Larouche, Karim Ghani, Elena Pope, Manuel Caruso, Lucie Germain.
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Introduction: Recessive dystrophic epidermolysis bullosa (RDEB) is a very rare genodermatosis (3 per million births) in which minor mechanical stress to the skin results in blisters, erosions and scarring leading to severe pain and decreased life expectancy. RDEB is caused by mutations in the *COL7A1* gene, encoding type VII collagen (Col7). The mutation leads to defective anchoring fibrils at the dermo-epidermal junction (DEJ) resulting in a loss of adhesion between the epidermis and the dermis.

Methods: RDEB cells producing no Col7 were transduced using a SIN COL7A1 vector. Transduction efficiency and transduced stem keratinocytes, expressing keratin 19, were assessed through flow cytometry. These corrected cells were used to produce self-assembled skin substitutes.

Results: Up to 55% of fibroblasts and 60% of keratinocytes were transduced. Moreover, 60% of keratin 19-expressing keratinocytes were transduced and maintained in the reconstructed skin. Col7 production and assembly at the DEJ was observed through immunofluorescence and electronic microscopy in skin substitutes produced from transduced RDEB cells. The dermo-epidermal adhesion was restored and comparable to skin produced from healthy cells and vastly superior to skin produced with untreated RDEB cells. Finally, grafting on athymic mice for up to 6 months showed that the production of Col7 and stem cells were maintained over time in genetically modified skin substitutes.

Conclusions: We developed an efficient method to restore Col7 production in RDEB cells while maintaining stem cell keratinocytes, allowing for potential long-lasting therapeutic effect. Our results indicate that this method is suitable for the treatment of RDEB skin lesions.

Learning objectives:

- RDEB: etiology & clinical manifestations
- Gene therapy strategy for the treatment of RDEB
- Self-assembly approach to produce graftable skin substitutes

Takeaway Message: The progresses in gene therapy and tissue engineering allows researchers to produce genetically modified autologous self-assembled skin substitutes that could be grafted on RDEB patients for the treatment of wounds.

Nadia Kashetsky	3:40 – 3:50pm

Light and Laser-based Treatments for Granuloma Annulare: A Systematic Review

Nadia Kashetsky1*, Ilya M. Mukovozov2*, and Vincent Richer1,3

**** Equal contribution***

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2 Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

3 Pacific Derm, Vancouver, BC, Canada

Introduction: Granuloma annulare (GA) is challenging to treat, especially when generalized. A systematic review to support the use of light and laser-based treatments for GA is lacking.

Methods: We performed a systematic review by searching Cochrane, MEDLINE and Embase. Title, abstract, full text screening and data extraction were done in duplicate. Quality appraisal was performed using the Joanna Briggs Institute critical appraisal tool for case series.

Results: Thirty-one case series met the inclusion criteria, representing a total of 336 patients. Overall, treatments with the most reported cases were psoralen plus ultraviolet A (PUVA), ultraviolet A1 phototherapy (UVA1) and ultraviolet (UVB) and/or narrowband UVB (nbUVB) which showed a complete response in 59% (n=77/131), 31% (n=27/86) and 39% (n=17/44) of patients respectively. Pooled complete response rates for other treatments were 68% (n=21/31) for laser/energy-based devices and 52% (n=13/25) for photodynamic therapy (PDT). Available data reported recurrence rates of 51% (n=52/101) for PUVA, 38% (n=8/21) for UVA1, 45% (n=5/11) for UVB/nbUVB, and 44% (7/16) for PDT.

Conclusions: The body of evidence for light and laser-based treatment of GA is sparse. Our results suggest that PUVA has a high clearance rate for GA but its use may be limited by concerns of carcinogenesis. Laser devices and PDT have high clearance rates for patients with GA, but data is limited by small sample sizes. Further, they may be limited by access to technology and impractical treatment delivery for generalized GA. Although UVB/nbUVB appeared slightly less effective than other light therapies, we recommend UVB/nbUVB therapy as a first-line treatment for patients with generalized GA given wider availability and a favourable long-term safety profile.

Learning objectives:

- Identify light and laser-based treatment modalities employed for GA,
- their reported treatment outcomes,
- and associated recurrence rates.

Takeaway Message: Although UVB/nbUVB appeared slightly less effective than other therapies, in light of widespread availability and a favourable long-term safety profile, we recommend that UVB/nbUVB can be considered an appropriate first-line treatment for patients with GA.

Friday, 12 November
Plenary Session III Inflammatory Skin Diseases
9:00 - 10:30am

Andrew Leask	**9:00 – 9:20am**
Targeting the Tumor Stroma in Checkpoint Inhibitor-Resistant Melanoma	
Andrew Leask *University of Saskatchewan*	
Abstract not available	

Katlyn Richardson	**9:20 – 9:30am**

Granzyme K: A Novel Therapeutic Target for Psoriasis

Katlyn C. Richardson1,2, Christopher T. Turner1.2, Lorenz Nierves2,3, Rachel A. Cederberg2,4, Hongyan Zhao1,2, Angela Burleigh5, Matthew R. Zeglinski1.2, Sho Hiroyasu1,2, Megan A. Pawluk1,2, Layla Nabai1,2, Kevin L. Bennewith2,4,6, Philipp F. Lange2,3, Richard I. Crawford2, David J. Granville1,2,7.

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7. British Columbia Professional Firefighters' Burn and Wound Healing Group, Vancouver, Canada.

Introduction: Psoriasis affects over one million Canadians and is characterized by increased skin inflammation and epidermal proliferation. Current therapies are expensive, ineffective and/or associated with significant side effects. Thus, for new therapies to be developed, a deeper understanding of the pathological mechanisms of psoriasis is necessary. Granzyme K (GzmK) is a serine protease recently shown to promote skin inflammation. GzmK is abundant in human psoriasis skin. We *hypothesize* that GzmK contributes to the onset and progression of psoriasis through the augmentation of inflammation and/or epidermal proliferation.

Methods: GzmK levels were assessed histologically in skin biopsies with and without psoriasis. The role of GzmK was investigated in a murine model of psoriasis, comparing GzmK knockout (K-KO) to wild-type (WT) mice. Psoriasis severity (erythema, squamae) was assessed macroscopically. Skin tissue extracts were examined for pro-inflammatory markers and epidermal thickness via histology, ELISA, qPCR, and validated in vitro. To elucidate a mechanism, we are defining the GzmK degradome within the skin using High-efficiency Undecanal-based N Termini EnRichment (HUNTER), a mass spectrometry-based method for N-termini enrichment.

Results: GzmK-positive cell numbers were elevated 40-fold (p=0.045) in lesional psoriasis skin compared to healthy skin. K-KO mice exhibited an average 60% decrease in psoriasis severity compared to WT mice. K-KO mice exhibited a reduction by approximately 50% (p=0.0053*)* in inflammatory cell infiltrate compared to WT mice. Pro-inflammatory cytokines, IL-17 and IL-23, commonly elevated in human psoriasis, were reduced an average of 46% (p=0.044) and 48% (p<0.001) in K-KO mice, respectively. Preliminary in vitro work suggests GzmK-treated macrophages secrete increased IL-23. K-KO mice also exhibited an average 30% decrease (p=0.014) in epidermal thickness, and 98% decrease (p=0.03) in proliferation markers, compared to WT mice. In vitro, GzmK induced PAR-1-mediated keratinocyte proliferation ($p \leq 0.002$).

Conclusions: Based on the results observed thus far, inhibition of GzmK may represent a novel therapeutic approach for treating psoriasis.

Learning objectives:

- GzmK is elevated in human psoriasis lesions where it is secreted by mast cells, macrophages and neutrophils;
- GzmK depletion attenuates psoriasis severity in a murine model of psoriasis;
- GzmK promotes inflammation in psoriasis by increasing pro-inflammatory cell infiltrate and cytokine release, including IL-23 from macrophages;
- GzmK promotes epidermal proliferation in psoriasis by inducing PAR-1-mediated keratinocyte proliferation.

Takeaway Message: GzmK is elevated in human psoriasis lesions and may contribute to disease onset and severity. This study could provide important insights into disease mechanisms and provide the first evidence for GzmK as a therapeutic target for psoriasis.

Megan Pawluk	**9:30 – 9:40am**

Granzyme B Contributes to Radiation Dermatitis through E-Cadherin Cleavage and Loss of Epithelial Barrier Function

***Megan A. Pawluk** 1,2, Sho Hiroyasu 1,2, Layla Nabai 1,2, Brennan Wadsworth 2,3, Yue Shen 1,2, Kevin L. Bennewith 2,3, David J. Granville 1,2,4.*

1 International Collaboration On Repair Discoveries (ICORD), Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, Canada. 2 Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada. 3 BC Cancer Research Center. 4 British Columbia Professional Firefighters' Burn and Wound Healing Group, Vancouver, Canada.

Introduction: Radiation dermatitis (RD) is an adverse event that occurs in up to 95% of patients receiving radiation therapy for cancer treatment. Symptom severity may delay or prevent further radiation treatments. Current RD treatments are not effective. Granzyme B (GzmB), a serine protease, is expressed and secreted by numerous immune as well as non-immune cell populations. Extracellular GzmB is dramatically elevated in RD. Previous studies suggest that GzmB cleaves numerous cell-cell junction proteins leading to reduced epithelial barrier function.

Hypothesis: GzmB contributes to increased severity and delayed healing of RD through the cleavage of cell-cell junction proteins resulting in impaired epidermal barrier function leading to increased inflammation.

Methods: GzmB expression and E-cadherin levels were assessed using immunohistochemical analysis of biopsies taken from patients exhibiting RD. The role of GzmB was investigated in an established murine model of RD, comparing GzmB knockout (GzmB-KO) to wild type (WT) mice. RD was induced in mice by applying a single 40gy dose of radiation to the upper back. RD severity was blindly scored by pathologists. Tissue samples were collected on day 14 (N=14) and examined by histology and ELISA for pro-inflammatory markers and GzmB levels.

Results: Elevated GzmB and reduced E-cadherin was observed in RD human skin tissues compared to healthy human skin tissues. GzmB-KO mice exhibited a significant decrease in RD severity compared to WT mice at day 4 ($p=0.03$), day 6 ($p=0.02$), day 8 ($p \leq 0.001$), day 10 ($p=0.01$), and day 12 ($p=0.01$) post-radiation. A significant reduction in skin erythema, scaling, and crusted wounds were observed 4-12 days post-radiation. Future studies will examine the utility of a topical GzmB inhibitor.

Conclusions: GzmB is abundant in human RD. GzmB may contribute to RD severity through E-cadherin cleavage and the loss of epithelial barrier function. GzmB may be a novel therapeutic target for the treatment of RD.

Learning objectives:

- GzmB is highly elevated in human radiation dermatitis tissue samples when compared to normal human skin samples
- GzmB may cleave cell-cell junction protein E-cadherin resulting in a loss of epithelial barrier function.
- GzmB may be used as a novel therapeutic target for decreasing the severity of radiation dermatitis and increasing the epithelial barrier function integrity.

Takeaway Message: GzmB may contribute to RD through the proteolytic cleavage of E-cadherin and other cell adhesion proteins leading to a loss of epidermal barrier function. GzmB may be a novel therapeutic target for treating RD.

Geneviève Rioux	**9:40 – 9:50am**

Study of The Role Of Pathological Keratinocytes And Their Communication With T Cells Using Tissue Engineered Psoriatic Skin

<u>Geneviève Rioux</u> (1,3), Roxane Pouliot (1,3) and Sylvain L. Guérin (1,2,4)

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4 Département d'ophtalmologie, Faculté de médecine, Université Laval, Québec, Qc, Canada.

Introduction: Psoriasis is a chronic inflammatory skin disease involving a variety of epithelial and immune cells. The main challenge in studying psoriasis is that it is an exclusively human condition and there is no natural animal equivalent of this disease. In order to analyze the different mechanisms governing psoriasis, it is essential to develop adapted models that are as close as possible to the native psoriatic skin. The aim of this project was to develop an advanced psoriatic model enriched in T cells.

Methods: For this purpose, healthy and psoriatic skin substitutes were reconstructed by the LOEX self-assembly method. T cells were isolated from whole blood by immunomagnetic negative selection and activated with phorbol 12-myristate 13-acetate (25 ng/ml) and ionomycin (1 µg/ml) before being seeded into the dermal compartment of healthy and psoriatic skin models.

Results: Secretory profile analysis reveals that psoriatic skin substitutes enriched in T cells exhibit an inflammatory microenvironment marked by significantly greater production of CCL2, CXCL1, CXCL10, IL-1ra, IL-6, CXCL8, IL-17A, and IFNγ compared with healthy T-cell-enriched substitutes. Several of these cytokines are secreted by keratinocytes and are involved in leukocyte attraction, thus explaining the marked T-cell infiltration in the epidermis of psoriatic substitutes.

Conclusions: These results highlight the role of pathological keratinocytes in the initiation of skin inflammation. This first immunocompetent model using primary skin cells derived from psoriatic skin and producing an inflammatory microenvironment characteristic of the pathology may stand out as a compelling tool for studying epithelial-immune cell communication in psoriasis.

Learning objectives:

- Possible collaborations to use this psoriatic skin model enriched with T-cell to test molecules with anti-psoriatic potential.
- Meet experts in the field of skin immunity.
- See the latest advances in tissue engineering and skin models (healthy and pathological).

Takeaway Message:

The aim of this study was to provide an innovative 3D immunocompetent human psoriatic skin model. We demonstrated that the T-cell enriched psoriatic model differs from T-cell enriched healthy model, highlighting efficient crosstalk between pathologic epithelial cells and T cells.

Sara Mirali	9:50 – 10:00am

Light and Laser-based Treatments for Hidradenitis Suppurativa: a Systematic Review

***Sara Mirali*1, Ilya M. Mukovozov2, Sophie Khaslavsky3, Sunil Kalia2, 4, 5**

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Introduction: Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterized by painful, disfiguring, recurrent lesions occurring mainly in intertriginous areas. HS is primarily managed by modifying lifestyle risk factors, medical, and procedural therapy. The aim of this systematic review was to critically assess HS treated with laser or light-based therapies and characterize their relative effectiveness.

Methods: Cochrane, MEDLINE, and Embase were searched on June 12, 2020 for articles describing laser and light-based treatments for HS. Data from 41 studies representing 668 patients were extracted and included in the analysis.

Results: The most commonly used light-based treatments were carbon dioxide (CO2) laser (59%, n=396/668), photodynamic therapy (PDT) (25%, n=167/668), and neodymium-doped yttrium aluminum garnet (Nd:YAG) laser (14%, n=92/668). Among those with reported treatment outcomes, CO2 laser was effective in 79% (n=311/396) of patients, PDT in 71% (n=118/167), and Nd:YAG laser in 86% (n=30/35). Adverse events were reported in 26% (n=103/393) of patients treated with CO2 laser, 15% (n=8/53) of patients treated with Nd:YAG laser, and 36% (n=23/64) of patients treated with PDT. Lasers used for surgery were more effective compared to lasers used for field treatment, showing overall response rates of 80% (n=344/431) and 71% (n=84/118), respectively. However, patients receiving laser surgery experienced significantly higher rates of adverse events (25%, n=105/424) compared to those receiving laser field treatment (18%, n=24/134). Limitations included a lack of comparative randomized clinical trials, treatment being offered at different HS stages, and the majority of studies used different outcome assessments.

Conclusions: Our results suggest that laser and light devices are effective in treating patients with both mild and severe HS. However, limited access to laser and light-based therapies are barriers to treatment. Larger comparative studies with standardized outcome assessments are needed to compare the efficacy of laser and light therapy devices to medical therapy used in HS patients.

Learning objectives:

- Summarize light and laser-based treatments used in HS
- Compare pooled response rates and side effect profiles across different laser and light-based treatment modalities for patients with early and advanced disease
- Recognize the difference between lasers used for surgery and those used for field treatment

Takeaway Message: Laser and light-based therapies showed beneficial effects in both early and advanced disease. Lasers used for surgery showed greater clinical improvement compared to lasers used for field treatment but had higher rates of adverse events

Jordanna Roesler	**10:00 – 10:10am**

Dermatological Conditions in Rural and Remote Indigenous Communities of North America: A Systematic Review

Rachel Netahe Asiniwasis, MD FRCPC
Principal Investigator and Primary Contact - Origins Dermatology Centre
Assistant Professor (Dermatology), University of Saskatchewan College of Medicine
Gregory Kost, MD, Odeshi, Oluwatosin MD, Jordanna Roesler, BSc, Colton Jensen, BSc, Trisha Campbell, BSc, Mamata Pandey, PhD

Introduction: North American Indigenous populations face unique systemic barriers and numerous health disparities in comparison to the general population. Rural and remote Indigenous populations within Canada are especially underserviced in dermatology and lack access to adequate dermatologic services and treatments. Dermatological conditions affecting Canadian and North American Indigenous communities is poorly understood and documented within dermatology. This systemic review provides novel data on these underrecognized and undertreated conditions to guide future recommendations to improve patient care.

Methods: A systematic review of dermatological conditions in North American Indigenous remote and rural communities with a primary Canadian focus was conducted using the Rayyan web-based software platform. Multiple electronic databases (e.g., Medline, Embase, Scopus, PubMed) and manual searches of journals were used to locate literature from published, peer-reviewed, randomized controlled and cross-sectional studies of any size dating from 1970 to present. Two review authors independently screened titles and abstracts of all records identified by the searches followed by full-text review. Any discrepancies were resolved through discussion until a consensus was reached.

Results: The number of articles, inclusion, and exclusion criteria are pending. Full results will be available before November.

Conclusions: Findings from this systematic review indicate that there is a paucity of dermatologic literature in North American Indigenous communities. Concerns surrounding atopic dermatitis, skin and soft tissue infections, and (other identified concerns – TBA) needs further exploration.

Learning objectives:

- To understand current barriers to health within rural, remote, and Indigenous communities within Canada and North America from a dermatologic perspective.
- To discuss quality of life impact, chronicity, and severity of dermatologic conditions in rural, remote, and Indigenous communities within Canada and North America.
- To discuss strategies and recommendations to improve dermatological health services to these communities.

Takeaway Message: Rural and remote Indigenous populations within Canada and North America are underserviced and lack access to adequate dermatologic services and treatments. Dermatological conditions affecting these communities, including their chronicity and severity, is poorly understood and documented within dermatology and is considered an area of high need.

Sophie Morin	10:10 – 10:20am

Investigation of The Influence of Alpha-Linolenic Acid In A 3-D Engineered Immunocompetent Psoriatic Skin Model

Sophie Morin1,2, Mélissa Simard1,2, Geneviève Rioux1,2, Pierre Julien3,4, Roxane Pouliot1, 2

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Introduction: Psoriasis is a skin disease with an over proliferation of keratinocytes. The pathology presents an exaggerative response to external aggressions, which triggers an excessive activation of the immune system. N-3 polyunsaturated fatty acids (n-3 PUFAs), in particular alpha-linolenic acid (ALA), are anti-inflammatory molecules and their dietary consumption beneficially impacts psoriatic patients. The aim of this study was to elucidate the bio-action of ALA on the immune component of psoriasis, by using a psoriatic skin model.

Methods: Psoriatic skin substitutes were produced according to the self-assembly method. T cells were isolated from blood samples of healthy donors and ALA supplementation was maintained at a concentration of 10 mM throughout cell culture.

Results: In this psoriatic skin model enriched with T cells, ALA regulated the hyperproliferation and abnormal cell differentiation of psoriatic keratinocytes, which were highly stimulated by T cells. The exogenous ALA was incorporated into the phospholipids fraction of keratinocytes, which resulted in increased levels of ALA, EPA and n-3 DPA. Moreover, the addition of ALA in the culture medium slowed down the infiltration of T cells into the epidermis, which was represented by a diminution in the expression of CD45 and CD11a. Finally, psoriatic skin substitutes produced with T cells exhibited high quantities of inflammatory cytokines and chemokines, such as CXCL1, IL-6 and IL-8, whereas the supplementation of the media with ALA potentiated the production of those cytokines.

Conclusions: Our results showed that in this psoriatic skin model enriched with T cells, ALA mainly exerts its anti-inflammatory actions by decreasing inflammatory mediators released by T cells.

Learning objectives:

- Describe the regulation of n-3 PUFAs on keratinocyte differentiation
- Illustrate the influence of ALA on T cells migration
- Report the effects of ALA on cytokine production

Takeaway Message: n-3 PUFAs lowers the inflammation caused by the addition of T cells in the psoriatic model.

Maha Alsharqi	10:20 – 10:30am

Regulation of Pulmonary Fibrosis by CD109 In A Murine Model

Maha Alsharqi1,3, Yumiko Ishii2,3, Meryem Blati1,3, James Martin2,3 and Anie Philip1,2,3

1Division of Plastics Surgery, McGill University,

2Department of Medicine, McGill University and 3The Research Institute of the McGill University Health Centre.

Introduction: Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease characterized by inflammation, excessive fibroblasts proliferation, and deposition of extracellular matrix (ECM) in the interstitium. It leads to impairment in the quality of life and decline in lung functions.TransformingGrowthFactor-ß1(TGF-ß1)isa multifunctionalgrowthfactor,with a wide range of functions in homeostasis and tissue repair. TGF- ß1 signaling is mediated via Smad2/3 intracellularproteinsleading to genetranscriptionand ECM protein expression. TGF- ß1/Smad2,3 signaling pathway plays an important role in the pathogenesis of lung fibrosis and other fibrotic disorders. Our team has previously identified CD109 a glycosylphosphatidylinositol (GPI)-anchored protein as a TGF-ß1 co-receptor that negatively regulates TGF-ß1 signaling and responses. . Our group has previously shown that CD109 deficient mice display enhanced TGF-ß1 signaling leading to an increasedfibroblastproliferation and ECMdeposition in a skin fibrosis model.Inthisstudy,weaim to investigate the role of CD109 in lung fibrosis using a CD109 deficient mouse model.

Methods: Cellular migration was analyzed using invitro wound healing assay. The architecture of the lung alveoli and collagen deposition were analyzed by hematoxylin and eosin staining, and Masson'strichromestaining, respectively. Immunohistochemistry was performed to evaluate the expression of different ECM markers, and the number of neutrophils and M1 and M2 macrophages. Finally,we evaluated lung compliance using FlexiVent in CD109 deficient mice in comparison to WT mice.

Results: In vitro wound healing assay shows that CD109 KO lung fibroblasts display greater TGF-β induced migration than WT lung fibroblasts ($p<0.05$). Interestingly, H&E staining reveals that the KO lungsexhibitincreased cellularityanddistinctalveolarmorphologythatcouldbeduetoobliteration of the alveolar sacs, when compared to WT lungs. Trichrome staining demonstrates a markedly increased collagen content in CD109 KO lungs compared to WT lungs. Furthermore, the KO lung tissue shows increased expression of collagen, fibronectin and alpha smooth muscle actin, as detected by immunohistochemistry. In addition, the KO lung tissue shows markedly increased macrophage numbers while the neutrophil count remains unchanged.

Conclusions: Our finding that CD109 deficiency results in markedly enhanced TGF-β signaling, fibrotic responses, andcellularity in the mouselung, implicates not only anessentialrole forCD109 in lunghomeostasis, butalsoits potential asananti-fibroticmoleculefortherapeuticintervention inlungfibrosis.

Learning objectives:

- To determine whether CD109 regulates migration and ECM synthesis in the mouse lungs *in vivo.*
- To determine whether CD109 regulates inflammatory responses.
- To determine whether CD109 affect lung functions and morphology.

Takeaway Message: Immune mechanisms contribute to fibrogenesis in CD109 KO mice evident by the increase number of macrophages. Contradictory effects was seen when Neutrophil numbers remain unchanged - and future studies are required to clearly define their role in CD109 KO mice.

Friday, 12 November
Plenary Session IV Skin Cancer
3:00 - 4:20pm

Philippe Lefrançois	**3:00 – 3:20pm**

The Transcriptional Landscape Analysis of Basal Cell Carcinomas Reveals Novel Signaling Pathways and Actionable Targets

Ivan V. Litvinov M.D., Ph.D., FRCPC (1), Pingxing Xie M.D., Ph.D. (1), Scott Gunn B.Sc. (1), Denis Sasseville M.D., FRCPC (1), and Philippe Lefrançois M.D., Ph.D. (1,2)
(1) Division of Dermatology, Department of Medicine, McGill University, Montreal, QC, Canada
(2) Present: Jewish General Hospital Division of Dermatology; Lady Davis Institute; McGill University Department of Medicine

Introduction: Basal Cell Carcinoma (BCC) is the most common skin cancer and human malignancy. Although most BCCs are easily managed, some are aggressive locally, require Mohs micrographic surgery or can even metastasize. In the latter, resistance to Sonic Hedgehog inhibitors may occur. Despite their frequent occurrence in clinical practice, their transcriptional landscape remains poorly understood.
Methods: We re-analyzed 3 cohorts of BCC RNA-Seq patients and performed pathway analysis and clustering for biomarker discovery. We validated our findings in patient-derived BCC samples from McGill dermatology clinics.
Results: By analyzing BCC RNA-Sequencing data according to clinically important features (all BCCs *vs.* normal skin, high-risk *vs.* low-risk BCCs based solely on histopathological subtypes with aggressive features, advanced *vs.* non-advanced BCCs, and vismodegib-resistant *vs.* vismodegib-sensitive tumors), we have identified novel differentially-regulated genes and new targetable pathways implicated in BCC tumorigenesis. Pathways as diverse as *IL-17*, *TLR*, *Akt/PI3K*, cadherins, integrins, *PDGF* and *Wnt/β-catenin* are promising therapeutic avenues for local and systemic agents in managing this common malignancy, including through drug re-purposing of existing medications. We experimentally validated several of these targets as biomarkers in our patient-derived cohort of primary BCC tumors.
Conclusions: By analyzing BCC RNA-Sequencing data according to clinically important features, we identified novel differentially-regulated genes and new targetable pathways, many of which could be altered through drug re-purposing. Several biomarkers were validated in patient-derived BCC samples.
Learning objectives:
- Discover new differentially regulated pathways for BCC pathogenesis
- Understand key gene expression patterns underlying resistance to vismodegib and aggressive disease
- Appreciate a simple biomarker panel for routine BCC

Takeaway Message: Pathways as diverse as IL-17, TLR, Akt/PI3K, cadherins, integrins, PDGF and Wnt/β-catenin are promising therapeutic avenues for local and systemic agents in managing BCC, including through drug re-purposing of existing medications. Wnt/β-catenin upregulation is a hallmark of vismodegib-resistant tumors.

Shu Feng Zhou	**3:20 – 3:30pm**

Unraveling the Contribution of ACTL6A, A Chromatin Remodeling Factor, To Immune Evasion In Head And Neck Squamous Cell Carcinoma

Shu Feng Zhou

Massachusetts General Hospital Cancer Center, Harvard medical school

Introduction: The gene encoding ACTL6A, a subunit of the SWI/SNF complex, is frequently amplified in head and neck squamous cell carcinoma (HNSCC). Elevated ACTL6A in HNSCC deregulates SWI/SNF function and enhances EZH2-mediated transcriptional repression. Anti-programmed cell death protein (PD-1) immune checkpoint inhibitor (ICI) therapy has resulted in remarkable clinical response, but most of HNSCCs develop resistant to ICIs. We hypothesize that amplified ACTL6A promotes EZH2-mediated repression via H3K27me3 at key loci of immune responses genes, resulting in immune cold tumors that are resistant to ICI therapy.

Methods: RNA-seq, Chip-seq, ATAC-seq, FACS, inducible shRNA, autochthonous and syngeneic immunocompetence murine models were used in this study

Results: Inhibition of the ACTL6A/EZH2 axis enhances tumor cell antigen presentation and immune cell recruitment and subsequently sensitizes resistant tumors to anti–PD-1 therapy. ACTL6A deletion markedly increased tumor-free survival in the 4NQO autochthonous HNSCC model. In the syngeneic transplantable SCC model, although we observed significant anti-tumor effects of either inducible shRNA knockdown (KD) of endogenous ACTL6A or treatment with the catalytic EZH2 inhibitor (EPZ) or anti-PD-1 alone, combining either shACTL6A or EPZ with anti-PD-1 completely abrogated tumor progression. Correspondingly, we observed a >4-fold increase in the proportion of T cells and CD8+ T cells with the combination with anti-PD-1 and either shACTL6A or EPZ. Importantly, combination treatment of ACTL6A KD with anti-PD-1 contributed to a long-term immune memory.

Conclusions: ACTL6A/ EZH2 inhibition upregulates antigen presentation, Th1 chemokine signaling and interferon response, including (PD-L1 by activating interferon-STAT1 pathways, resulting in increasing intratumoral trafficking of activated CD8+ T cells and reversing resistance to ICI.

Learning objectives:

- ACTL6A expression identifies a tumor subset that could be therapeutically targeted with ACTL6A/EZH2 inhibition to modulate the TME and thereby promote synergy with immunotherapy.

Takeaway Message: These data provide important evidence for targeting chromatin and epigenetic regulators to overcome immunotherapy resistance.

Amani Hassan	**3:30 – 3:40pm**

Targeting the CD109-IL6 pathway in Squamous Cell Carcinoma

Amani Hassan1, Tenzin Kungyal1, Shufeng Zhou1, Meryem Blati1, Julie Berube1, Nicholas Bertos1,2, Nader Sadeghi2, Veena Sangwan1 and Anie Philip1.

1 Division of Plastic Surgery, Department of Surgery, Faculty of Medicine, McGill University, Montreal, Quebec, Canada

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Introduction: Squamous cell carcinoma (SCC), is one of the most prevalent types of malignancy and its incidence is increasing globally. Despite intensive research, there has been limited success in blocking recurrence and metastasis that occurs in a sizable proportion of SCC patients. The GPI-anchored membrane protein CD109 is frequently overexpressed in squamous cell carcinoma (SCC) and this overexpression is associated with malignant transformation. The molecular mechanisms by which CD109 may regulate SCC progression are still unknown. CD109 was found to strongly enhance interleukin-6 (IL-6)/Jak/STAT3 signaling in lung cancer cells. Interleukin-6 (IL-6) is a pleiotropic cytokine playing important roles in proliferation, survival, differentiation, migration and invasion. IL-6 levels are elevated in SCC tumors and its elevated expression is associated with increased recurrence and lower survival, and anti-IL-6/anti-IL-6 receptor-targeted therapies have been proposed for the treatment of SCC. In the proposed research, we aim to delineate the molecular mechanisms by which CD109 may promote the progression of SCC.

Methods: CD109 KO and parental A431 and SCC-9 cells were left untreated or treated with IL6 for various time periods. CD109 and IL6R expression and IL6-induced phosphorylation of STAT3 were measured by western blot and immunohistochemistry. CD109 association with the IL6R was studied by co-immunoprecipitation and co-localization was studied using immunofluorescence. Organoid cultures were also employed using patient tissue from SCC tumors.

Results: In the current work, we found that CD109 is a pivotal regulator of IL6R expression and function in SSC. Our preliminary data shows that CD109 potentiates IL6R/STAT3 signaling pathways. Moreover, CD109 also interacts with IL6R and that the loss of CD109 leads to decreased IL6R expression as determined by co-immunoprecipitation and co-localization studies. Furthermore, our preliminary data show that CD109 and IL6Rs are upregulated in patient derived organoids compared to controls. This is consistent with our in vivo finding that deletion of CD109 markedly decreases tumor formation and metastasis.

Conclusions: Our findings show that the loss of membrane CD109 attenuates IL6R signaling pathways in SCC cells and reveal a fundamental role for CD109 in SCC progression. These findings highlight a potential clinical utility for CD109 as a therapeutic target in SCC.

Learning objectives:

- Identify molecular mechanisms through which CD109 drives SCC progression.
- Determine whether CD109 regulates IL6 signaling pathways in human SCC cells in vitro.
- Identify the effect of CD109 deletion on IL6 signalling.

Takeaway Message: We present CD109 as an important regulator of IL6R/STAT3 signalling and that could be one of the possible mechanisms through which CD109 promotes SCC progression.

Tenzin Kungyal	**3:40 – 3:50pm**

Therapeutic Targeting of Oncogenic CD109/EGFR Signaling and mechanism of action.

Tenzin Kungyal, ***Amani Hassan, Shufeng Zhou, Kenneth Finnson and Anie Philip***
Division of Plastic Surgery, McGill University

Introduction: CD109 is a GPI-anchored membrane protein that is expressed on the surface of many cell types. CD109 levels are upregulated in squamous cell carcinoma (SCC), and CD109 is strongly implicated in SCC progression. Previous work from our lab has shown that CD109 is pro-tumorigenic and that it interacts with the EGFR protein, another key receptor overexpressed in SCC and well-documented to promote malignant progression, neoplastic angiogenesis, and enhanced metastatic potential, leading to decreased survival. Deletion of CD109 gene in A431 cells resulted in the loss of cell surface EGFR expression. So, we hypothesized that CD109 is required for the stability and the activation of EGFR signaling. We sought to determine the mechanism in which CD109 promotes EGFR activation and stability and whether interfering with the interaction between CD109 and EGFR in SCC cells can block EGFR signaling and thus SCC progression.

Methods: To determine whether CD109 regulates the Expression of EGFR, we performed microarray analysis of A431 control SCC cells versus CD109 knockout (KO) A431 cells. We also determined the relationship between the expression of CD109 expression and CD109 and EGFR co-expression using the available TCGA data set of 515 head and neck squamous cell carcinoma patients. Also, at the protein level, the relationship between CD109 and EGFR was studied in three SCC cell lines, A431, FaDu and SCC9, and their respective CD109 KO cells. The interaction between the two proteins was analyzed by the co-immunoprecipitation method. Regulation of EGFR signaling by CD109 was also analyzed. In addition, we determined whether CD109 regulates the stability of EGFR on the cell surface, using CD109 overexpressing A431 SCC cells and A431 empty vector cells.

Results: Our results show that loss of CD109 leads to decreased EGFR expression and that CD109 protein associates with EGFR on the cell surface. Furthermore, CD109 promotes EGFR signaling in SCC cells via AKT, STAT3 and ERK pathways. Importantly, CD109 promotes EGFR stability by inhibiting EGFR internalization and degradation.

Conclusions: Increased EGFR signaling is a hallmark of many cancers, especially SCC, and EGFR signaling is a well-documented therapeutic target for SCC. CD109 interacts with EGFR and stabilizes EGFR levels by inhibiting EGFR degradation, leading to enhanced EGFR signaling via STAT3, AKT and ERK pathways. Decreasing CD109-EGFR interaction and thereby blocking EGFR signaling and EGF-induced cellular responses as demonstrated in the current study may provide a novel therapy for SCC treatment.

Learning objectives:

- Understand the importance of CD109 in the regulation of EGFR levels and EGFR signaling
- Learn about the mechanism by which CD109 may regulate EGFR levels.
- Obtain a basic understanding of why CD109-EGFR interaction can be used as a therapeutic target for the treatment of SCC patients.

Takeaway Message: CD109 protein regulates EGFR levels by regulating EGFR internalization and degradation.

Meagan-Helen Henderson Berg	**3:50 – 4:00pm**

Intralesional Rituximab in The Treatment of Indolent Primary Cutaneous B-Cell Lymphoma

Anissa Chirico, *Division of Anesthesia, University of Manitoba*
Meagan-Helen Henderson Berg, *Division of Dermatology, McGill University*
David Roberge, *Division of Radiation Oncology, Université de Montréal*
Kevin Pehr, *Division of Dermatology, McGill University*

Introduction: Intralesional (IL) injection of the anti-CD20 antibody rituximab has been reported as a successful therapy for primary cutaneous B cell lymphomas (PCBCLs). However, there remain few published studies of patients treated with IL rituximab, and the ideal administration schedule remains unclear.

Methods: We retrospectively reviewed the charts of 12 patients with PCBCL, 7 with primary cutaneous marginal zone lymphoma (MZL) and 5 with primary cutaneous follicle centre lymphoma (FCL), who were treated with IL rituximab 3 times/week (previously reported), or our novel once/week schedule.

Results: The objective response rate was 92% (11/12), with complete response in 83% (10/12) patients. All 4 patients who received 3-times-weekly IL rituximab attained an objective response compared to 88% (7/8) of those who were treated once weekly. Of the 10 patients with a complete response, 50% remained disease-free at the end of follow-up. Median follow-up was 3.2 years (range: 1.9-6.1 years). Adverse events were limited to CTCAE grade 1, reported in 50% (6/12), including injection site reaction, headache, and urticaria. Ninety-two percent (11/12) of patients expressed overall satisfaction with the treatment.

Conclusions: IL rituximab is a safe and well-tolerated treatment for MZL and FCL. This series provides evidence to support the use of a novel weekly dosing regimen for PCBCL.

Learning objectives:

- To assess the efficacy of IL rituximab in PCBCL in a real-world setting, including novel once/week dosing.
- To evaluate the real-world safety and tolerability of IL rituximab.
- To describe patient satisfaction with IL rituximab treatment.

Takeaway Message: Weekly IL rituximab demonstrates favorable efficacy and safety in indolent PCBCLs and may be especially beneficial in areas less amenable to radiotherapy and/or surgery.

Jennifer Gantchev	4:00 – 4:10pm

How the Meiosis Gene HORMAD1 Contributes to the Development of Squamous Cell Carcinomas in Melanoma Patients

Jennifer Gantchev1,2, Amelia Martinez Villarreal1,2, Ivan V. Litvinov1,2,3

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2 Division of Experimental Medicine, Faculty of Medicine, McGill University, Montreal, Canada.

3 Division of Dermatology, McGill University, Montreal, Canada.

Introduction: BRAF inhibitor (BRAFi) therapies are highly effective treatments for metastatic melanoma. However, BRAFi monotherapies are associated with a significant risk of squamous cell carcinoma (SCC) development in melanoma patients. Consequently, BRAF inhibition results in an unanticipated activation of the MAPK pathway in surrounding cells that harbour wildtype BRAF. Fortunately, a combination approach with both a BRAFi and the selective MAPK inhibitor (MEKi), trametinib, attenuates BRAFi-induced risk of SCCs. Despite the fact that this combination therapy is widely used in clinical practice, the mechanisms associated with SCC induction and why this effect is attenuated with a MEK inhibitor remain poorly understood. HORMAD1, a meiosis specific gene, has been shown to have an impact on genomic instability and proliferation in the development of SCCs. Moreover, recent work in our lab has demonstrated that the MAPK pathway regulates HORMAD1 expression in SCC cell lines. Therefore, we sought to investigate a potential role of HORMAD1 in the risk and development of SCCs as a mechanism of BRAFi that is attenuated with the co-administration of the MEKi, trametinib.

Methods: Using the BRAFi, vemurafenib, we inhibited the kinase activity of activated BRAF (V600E) and the MEKi, trametinib to evaluate the expression of HORMAD1 in melanoma and normal keratinocyte cell lines. To determine the effects of these two inhibitors, a cell proliferation assay was conducted followed by the evaluation of various components of cell cycle regulation and genomic instability.

Results: We found that HORMAD1 protein expression levels increased following treatment with the BRAFi, vemurafenib, in the normal keratinocyte cell line, HaCaT, but not in the melanoma cell line, A375. In contrast, HORMAD1 expression decreased following treatment with the MEKi, trametinib in both HaCaT and A375. Cell proliferation assays depict a vulnerability to both vemurafenib and trametinib in both normal and melanoma cell lines, however, HaCaT cells appear to be more susceptible to increased levels of genomic instability following treatment with vemurafenib when compared to A375.

Conclusions: Our results suggest that HORMAD1 likely plays a key role in the development of SCCs by increasing genomic instability and proliferation in normal keratinocytes following BRAFi mono treatment. The increased risk of SCC formation is attenuated by dampening HORMAD1 levels with the co-administration of the MEKi, trametinib.

Learning objectives:

- Squamous cell carcinoma, meiomitosis, MAPK pathway

Takeaway Message: Dual treatment of vemurafenib and trametinib in melanoma patients diminishes the development of SCCs due to attenuated expression of the meiosis gene HORMAD1.

Brandon Ramchatesingh	**4:10 – 4:20pm**

PRAME Enhances Proliferation and Attenuates Retinoid Response in Keratinocyte Carcinoma and in Head and Neck Squamous Cell Carcinoma

Brandon Ramchatesingh1, 2, Ivan V. Litvinov1, 2, 3

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Introduction: Preferentially Expressed Antigen of Melanoma (PRAME) is a cancer-testis antigen that represses retinoid signaling and fosters aggressive phenotypes in cancer cells. Retinoids normalize cell differentiation and promote turnover. Hence, these compounds have applications in cancer treatment and prevention. Retinoids are used to prevent the development of keratinocyte carcinomas (KC): basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC). The expression and function of PRAME in KC has never been studied.

Methods: PRAME expression was evaluated in human KC tumors, KC cell lines and head and neck SCC (HNSCC) cell lines by immunoblotting and qRT-PCR. PRAME-overexpressing KC and HNSCC cell lines were generated. shRNA-mediated knockdown of PRAME was performed in a cSCC and a HNSCC cell line. Cells were treated with all-trans retinoic acid (ATRA) for 24, 48 or 72 hours. Expression of differentiation markers was assessed by immunoblotting and qRT-PCR. Cell counting assays, immunoblot analysis of cell cycle genes and Ki67 immunofluorescence staining were used to assess proliferation.

Results: PRAME expression was detected in subsets of BCC and cSCC tumors and in cell lines. Overexpression of PRAME in HNSCC cells enhanced cell proliferation compared to control cells. ATRA did not promote differentiation of PRAME-expressing cells. Furthermore, PRAME overexpression attenuated the anti-proliferative effect of ATRA in HNSCC cells.

Conclusions: We conclude that PRAME is expressed in KC tumors. PRAME overexpression enhances proliferation of malignant keratinocytes in vitro and may confer resistance to retinoid-induced differentiation and proliferation arrest.

Learning objectives:

- To assess the expression of PRAME in KC tumors and cell lines
- To investigate how PRAME modulates retinoid-induced cell differentiation in vitro
- To investigate how PRAME modulates the effects of retinoids on cell proliferation in vitro

Takeaway Message: PRAME may alter cell proliferation and confer resistance to retinoid-induced differentiation and proliferation arrest. Investigations to assess the prognostic and therapeutic significance of PRAME expression are warranted.

Friday, 12 November
Virtual Plenary Session
4:30 - 5:50pm

Aziz Ghahary	**4:30 – 4:50pm**

Application of A Liquid Dermal Scaffold Promotes Wound Healing in A Mouse Model

Mohammadreza (Sam) Pakyari, Reza B Jalili, Ruhangiz T Kilani, Erin Brown, Aziz Ghahary*
University of British Columbia

Introduction: Lack of matrix deposition is one of the main factors that complicates the healing process of wounds. The aim of this study was to test the efficacy and safety of a liquid dermal scaffold, referred to as MeshFill (MF), that can fill the complex network of tunnels and cavities which are usually found in chronic wounds and hence improve the healing process. The flowable in situ-forming scaffold is liquid at cold temperature and solidifies after application to the wound site. Therefore, it would conform to the topography of the wounds when liquid and provides adequate tensile strength when solid.

Methods: We evaluated the *in vitro* and *in vivo* properties of a novel liquid dermal scaffold in a delayed (splinted) mouse full thickness wound model. We also compared this scaffold with a commercially- available granular collagen-based products.

Results: Liquid dermal scaffold significantly accelerated wound closure as compared to no-treatment control and collagen-based injectable composites in a delayed splinted wound model. When we compared cellular composition and count between control and treated group, it was found that MF is the most analogous and consistent to the normal anatomy of the skin. We also found an earlier phase of immune cell infiltration and clearance in MeshFill treated wounds as compared to control wounds.

Conclusions: Evaluating and comparing clinical appearance, tissue cellularity, immune cell infiltration, collagen expressing cells and thickness of dermis and epidermis well indicated that MF treatment markedly improves the healing outcome of delayed wounds.

Learning objectives:

- Application of liquid scaffold accelerates the healing process.
- The phases of immune cell infiltration and clearance are earlier than those of control.
- Liquid scaffold can be used for irregular shape wounds

Takeaway Message: Applying an injectable liquid scaffold that can fill wound gaps and generate a matrix to promote keratinocytes and fibroblasts migration, can result in improvement of the healing process of complex wounds.

Elodie Labit	**4:50 – 5:00pm**

Preferential Recruitment of Immature Neutrophils Enables Robust Skin Regeneration

Labit E1,3, Sinha S1, Kutluberk E1, Jaffer A1, Arora R1, Cao L1, Shin W1, Rosin NL1, Granton E2, Yipp B2, Biernaskie J1,3,4

1 Department of Comparative Biology and Experimental Medicine, Faculty of Veterinary Medicine, University of Calgary, 2 Snyder Institute, 3Alberta Children's Hospital Research Institute, and 4 Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, 3330 Hospital Drive N.W., Calgary, Alberta T2N 4N1, Canada

Introduction: After severe injury or burn, adult mammalian wound healing occurs by formation of fibrotic scar, loss of skin appendages and permanent functional impairment. In mice, severe skin injuries exhibit partial regeneration, including formation of new hair follicles (HFs) in the center of the wound, whereas the periphery remains fibrotic. Our recent work has established that fibroblasts residing within the regenerative zone exhibit activation of unique transcriptional programs reminiscent of early skin development (Abassi et al, Cell Stem Cell 2021). How these programs are engaged within certain subsets of fibroblasts remains unclear. Immune cells dominate the early response, providing an inflammatory environment that is thought to drive fibroblasts to adopt a fibrotic fate, resulting in the formation of a dysfunctional scar.

Methods: To test this hypothesis, we microdissected then compared the microenvironment of fibroblasts by scRNAseq in the center vs periphery of the wound.

Results: An unbiased assessment of matched cell states revealed neutrophils as the most discrepant cells distinguishing regenerative domains from their fibrotic counterparts. Systemic application of aLy6G/C after injury depleted Ly6G+ neutrophils in bone marrow and in the wound bed, resulting in a 15-fold expansion of neogenic hair follicles within the wound. Single-cell transcriptomics of aLy6G/C-treated wounds revealed the emergence of Ly6GNEG MPO+ neutrophils that generate large quantities of reactive oxygen species, a feature essential for invigorating regenerative programs. Finally, we show that purposeful recruitment of these immature neutrophils repatterns immune-stromal crosstalk, resulting in an expanded pool of regeneration-competent fibroblasts to drive robust skin regeneration.

Conclusions: Together, our work identifies neutrophils as the cellular linchpin connecting innate immunity to tissue repair outcomes and defines a temporal window wherein their dynamics remain pharmacologically amenable to achieve near-complete skin regeneration.

Learning objectives:

- Neutrophil biology
- Innate immune cells and skin regeneration
- Improving skin regeneration
- Single cell RNAseq analysis

Takeaway Message: Recruitment of immature neutrophils into the skin wound can switch the fibroblasts fate in regenerative fibroblasts, resulting in a 15-fold expansion of neogenic hair follicles within the wound.

Eren Kutluberk	**5:00 – 5:10pm**

Investigating the Effects of CSF1R Inhibition on Skin Regeneration

Eren Kutluberk, Elodie Labit, and Jeff Biernaskie
Faculty of Veterinary Medicine, University of Calgary

Introduction: After injury, mammalian skin heals by producing fibrotic non-functional scar devoid of hair follicles (HFs). Interestingly, in mice, after a large open wound, regeneration of new HFs is observed in the center of the wound. CSF1 is a cytokine that acts via the CSF1R, expressed by monocytes and macrophages and stimulates proliferation and differentiation. The CSF1-CSF1R axis has been suggested to influence regenerative outcomes in the gut and liver. Here we asked whether CSF1 signaling influences skin regeneration.

Methods: To test this, CSF1R inhibitor or control chow diets were given to mice for two-time courses: 7 days before LOW until D0 (time of injury) (early) or 2 days before LOW until D5 post-injury (late).

Results: Only late CSF1R inhibition changed wound healing outcomes. Indeed, CSF1R inhibition induced faster wound closure and an increase in HF regeneration. After validating the CSFR1-inhibitor mediated depletion of F4/80+ macrophages, we will perform scRNA-seq on macrophages and fibroblasts to evaluate the diversity of macrophage populations and their state changes after CSF1R inhibition, and how the connectome between macrophages and fibroblasts evolves with CSF1R inhibition.

Conclusions: In the end, identification of a novel, macrophage-mediated, pathway responsible for activating regenerative skin fibroblasts (or suppressing scarring fibroblasts) could allow for new regenerative therapies to improve wound healing in humans and animals.

Learning objectives: Understand the large open wound model and how the regenerative response in the center of the wound is a quantifiable example of genuine skin regeneration. Appreciate the enhanced skin regeneration and hastened wound healing seen in mice with systemic CSF1R inhibition. Hypothesize about how CSF1R inhibition may be changing macrophage states and the fibroblast-macrophage connectome.

Takeaway Message: Systemic CSF1R inhibition improved mouse skin regeneration and hastened wound healing. Whether macrophage depletion also took place will be seen by in situ macrophage quantification. scRNA-seq will show how CSF1R inhibition changes macrophage states and the macrophage-fibroblast connectome.

Richard Henry	5:10 – 5:20pm

Mental Health Prior to and Longitudinally During COVID-19: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

Richard S. Henry, PhD;1,2 Linda Kwakkenbos, PhD;3,4 Marie-Eve Carrier, MSc;1 Zelalem Negeri, PhD;1,5 Angelica Bourgeault, MSc;1 Scott Patten, PhD;6-8 Susan J. Bartlett, PhD;9,10 Luc Mouthon, MD;11,12 John Varga, MD;13 Andrea Benedetti, PhD;5,9,14 Brett D. Thombs, PhD;1,2,5,9,15-17 and the SPIN COVID-19 Patient Advisors on behalf of the SPIN Investigators

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Introduction: The COVID-19 pandemic has caused over 4 million deaths and had devastating health, social, and economic consequences. Concerns exist about mental health implications during and beyond the pandemic, especially among people with pre-existing medical conditions. We assessed mental health symptoms among people with systemic sclerosis (SSc; scleroderma) from pre-COVID-19 to March 2021.

Methods: Participants were recruited from the ongoing Scleroderma Patient-centered Intervention Network (SPIN) Cohort and externally between April 9 and April 27, 2020. Pre-COVID-19 SPIN Cohort data were linked to data collected during COVID-19. We graphically displayed symptom patterns pre-COVID-19 (anxiety and depression symptoms) and at 15 assessments between April 2020 and March 2021 (anxiety and depression symptoms, fear, loneliness, boredom) and calculated standardized mean difference (SMD) changes.

Results: Among 435 participants with pre-COVID-19 data, anxiety symptoms initially increased substantially in April 2020 (SMD=0.51, 95% CI 0.37 to 0.64) then returned to pre-COVID-19 levels in March 2021 (SMD pre-COVID-19-March 2021 =0.05, 95% CI -0.08 to 0.19). Depression symptoms did not initially change (SMD pre-COVID-19-April 2020=-0.05, 95% CI -0.19 to 0.09) then decreased significantly (SMD pre-COVID-19-March 2021=-0.20, 95% CI -0.35 to -0.06). Among all participants (N=800) fear and boredom decreased significantly after April 2020, whereas loneliness was unchanged. Patterns did not differ by age, sex, country, or disease subtype.

Conclusions: Apart from an initial increase in anxiety, mental health did not worsen in COVID-19 for people with SSc. Health care providers should, nonetheless, be alert to individuals with new onset or worsened symptoms that need attention.

Learning objectives:

- To describe changes in anxiety and depression symptoms among individuals with pre-existing medical conditions, specifically SSc, prior to and during COVID-19.
- To describe changes in fear, boredom, and loneliness among individuals with SSc during COVID-19.
- To demonstrate how SPIN's centralized cohort infrastructure and extensive collaborative network were key factors in rapidly addressing knowledge needs in COVID-19.

Takeaway Message: No studies have documented mental health among medically ill individuals pre-COVID-19 and during the pandemic. Anxiety initially increased substantially then returned to pre-COVID-19 levels. Overall, mental health in SSc has not worsened, but some individuals may be affected.

Simon-Pierre Gravel	5:20 – 5:30pm

The PGC-1 Coactivators Control Inflammation And Immunosuppression In Melanoma

Karl Larin, Katherine Coutu-Beaudry, Nour Meribout, Simon-Pierre Gravel
Faculté de pharmacie, Université de Montréal

Introduction: Advanced stage melanoma is a fatal disease that presents a significant therapeutic challenge due to the capacity of melanoma cells to develop resistance to treatments and to evade the immune system. Immune checkpoint therapy remains unfortunately ineffective in a large portion of patients due to primary or acquired resistance. A better understanding of the mechanisms by which melanoma cells can modulate T cell functions should bolster the design of new therapeutic approaches to increase clinical efficacy of immune checkpoint therapy. Melanoma is characterized by metabolic remodeling which bolster survival, metastasis, and therapeutic resistance. The peroxisome proliferator-activated receptor gamma coactivators (PGC-1s), which control mitochondrial biogenesis gene expression programs, have recently emerged as important mediators of this remodelling. Since various mitochondrial inputs can drive the immune response, we hypothesized that PGC-1s dysfunction or deregulated expression may shape tumour inflammation and immunosuppression.

Methods: We analyzed the correlation between PGC-1s, metabolic, and immune transcripts in RNA-seq datasets from the TCGA PanCancer Atlas and the Cancer Cell Line Encyclopedia. We performed RNA interference in a panel of human melanoma cell lines. We studied cell proliferation and performed cell cycle analysis by FACS, studied glycolysis and mitochondrial respiration with Seahorse analyzers, and assessed changes in gene expression by qRT-PCR and protein levels by immunoblotting and cytokine arrays. We also use a panel of compounds, gene reporter assays, and performed cell partitioning to investigate molecular mechanisms.

Results: We show that the depletion of PGC-1s in human melanoma cell lines recapitulates the immunosuppressive and pro-inflammatory signature observed in human tumours. We show that PGC-1s depletion induces proliferative arrest and reduces the expresssion of HSPA9, which is linked with metabolic and immune rewiring. We further show that the IKK and MEK signaling pathways bolster the immune effects of PGC-1s depletion.

Conclusions: Our analyses suggest that PGC-1s expression level in tumors may influence immune evasion programs and the response to immunotherapy.

Learning objectives:

- Discover melanoma-cell-intrinsic immunosuppressive mechanisms
- Describe classic and novel functions of the PGC-1s
- Describe the mechanistic links between metabolic dysfunction and immune response

Takeaway Message: We show that the metabolic coactivators PGC-1s, mostly known for their role in mitochondrial biogenesis, have overlooked functions in shaping tumour immune response. Our study shed light on a link between mitochondrial dysfunction and transcriptional programs that mediate immune evasion.

Samar Sayedyahossein	**5:30 – 5:40pm**

Loss of Kindlin-1 Causes Actin Cytoskeleton Dysregulation and Impaired Keratinocyte Cellular Function

S. Sayedyahossein**, I.A. Ivanova*, E. Mahdipour*, F. Wahba Hassan*#, M. Karimi‡, M. Bahmanif, and L. Dagnino*†.

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Introduction: Kindlin-1 is a FERM domain-containing scaffold protein, indispensable for integrin activation and a key component of focal contacts in epidermal keratinocytes. Loss of function mutations in the *FERMT1* gene, which encodes Kindlin-1, lead to epidermal fragility, blister formation, photosensitivity, and increased risk for mucocutaneous malignancies.

Methods: To better understand the mechanisms involved in Kindlin-1-modulated processes in the epidermis, we generated monoclonal lines of N/TERT keratinocytes with *FERMT1* inactivation using CRISPR/Cas9 gene editing (hereafter termed Kin-1KO cells).

Results: Kin-1KO keratinocytes exhibit reduced proliferation, decreased migratory capacity and impaired spreading, compared to parental cells. Reverse Phase Protein Array (RPPA) analysis revealed that Kindlin-1-deficiency is associated with changes in the abundance of proteins involved in major signaling cascades, including actin cytoskeleton dynamics. Further, we found altered arrangement of filamentous actin and cytokeratin 14 intermediate filaments in Kin-1KO keratinocytes compared to control parental cells.

Conclusions: We conclude that Kindlin-1 is essential for normal cytoskeletal assembly in keratinocytes. These findings may be applicable to other Kindlin-1-expressing epithelial cell types.

***Supported with funds from the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council.

Learning objectives: This study enhances our understanding of the role of Kindlin-1 in regulation of actin cytoskeleton dynamics and provides mechanistic insight into how Kindlin-1 modulates signaling cascades involved in key cellular functions of keratinocytes. The findings of our study potentially help to illustrate molecular aspects of Kindler Syndrome.

Takeaway Message: Kindlin-1 is essential for normal cytoskeletal assembly in keratinocytes.

Maggie Xiao	5:40 – 5:50pm

Transcriptomic Changes During Stage Progression of Mycosis Fungoides

Maggie Z.X. Xiao*[1], Dylan Hennessey[1], Aishwarya Iyer[1], Sandra O'Keefe[1], Frederick Zhang[2], Arunima Sivanand[1], Robert Gniadecki[1]

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**Principal investigator*

Introduction: Mycosis fungoides (MF) is the most common cutaneous T cell lymphoma, which in the early patch/plaque stages runs an indolent course. However, ~25% of MF patients develop skin tumors, a hallmark of progression to the advanced stage and is associated with high mortality. The mechanisms involved in stage progression are poorly elucidated.

Methods: We performed whole-transcriptome and whole-exome sequencing of malignant MF cells from skin biopsies obtained by laser-capture microdissection. We compared three types of MF lesions: early-stage plaques (ESP, n=12), and plaques and tumors from patients in late-stage disease (late-stage plaques, LSP, n=10, and tumors, TMR, n=15). Gene Ontology (GO) and KEGG analysis were used to determine pathway changes specific for different lesions which were linked to the recurrent somatic mutations overrepresented in MF tumors.

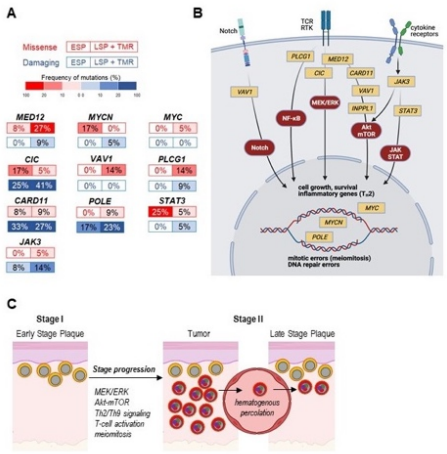
Results: The key upregulated pathways during stage progression were those related to cell proliferation and survival (MEK/ERK, Akt-mTOR), Th2/Th9 signaling (IL4, STAT3, STAT5, STAT6), meiomitosis (CT45A1, CT45A3, STAG3, GTSF1, REC8) and DNA repair (PARP1, MYCN, OGG1). Principal coordinate clustering of the transcriptome revealed extensive gene expression differences between early (ESP) and advanced-stage lesions (LSP and TMR). LSP and TMR showed remarkable similarities at the level of the transcriptome, which we interpreted as evidence of cell percolation between lesions via hematogenous self-seeding.

Conclusions: Stage progression in MF is associated with Th2/Th9 polarization of malignant cells, activation of proliferation, survival, as well as increased genomic instability. Global transcriptomic changes in multiple lesions may be caused by hematogenous cell percolation between discrete skin lesions.

Learning objectives:

- Identify the clinical stages of mycosis fungoides (MF)
- Describe the transcriptomic changes in advanced vs. early MF
- Understand how the percolating of circulating tumor cells between the skin and blood compartments may be essential for the progression of MF.

Takeaway Message: Tumor progression in MF is associated with recurrent mutations which can be linked to the upregulation of signaling pathways controlling cell proliferation, survival, mitosis, and DNA repair. We speculate that percolation of malignant cells between lesions and tumor self-seeding may mediate stage progression in MF.



Muthu Lakshmi Muthu	**3:00 – 3:10pm**

Sex Specific Role of Fibrillin-1 In Adipose Tissue Development and Function

Muthu L. Muthu1*, Kerstin Tiedemann2,3*, Rajpreet Kaler1, Julie Fradette4,5,6, Svetlana Komarova1,2,3#, Dieter P. Reinhardt1,2#

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** Co-first authors, # Co-senior authors*

Introduction: Fibrillin-1 is an extracellular glycoprotein present throughout the body. Mutations in fibrillin-1 cause a wide spectrum of type I fibrillinopathies, including Marfan syndrome and stiff skin syndrome characterized by manifestations in adipose tissues and skin, among others. This study addresses the hypothesis that fibrillin-1 regulates adipocyte development and plays a vital role in normal adipose tissue homeostasis.

Methods: We employed two mouse models - *Fbn1*mgR/mgR (20-25% of normal fibrillin-1) and *Fbn1*C1041G/+ (missense mutation in fibrillin-1) to examine the role of fibrillin-1 in adipose tissue development. To further elucidate the fibrillin-1 dependent adipogenic mechanisms, we used primary bone marrow derived mesenchymal stem cells (MSCs) from *Fbn1*mgR/mgR, *Fbn1*C1041G/+ mice and littermate controls (Wt).

Results: Fibrillin-1 was present around mature adipocytes in both mouse and human white adipose tissues. As expected, Fbn1mgR/mgR mice displayed a significant reduction in fibrillin-1 levels, whereas no change was observed in Fbn1C1041G/+ mice. Male Fbn1mgR/mgR mice displayed a higher weight of subcutaneous (underneath the dermis) white and brown adipose tissues and visceral (abdominal) white adipose tissue, whereas female Fbn1mgR/mgR and Fbn1C1041G/+ showed no difference compared to littermate controls. Consistently, male Fbn1mgR/mgR mice displayed an insulin resistant phenotype and higher levels of cholesterol and high-density lipoproteins in the serum. Fibrillin-1 deficiency in male mice also promoted adipogenic gene expression and led to hypertrophic expansion of mature adipocytes. Increased adipogenic differentiation and pAkt levels were observed when MSCs were differentiated from Fbn1mgR/mgR mice. Finally, a C-terminal fibrillin-1 fragment significantly reduced adipocyte differentiation and specifically the adipogenic commitment by sequestering insulin and suppressing the Akt signaling pathway.

Conclusions: Overall, our study shows that altered adipose tissue metabolism observed in fibrillin-1 deficient mice depend on the type of fibrillin-1 deficiency and the biological sex. Precisely, fibrillin-1 negatively regulates adipogenesis in the early commitment phase establishing its importance in adipose tissue development and homeostasis.

Learning objectives:

- To study the function of fibrillin-1 in adipose tissue development,
- To elucidate the role of fibrillin-1 in adipogenesis, and
- To distinguish the sex specific consequences of fibrillin-1 in adipogenesis and adipose tissue development

Takeaway Message:

i) Fibrillin-1 deficiency but not a missense mutation promotes excess fat deposition and metabolic disturbances in male mice only, and
ii) Fibrillin-1 acts as a negative regulator of adipogenesis.

Valentin Nelea	3:10 – 3:20pm

Role Of N-Linked Glycans In Fibulin-5 And LTBP-4S Mediated Matrix Assembly And Function

V. Nelea*1, H. Kumra*1, R.M. Zhang 1, H. Hakami 1, E. Mirzarazi 1, D.P. Reinhardt1,2 * co-first authors

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Introduction: Skin requires various extracellular proteins, including fibulin-4 and -5 and the latent TGFβ binding protein-4 (LTBP-4) long and short isoforms (LTBP-4L and LTBP-4S) to synthesize functional elastic fibers. Mutations in these proteins cause heritable diseases such as cutis laxa, and result in deficient elastic fibers and compromised skin elasticity. We recently demonstrated new mechanisms in elastogenesis involving a dual role of fibulin-4 in i) inducing a stable conformational and functional change of LTBP-4L, and ii) promoting deposition of tropoelastin onto the elongated LTBP-4L [1]. The role of N-linked glycosylation in these processes are not understood.

Methods: Fibulin-4, fibulin-5, LTBP-4S and LTBP-4L were recombinantly produced by HEK293 cells and chromatographically purified. Deglycosylation was performed with PNGase F enzyme. The binding affinity of the proteins was studied by Biacore surface plasmon resonance spectroscopy. Atomic force microscopy was used to visualize the proteins. Dynamic light scattering was employed to analyze protein conformations in solution.

Results: Here, we show that fibulin-5, but not fibulin-4 can induce a similar but not identical extension and functional change of LTBP-4S, resulting in an increase in LTBP-4 assembly and in tropoelastin assembly/deposition. This provides a mechanism for the previous in vivo observations and suggest the existence of two separate development axes in elastogenesis (fibulin-4—LTBP-4L and fibulin-5—LTBP-4S). We next asked if N-linked glycans on fibulins and LTBP4s play a key role in fibulin-mediated LTBP-4 structure, function, assembly, and elastogenesis. Our results show that overall deglycosylation influences LTBP4 assembly as well as tropoelastin deposition. Preliminary data demonstrate that fibulin-5 N-linked glycans are essential for promoting LTBP4S binding, extension, assembly, and tropoelastin deposition. Conversely, in the LTBP-4—fibulin-4 axis, the N-linked glycans in LTBP-4L but not in fibulin-4, are crucial to allow LTBP-4L structure, function, and assembly changes. The N-linked glycans of fibulin-4 play an inhibitory role in binding to tropoelastin and promoting tropoelastin assembly. Enzymatic or genetic removal of N-linked glycans from fibulin-4 increases its binding to tropoelastin. N-glycosylation mutants of fibulin-4, when endogenously expressed, enhanced elastin assembly.

Conclusions: The data elucidate new mechanisms which regulate the process of elastic fiber formation in skin including the fibulin-5—LTBP-4S axis and suggest that the presence of N-linked glycans in fibulins and in LTBP4s affect the LTBP4 assembly and tropoelastin deposition.

Learning objectives:

- To investigate the contributions of the fibulin-5—LTBP-4S axis to elastogenesis.
- To determine whether the glycosylation status of the proteins has a functional role for LTBP-4 assembly and tropoelastin deposition.
- To determine which N-linked glycan in fibulin-4, fibulin-5, LTBP-4L and LTBP-4S is ultimately required for elastogenesis.

Takeaway Message: New mechanisms that regulate the process of elastic fiber formation in skin including the fibulin-5—LTBP-4S axis was presented. The presence of N-linked glycans in fibulins and in LTBP4s affect the LTBP4 assembly and tropoelastin deposition.

Brice Magne	**3:20 – 3:30pm**

Exploring the Role of Autophagy in Skin Pigmentation

***Brice Magne*, Karel Ferland et Lucie Germain.**

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Introduction: The skin pigmentation barrier is regulated by a complex network of cells including (i) melanocytes, that synthesize and deliver melanin granules, (ii) keratinocytes, that capture and sequester melanin around the nucleus to form "nuclear caps", and (iii) neural, immune and fibroblast cells, secreting paracrine factors that regulate pigmentation. While the mechanisms of melanin production and transport in melanocytes are well described, melanin transfer, sequestration and degradation in keratinocytes still remain barely understood. Previous observations indicate that melanin distribution in the epidermis varies according to skin phototype and epidermal layer, but no precise mechanism has been delineated yet. Autophagy is a cellular degradation process that is necessary for cell maintenance and homeostasis. Recently, different studies have shown that autophagy-related genes were upregulated (i) in suprabasal epidermal cells compared to basal epidermal cells, and (ii) in skin cells derived from light phototypes compared to dark phototypes. Therefore, the aim of this study was to evaluate the role of autophagy on melanin degradation in keratinocytes.

Methods: Skin samples from light and dark phototype donors were collected and processed for histological analyses and fluorescent activated cell sorting (FACS). Pigmented skin substitutes were produced from extracted cells and treated with an autophagy inductor or inhibitor. Immunofluorescence and western blots were used to analyze the results.

Results: Systemic treatment with an autophagy inhibitor reduces melanin degradation in keratinocytes. However, long-term treatment is deleterious for melanocytes and epidermal cell differentiation.

Conclusions: Autophagy plays a role in pigmentation at both keratinocyte and melanocyte levels. Future investigations will aim to clarify the relationship between melanin degradation and epidermal cell differentiation.

Learning objectives:

- Learn about pigmentation processes,
- gather information about autophagy and its effects on pigmentation,
- Familiarize with the use of combined techniques to answer a complex research question.

Takeaway Message: Melanin production and degradation are influenced by autophagy.

Emilie Attiogbe	**3:30 – 3:40pm**

Immunocompetent, Vascularized, Autologous 3D Skin Model Reconstructed by Tissue Engineering For Wound Healing Studies

Emilie Attiogbe1,2, Sébastien Larochelle1,2, Carine Mainzer3, Adèle Mauroux3, Sylvie Bordes3, Brigitte Closs3 Caroline Gilbert2, Véronique J Moulin1,2

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Introduction: Skin wound healing is a normal biological process occurring after injury and is categorized into hemostasis, inflammation, proliferation, and remodeling. The early phases require the recruitment of several immune cells from the blood that regulate the fate of wound healing. However, the role of skin's resident immune cells is not well defined and could perpetuate a distinct contribution to the healing process.

Methods: To investigate their contribution to wound healing, we first developed a cell extraction technique that isolates skin resident cells from the same donor (keratinocytes, fibroblasts, immune and endothelial cells). From this isolation, an autologous *in vitro* three-dimensional (3D) human skin model was developed.

Results: Analysis by flow cytometry reveals the presence of resident skin macrophages CD45+ CD14+ CD163+; lymphocytes, CD45+CD3+; dendritic cells CD45+, CD14-, CD1a+ and endothelial cells CD45-CD31+ in freshly isolated skin cells. Their presence was then confirmed in the 3D skin model by immunofluorescence staining. Endothelial cells self-assemble to form capillary like networks and the number of immune cells is maintained after 14 days in culture. The rate of proliferation at the level of the basal layer of the epidermis was characterized by Ki67 staining and reveals a difference between reconstructed skin supplemented with resident immune and endothelial cells compared to reconstructed skin containing only fibroblasts and keratinocytes.

Conclusions: This skin model provides a great tool to study wound healing process and the interaction of skin's dermal resident immune cells.

Learning objectives:

- Developing a cell extraction technique for skin's resident immune cells
- Maintaining immune cells and their function into a 3D skin model
- Understanding the contribution of skin's resident immune cells to wound healing process

Takeaway Message: We developed a vascularized, autologous 3D skin model reconstructed by tissue engineering and containing resident immune cells for wound healing studies.

Valentin Nelea	3:40 – 3:50pm

Differential Interaction of LOXL1 Variants Linked to Pseudoexfoliation Syndrome with Fibulin-4, Fibulin-5 And Tropoelastin

Nelea V*1; Hoja U*2; Schlotzer-Schrehardt U#2; Reinhardt DP#1,3 *Co-first authors; #Co-last authors

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Introduction: Pseudoexfoliation syndrome (XFS) is an age-related systemic disorder involving excessive production and accumulation of abnormal elastic fiber components. It is manifested prominently in the eye with XFS being the most common factor of severe blindness-inducing glaucoma, but it is also present in skin and other tissues. XFS pathology has been linked to variants in *LOXL1*, a gene encoding the elastic fiber cross-linking enzyme lysyl oxidase-like 1. Combinations of LOXL1 single nucleotide polymorphisms (SNPs) leading to different amino acid substitutions at p.141, p.153 and p.407 were found to be associated with XFS, but the contribution of these SNPs to the disease severity varies widely among different populations.

Methods: Triple variants of LOXL1 were recombinantly produced by HEK293-EBNA cells and purified. These included wild-type GGA described as a risk factor in the German population and TGA categorized as risk factor in the Japanese population, as well as German (GAA) and Japanese (GAT) protective variant combinations. Molecular interactions of these LOXL1 variants with fibulin-4, fibulin-5 and tropoelastin were investigated by surface plasmon resonance spectroscopy and their binding affinities determined.

Results: The German protective variant GAA binds significantly stronger (KD=4.5 nM) to fibulin-4 than the German risk variant GGA (KD=10 nM). The Asp at p.153 replacing Gly contributes to the increase in binding. The Japanese protective GAT and German protective GAA bind fibulin-4 with similar very high affinity (KD=3 nM and KD=4.5 nM). The replacement of Tyr at p.407 with Phe had no effect in binding. The Japanese risk TGA does not bind to fibulin-4 with Leu at p.141. On the other hand, all LOXL1 variants bind fibulin-5 similarly with moderate affinity (KD=95-207 nM). The German protective variant GAA binds weaker (KD=78 nM) to tropoelastin than the German risk variant GGA (KD=11 nM). The Asp at p.153 replacing Gly accounts for this binding reduction. The Japanese risk TGA binds tropoelastin considerably weaker (KD=73 nM) than its German risk GGA counterpart. This implies that Leu at p.141 should account for this binding decrease. The binding site includes p.141 in addition to p.153. The Japanese protective GAT binds much stronger to tropoelastin (KD=3.5 nM) than the German protective GAA (KD=78 nM). The replacement of Tyr at p.407 with Phe is responsible for this high binding increase, suggesting the existence of a tight tropoelastin binding interaction at p.407.

Conclusions: This is the first study that aims to define the link between LOXL1 SNPs relevant for XFS and their interaction with elastogenic proteins. SNPs in LOXL1 clearly change the binding behaviour to fibulin-4 and tropoelastin, but not to fibulin-5. The stronger the binding to fibulin-4, the higher the level of protectiveness. The binding site to fibulin-4 includes the SNP at p.153 in the N terminal domain. A new potential binding site to tropoelastin has been identified at p.407 in the C terminal catalytic domain of LOXL1

Learning objectives:

- To analyse LOXL1 variant interactions with elastogenic proteins fibulin-4, fibulin-5 and tropoelastin and map the interaction sites.
- To determine the functional link of the interactions with LOXL1 SNP-related XFS.

Takeaway Message: LOXL1 single nucleotide polymorphism variants bind differently to elastogenic proteins fibulin-4 and tropoelastin, but not to fibulin-5. The binding affinities to these proteins induce differences in elastogenesis and proper development of elastic tissues including skin with clinical manifestations in the systemic disorder pseudoexfoliation syndrome.

Karel Ferland	**3:50 – 4:00pm**

Using Physiological Factors to Improve Self-Assembled Skin Substitutes Pigmentation

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Introduction: Melanin, a chromophore derived from melanocytes, is responsible for skin pigmentation and protects the organism from ultraviolet's harmful effects. However, in patients treated with bilayered self-assembled skin substitutes (SASS), the pigmentation barrier is not fully restored. Pigmentation defects are probably due to melanocyte dilution during SASS culture. Thus, we hypothesized that the supplementation of the SASS culture medium with several physiological melanogenic factors, such as Fibroblast Growth Factor-2 (FGF-2), Endothelin-1 (ET-1), Growth Macrophage Colony-Stimulating Factor (GM-CSF), Stem Cell Factor (SCF) and Corticotropin-Releasing Hormone (CRH) would increase melanocyte growth and improve pigmentation.

Methods: We first evaluated the role of the five factors, in a dose-dependent manner, alone or in combination, on keratinocyte and/or melanocyte proliferation and melanin synthesis in 2D culture. The best candidates were then selected to be tested in the 3D SASS model.

Results: Our preliminary results suggest that FGF-2 promotes melanocyte proliferation, without stimulating keratinocyte proliferation, while GM-CSF, SCF, ET-1 and CRH seem to induce melanin synthesis in 2D culture. FGF-2 also stimulates melanocyte proliferation in SASS but has no effect on pigmentation. FGF-2 supplementation has no deleterious effect on epidermal development.

Conclusions: Our results suggest that FGF-2 supplementation could promote the maintenance of melanocytes in SASS. Future experiments will aim to confirm these results and determine whether the combined addition of melanogenic factors can induce melanin production

Learning objectives:

- Understand the cause of pigmentation defects presented by patients treated with SASS.
- Understand the importance of restoring the pigmentation barrier after burn.
- Learn about new approaches to stimulate melanocyte growth and melanin synthesis.
- Get more insights into proliferation and melanogenesis mechanisms of melanocytes.

Takeaway Message: The supplementation of keratinocyte culture medium with melanogenic factors such as FGF-2 could improve SASS pigmentation.

Melanie Laurin	**4:00 – 4:10pm**

Deciphering the Functions of FGD Rhogefs During Skin Development

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Introduction: Skin development requires the concerted action of developmental signaling pathways to regulate stem cell renewal and differentiation, while coordinating cytoskeletal remodeling to achieve tissue morphogenesis. Our understanding of the molecular effectors that regulate these processes remains rudimentary. Due to their ability to orchestrate cytoskeletal dynamics, the 20 Rho GTPases and their regulators, namely the RhoGEFs, the RhoGAPs and the RhoGDIs are emerging as key effectors of morphogenesis yet their contribution to skin development has been largely unaddressed.

Methods: The mouse skin is an excellent model organ to tackle this problem since the embryonic skin is abundant and easily tractable. Moreover, the skin is amenable to *in utero* lentiviral injections, a method that considerably improved our ability to genetically modify this tissue. Using the power of mouse *in utero* lentiviral injections, we functionally tested all of Rho GTPase network components for their contribution to skin development using a novel high-throughput shRNA mediated *in vivo* screen (*Laurin et al., elife 2019*).

Results: We revealed three members of the understudied FGD family of RhoGEFs i.e., FGD1/2/5 act as candidate regulators of skin development. Intriguingly, we observed that shRNAs targeting FGD1/2/5 were each individually depleted in different skin compartment, which suggests that these genes regulate different processes in this tissue. We now revealed that FGD1 is required for epidermal differentiation and cytoskeletal organization in this tissue.

Conclusions: Altogether, our work will unravel new functions for these understudied RhoGEFs and provide key understandings of the molecular mechanisms that orchestrate skin development.

Learning objectives:

- To gain fundamental insights into Rho GTPases signalling networks that orchestrate skin development.
- To unravel new function for understudied Rho GTPase network components
- To dissect the biological roles of FGD1/2/5 in skin development

Takeaway Message: In utero lentiviral injection is a powerful model to study skin development. We tested Rho GTPase network components for their contribution to skin development via a novel shRNA based high-throughput in vivo screen strategy. FGD1/2/5 are regulators of skin development.

Poster Presentation Abstracts

Wound Healing and Regeneration

Alvaro Sierra Sanchez | **WH01**

Comparison of Biomaterial-Free and Biomaterial-Based Human Bilayer Tissue-Engineered Skin Substitutes: Metabolic Activity and Mechanical Properties Analysis

Álvaro Sierra-Sánchez1,2, Brice Magne1, Etienne Savard1, Christian Martel1, Lucie Germain1, Salvador Arias-Santiago2.

1CHU de Québec – Université Laval Research Center, Division of regenerative medicine, LOEX-Hôpital de l'Enfant-Jésus and Department of Surgery, Faculty of Medicine, Université Laval, Québec, Canada. 2Cell Production and Tissue Engineering Unit. Virgen de las Nieves University Hospital, Andalusian Network of Design and Translation of Advanced Therapies, Granada, Spain.

Introduction: The use of human bilayer tissue-engineered skin substitutes (hbTESSs) for the treatment of dermatological pathologies is a promising therapy. Between both layers, dermis is responsible of hbTESSs' mechanical properties and for this reason, different manufacturing processes such as biomaterial-free approach (self-assembly of fibroblasts and their extracellular matrix) or biomaterial-based strategy (fibroblasts embedded in human plasma fibrin + others) will affect their final properties. Therefore, the aim of this study is to compare metabolic activity and mechanical properties of hbTESSs manufactured by i)self-assembly (SA) approach and ii)human plasma fibrin-based strategy.

Methods: 4 hbTESSs were manufactured by self-assembly (SA) method and 9 hbTESSs were fabricated using human plasma fibrin-based strategy combined with hyaluronic acid (F-HA), collagen (F-C) or alone (F) (n=3 for each condition). At the end of each manufacturing process, metabolic activity (Presto BlueTM), thickness, mechanical properties (ultimate tensile strength (UTS)), modulus of elasticity and dermoepidermal junction (DEJ) adhesive strength were analyzed.

Results: Metabolic activity was similar in all groups. F-HA and F-C substitutes were thicker (0.548 mm and 0.572 mm respectively) than SA (0.496 mm) and F groups (0.428 mm). SA skin substitutes were more resistant to tensile forces (UTS of 0.572 MPa) than those constituted of human plasma fibrin (0.344 MPa). SA group was stiffer than the rest (2.936 MPa), specially compared with F-C group (0.390 MPa). Finally, adhesive strength of DEJ was higher for SA and F-C groups (7.041 mN/mm and 3.251 mN/mm respectively) than F-HA and F (1.685 mN/mm and 1.618 mN/mm).

Conclusions: Self-assembly approach and human plasma fibrin-based strategy provide different properties to hbTESSs which could be interesting depending on the dermatological pathology to be treated.

Learning objectives:

- Compare metabolic activity and mechanical properties of hbTESSs manufactured by two different methods.
- Discuss their advantages and disadvantages.
- Evaluate their clinical applications depending on the dermatological pathology to be treated.

Takeaway Message: Self-assembly approach produces hbTESSs more resistant to tensile strengths but stiffer than those manufactured by human plasma fibrin-based strategy.

Wound Healing and Regeneration

Anabelle Demers | **WH02**

Development of A Tissue-Engineered Dermis Decellularization Protocol for Skin Substitute Production and An Eventual Grafting on Burn Patients

***Anabelle Demers*1,2, Brice Magne1,2, Marika Lemire-Rondeau1,2, Rina Guignard1,2 François A. Auger1,2 et Lucie Germain1,2.**

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2Centre de recherche du CHU de Québec-Université Laval (Québec, Canada).

Introduction: Autologous skin grafting in burn patients is limited when patients have small areas available for graft harvesting. Self-assembled skin substitutes (SASS) can be used to overcome this limitation, but their production is time-consuming. To shorten the process, decellularization and storage of allogeneic self-assembled dermis have been considered. Nevertheless, to be clinically applicable, decellularized allogeneic dermis (DM) should contain less than 50ng of DNA per mg of dry tissue and DNA residues should not exceed 200bp. The aim of this study was therefore to assess the effect of DNAse and storage on the nature and amount of DNA residues in the DMs.

Methods: We tested different doses of DNAse (0, 0.2, 0.4, 0.6, 0.8, and 1.0 mg/mL) during decellularization and assayed the amount of residual DNA before and after 1 month of wet storage. We also performed DNA electrophoresis, histology, and immunofluorescence to further characterize the structure and composition of DM.

Results: Our results indicate that the 0.4mg/ml dose of DNAse is sufficient to fall below the targeted DNA threshold. Storage also reduces residual DNA. DM thickness was reduced by decellularization and nuclei were absent.

Conclusions: The next challenges will be to validate the non-immunogenicity and the quality of the skin reconstructed from DM after grafting in vivo

Learning objectives:

- Understand the importance of shortening the SASS production process.
- Learn about the milestones that facilitate clinical translation.
- Gain more insights into decellularization and wet storage processes.

Takeaway Message: DNAse-driven decellularization and wet storage are efficient methods to reduce DNA residues in decellularized allogeneic dermis.

Wound Healing and Regeneration

Emilie Doucet | **WH03**

Development of An Additive for The Culture of Human Keratinocytes to Replace the Use of A Human Feeder Layer

Emilie Doucet*, *Line Cantin*, *Sergio Cortez Ghio*, *Martin Barbier*, *Sylvain Guérin*, *Christian Salesse* and *Lucie Germain

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Introduction: The production of human tissue-engineered skin substitutes (TES) requires massive amplification of keratinocytes. To obtain cultures of keratinocytes with a high proliferation rate that also preserve a high proportion of stem cells throughout successive passages, it is currently necessary to culture them with a feeder layer. It has been shown that, when cultured with a feeder layer, expression of the Sp1 transcription factor in keratinocytes is maintained throughout cell passages. On the other hand, in keratinocytes cultured without a feeder layer, Sp1 expression quickly decreases which consequently leads to cell senescence. It has been shown that the glycosylation level of Sp1 is reduced in the absence of a feeder layer. We hereby propose that the introduction of glycosylated Sp1 into keratinocyte cultures could efficiently replace a feeder layer. The aim of this study is to produce and purify the glycosylated form of Sp1 in order to use it as an additive that would substitute the feeder layer for culturing keratinocytes.

Methods: Plasmid vectors encoding for Sp1 and OGT (the enzyme responsible for its glycosylation) proteins have been produced and transformed in *Escherichia coli*. The glycosylated and non-glycosylated forms of Sp1 have been purified by column chromatography. These proteins will then be added to the medium of keratinocyte cultures to determine whether the addition of glycosylated Sp1 can mimic the effects of a feeder layer**.**

Results: The glycosylated and non-glycosylated forms of Sp1 have successfully been produced and purified.

Conclusions: We believe that the glycosylated Sp1 can eventually partially or totally replace the feeder layer.

Learning objectives:

- Keratinocyte cultures currently require a feeder layer.
- It would be better to avoid the use of a feeder layer.
- Adding recombinant Sp1 in its glycosylated form could mimic the effects of a feeder layer.

Takeaway Message: Because the feeder layer is allogeneic, replacing it with a recombinant protein would represent a significant advancement for clinical applications of human keratinocyte cultures.

Wound Healing and Regeneration

Etienne Savard | **WH04**

Effects of Static Pressure on The Adhesive Strength Between Two Dermal Sheets Reconstructed Using the Self-Assembly Method

Étienne Savard, Brice Magne, Anabelle Demers, Robert Gauvin, François A. Auger and Lucie Germain.

Centre de recherche en organogénèse expérimentale de l'Université Laval/LOEX and Department of Surgery, Faculty of Medicine, Université Laval, Québec, Canada.; CHU de Québec-Université Laval Research Centre.

Introduction: Reconstructed bilamellar skin grafts produced by the self-assembly approach are created from multiple sheets of confluent fibroblasts stacked to one another, with the top sheet previously seeded with keratinocytes. The culture at the air-liquid interface then promotes epidermal differentiation and fusion between cell sheets. To accelerate the production time, we developed a method to decellularize and preserve the self-assembled dermis before keratinocyte seeding and air-liquid interface switch. Using this method, the fibroblast sheets did not fuse properly, resulting in significant delamination after decellularization. We hypothesize that without appropriate mechanical surroundings, the fibroblast sheets are unable to fuse together. The objective of this study is thus to evaluate whether static pressure could increase the adhesive strength of decellularized dermal sheets.

Methods: We applied different static pressures on self-assembled dermis and measured the adhesive strength before and after decellularization using a "T" peel test. Biopsies were recovered for histological analysis of the thickness and delamination using Masson's Trichrome and Hematoxylin-Eosin stainings. Finally, we assessed matrix proteins content such as Collagen type I, Tenascin, and Decorin by western blotting.

Results: Static pressures above 150 Pa significantly improved fibroblast sheets adhesive strength and reduced delamination, with no effect on thickness or matrix protein expression. The decellularization process strongly decreased non-collagenous matrix protein content, leaving collagen type I to be accountable for the adhesive strength.

Conclusions: Proper control of cell sheets' mechanical surroundings results in improved mechanical properties without modifying matrix content and production.

Learning objectives:

Learn more about mechanical characterization possibilities concerning reconstructed skin substitutes, how to properly control mechanical surroundings of cell culture in a sterile environment, and how powerful image analysis can be to quantify morphological parameters.

Takeaway Message: Static mechanical pressure may play a significant role in matrix protein assembly and organization. Collagen type I could be accountable for most of the adhesive strength between two fibroblast layers.

Wound Healing and Regeneration

Jason Dagher | **WH05**

Bioengineering and Long-term Storage of Complex Tissue and Organ Constructs for Transplantation

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Introduction: In 2013, around 53 000 burn-related hospitalizations occurred in the USA, of which over 15 000 required skin grafts according to the *HCUP*. The corner stone in improving treatment prognosis of deep extensive burns remains fast and effective wound covering. Consequently, autologous engineered skin presents as a suitable treatment. Unfortunately, the production of personalized grafts incurs delays before transplantation. Thus, rapidly available tissue constructs are urgently needed to improve outcomes. We hypothesize that combining innovative tissue engineering with ice recrystallization inhibitors (IRIs) will enable cryopreservation of dermis suitable for immediate transplantation and/or autologous epithelial cell seeding.

Methods: Self-assembled skin substitutes (SASS) were used to obtain the dermis constructs. Briefly, fibroblasts were cultured for 28 days to form a single dermal sheet. Superimposing sheets can be achieved to form dermis of different thicknesses. For the freeze/thaw protocols, first, we assessed the ability of a single sheet to survive freezing within a 90% serum - 10% DMSO solution, 1.5% BSA – 10% DMSO solution. After thawing, tissue-viability was evaluated using one metabolic and one DNA-staining assay: AlamarBlue and SytoxGreen, respectively. We then tested a new product (N-2-fluorophenyl gluconamide) that has been previously tested as an IRI on single cell populations.

Results: Post thawing, a 50.6±9,5% viability was observed in presence of BSA and 47.3±8,2% with serum (p=0.43). N-2-fluorophenyl gluconamide did not modify viability, regardless of the carrier solution. Further testing is evaluating the efficacy of other gluconamide IRIs. Construct integrity will be evaluated following various concentrations of DMSO and ROCK-inhibitor. Toxicity assay results will be obtained shortly.

Conclusions: IRIs' mechanism of action remains to be elucidated when cells are embedded by matrix. Many experimenter-controlled variables affect the cryopreservation quality, while BSA presents as a non-inferior carrier solution compared to serum. Further testing is needed to determine which IRI can better preserve cutaneous constructs.

Learning objectives:

The key points of interest in this project remain the multiple techniques (physical, biochemical, logistical) employed to mitigate cryopreservation injury. Results obtained within cell suspension cannot be translated to a tissue model. Finally, while gluconamide IRIs seem promising in improving post-thaw viability in single cell solutions across a wide range of cell types, these results have not yet been obtained in a tissue construct.

Takeaway Message: Currently, we produce grafts that present similar histological characteristics to native skin and decellularize them to preserve the matrix used as a supporting scaffold for further cultures. Here, we go a step further by cryopreserving a complete dermal graft which would be suitable for transplantation immediately.

Wound Healing and Regeneration

Mathias Lemarchand | WH06

Development of A Glycated Tissue-Engineered Wound Healing Model to Mimic Diabetic Ulcers In Vitro

***Mathias Lemarchand* 1,2 Kiefer Thouin 1,2, Thiéry De Serres-Bérard 1,2, Sabrina Bellenfant 1,2, Sébastien Cadau 1,2 and François Berthod 1,2**

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2 Département de Chirurgie, Faculté de Médecine, Université Laval, Québec, Canada

Introduction: Diabetic ulcers (DU) are a major complication of diabetes. Their formation is notably caused by the accumulation of advanced glycation end-products (AGE) which induces diabetic neuropathy. To advance on a cure to DU, we developed a tissue-engineered skin treated with glyoxal, an AGE inducer, to mimic the diabetic skin environment. We studied the effect of two molecules on this wound healing model (WHM): aminoguanidine, an anti-glycation compound and substance P (SP), a neuropeptide involves in neurogenic inflammation. Our objective is to assess the potential of our WHM to adequately mimic DU and to be used to test new treatments.

Methods: The WHM is obtained by culturing human fibroblast, keratinocyte and endothelial cells on chitosan-collagen sponges. To induce glycation, the WHM is treated for two weeks with glyoxal. The wound is done with a biopsy punch in the epidermal part of the model. Keratinocytes are transfected with GFP in order to monitor the wound closure with an in vivo imaging system (IVIS).

Results: The topical deposition of aminoguanidine and SP improve wound closure of the glycated models.

Conclusions: The topical application of anti-glycation compounds on DU can minimize the deleterious effects of AGE and the deposition of SP speed up wound closure.

Learning objectives:

- Development of a robust in vitro study models
- Limitations and potentials of a tissue-engineered model
- Glycation in healthy cells to mimic diabetic ulcer environment

Takeaway Message: Wound closure of an in-vitro DU model is improved by SP and aminoguanidine.

Clinical Skin Research

Feras Al-Ghazawi | **CSR01**

Increased Risk of Second Malignancies in Patients with Extramammary Paget's Disease Patients: A Canadian Cancer Registry Analysis

Feras M. Ghazawi*[1], *Michelle Le, Akram Alakel, Elham Rahme, Denis Sasseville, Ivan Litvinov

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Introduction: Extramammary Paget's Disease (EMPD) is a rare intraepithelial adenocarcinoma that arises in apocrine gland-bearing skin and presents as a chronic rash that resembles several disorders such as eczema, cutaneous T cell lymphoma, Langerhans cells histiocytosis, intraepithelial neoplasia, fungal infections and psoriasis. EMPD is often associated with underlying or distant malignancies. The epidemiology of EMPD in Canada is incompletely understood. Further, the risk of developing second malignancies in Canadian EMPD patients was not evaluated prior to the presented study.

Methods: In this study, we thoroughly analyzed clinical characteristic, incidence and geographical distribution of EMPD patients in Canada from 1992 to 2015 using the Canadian Cancer Registry (CCR).

Results: In summary, in Canada, 845 patients were diagnosed with EMPD between 1992 and 2015. The mean incidence rate of EMPD in Canada was 1.1 cases per 1 million individuals per year with noteworthy variations in the incidence across the country. The male:female incidence ratio of EMPD was 1.00:1.87. The incidence of EMPD in Canada increased steadily within the aforementioned period. Analysis of the occurrence of second malignancies in EMPD patients revealed that 29.6% of EMPD patients developed at least one additional malignancy. These malignancies were predominantly adenocarcinoma at gastrointestinal and urogenital sites.

Conclusions: In conclusion, this study describes the epidemiology and patient distribution of EMPD patients in Canada. Further, the study also confirms increased risks of second malignancies in EMPD patients. Epidemiological studies, such as the presented one here, shed light on the risk factors associated with the development of EMPD and encourage regular screening of EMPD patients for second malignancies.

Learning objectives:

- The incidence rate of EMPD in Canada is ~1.1 cases per 1 million individuals per year with noteworthy variations in the incidence across the country.
- The male:female incidence ratio of EMPD was 1.00:1.87.
- About 30% of EMPD patients develop at least one additional malignancy, predominantly adenocarcinoma at gastrointestinal and urogenital sites.

Takeaway Message: EMPD patients are at increased risk of second malignancies.

Clinical Skin Research

Gaurav R. Isola | **CSR02**

Distinct IL-13 Production and Accumulation in Lesional And Non-Lesional Skin of Atopic Dermatitis Patients

***G. Isola* 1, V. A. Gimenez-Riviera 1, C. Jack 1,2**

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Introduction: IL-13 is a central mediator of atopic dermatitis (AD) pathophysiology. While strongly elevated in atopic dermatitis skin, the cellular origins and the localization of this cytokine in human tissue remain poorly defined, largely due to technical limitations.

Methods: Using confocal microscopy, we demonstrate IL-13 Protein by Immunofluorescence and mRNA using in-situ hybridization.

Results: We show that IL-13 protein is highly sensitive to paraformaldehyde (PFA) fixation, which masks key epitopes needed for optimal detection. We demonstrate that heat-induced epitope retrieval leads to successful detection and accurate quantification of this cytokine in human epidermis and dermis. In order to distinguish between accumulation and production of IL-13 in AD patient skin, we next compared the localization of IL-13 protein with mRNA expression by using confocal in-situ hybridization in lesional versus non-lesional skin of AD patients (n=8). Our results demonstrated that IL-13 protein mean fluorescent intensity was higher in epidermis compared to the dermis in both lesional and non-lesional skin of AD patients. IL-13 protein in lesional skin was also higher than non-lesional skin. In contrast, a greater number of IL-13+ cells were detected in the papillary dermis compared to the epidermal compartment (n=8), both in lesional and non-lesional AD skin. The majority of IL-13+ cells co-expressed mRNA for T-cell receptor as well as Th2 transcription factor GATA3 (n=4). Our findings also confirm the presence of TCR- IL-13+ cells.

Conclusions: The detection of IL-13 mRNA correlated with some but not all sites of IL-13 protein accumulation, indicating that the target epidermal compartment for IL-13 receptor binding in human skin is distinct from the predominantly dermal production site.

Learning objectives:

- To use validated methodologies for the detection of IL-13 protein and mRNA in human skin biopsies from atopic dermatitis patients
- To quantify IL-13 protein signal and cell count in epidermis relative to dermis in the lesional and non lesional skin of atopic dermatitis patients
- To immuno-phenotype IL-13 (mRNA) producing cell types in the AD lesional and non-lesional skin

Takeaway Message: These methods and results pave-the-way for more precise identification of the role of IL-13 in human skin during health and disease.

Clinical Skin Research

Jordanna Roesler | **CSR03**

Lagophthalmos as a Presenting Sign of Dermatomyositis with Muscle Involvement Limited to the Ocular Muscles Treated with Hydroxychloroquine: A Case Report

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Introduction: Dermatomyositis (DM) is an autoimmune myopathy commonly associated with a heliotrope rash and periorbital edema and erythema. Other ophthalmologic signs can occur with the disorder including ptosis and exophthalmos. Typically, ocular muscles are spared in DM even in untreated and advanced disease. The inability to completely close the eyelids, known as lagophthalmos, most commonly occurs from trauma, infection, and facial nerve palsy. No other cases of lagophthalmos as an ocular manifestation of DM without significant muscle involvement which later resolved with medical treatment has been described.

Methods: A 68-year-old woman with lagophthalmos and a past medical history of hypothyroidism and melanoma was referred by her ophthalmologist for a 7-month-history of a skin eruption on her face and upper chest.

Results: Upon examination, bilateral lagophthalmos and significant dermal atrophy of the eyelids with some sclerosis was present. The face and cape area had subtle skin induration, with poikilodermatous changes on the upper torso, neck, and face. There were no other findings on physical exam. Skin biopsy showed lichenoid type interface dermatitis with vacuolar changes. Full rheumatologic and neurologic investigations were unremarkable, including TSH, C3, C4, ENA, RF, anti-CPP, anti-Jo-1, and antineutrophilic cytoplasmic antibodies. ANA titer of 1:80 was deemed clinically insignificant. All other investigations, including imaging and EMG testing were normal. The patient was started on hydroxychloroquine 200 mg BID and responded well. 2 years later, a trial of 100 mg on alternating days lead to symptom exacerbation. Repeat EMG was again normal, and hydroxychloroquine 200 mg BID was restarted. Four years after initial presentation, the patient has no evidence of lagophthalmos or active DM.

Conclusions: Diagnosing DM can pose a challenge due to its various cutaneous and systemic features. This case highlights that ocular involvement, while rare, may be the initial presentation of systemic disease.

Learning objectives:

- To learn more about the various clinical presentations and management of DM.
- To appreciate the spectrum of myopathy and cutaneous subsets in DM.
- To understand that while rare, ocular involvement may be an initial presentation of systemic disease and requires further evaluation.
- To highlight the modes of investigations for DM.

Takeaway Message: The clinical spectrum of cutaneous manifestations and muscle involvement in DM is varied. Further awareness and understanding is needed to optimize patient outcomes.

Clinical Skin Research

Marleine Azar | **CSR04**

Factors Associated with Research Output in Academic Dermatology: A Canadian Study

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Introduction: Promotion in academia heavily relies on research productivity. The H-index is a standardized metric used to quantify research productivity at the individual level by combining the number of publications and citations to measure quantity and impact of publications. This index is particularly relevant when studying research output of individuals within a same field. Factors associated with higher H-Indices in dermatology, including sex, across Canadian academic centers remains unknown.

Methods: Medical academic centers throughout Canada with a dermatology department of at least ten faculty members were included (Dalhousie University, McGill University, Université de Montréal, Université de Sherbrooke, Université Laval, University of Alberta, University of British Columbia, University of Calgary andUniversity of Toronto). For each faculty member, we extracted sex (male, female), attainment of a masters of science or doctorate degree (yes/no), academic rank (Clinical Lecturer, Clinical Assistant Professor, Assistant Professor, Clinical Associate Professor, Associate Professor, Clinical Professor, Professor), number of years since obtaining their Fellow of the Royal College of Physician (FRCP) title or equivalent, recent Canadian Institutes of Health Research (CIHR) funding (yes/no) and H-index. Analyses were performed on the overall sample and on males and females separately. Linear regression analyses were performed to evaluate the association between H-Index and these factors using R.

Results: A total of 285 faculty members across Canada were analyzed, including 144 women (50.5%) and 141 men (49.5%). The overall H-index average was 8.44 and median was 4.00. A higher H-Index was associated with a greater number of years since FRCPC certification or equivalent (2.98, 95%CI(1.87, 4.08)), greater rank, the attainment of a graduate degree (10.25, 95%CI(6.28, 14.22)) and male gender (5.73, 95%CI(2.99, 8.48)). Similar trends were revealed within gender. However certain analyses could not be conducted due to the limited number of females in categories of higher academic ranking (Professor and Clinical Professor) and CIHR funding.

Conclusions: Academic output is associated with more years since dermatology certification, male sex, attainment of a graduate degree and recent CIHR funding. Despite making up half of dermatologists, female dermatologists showed significantly less academic productivity then their male colleagues. Further research aiming at identifying barriers to academic productivity in female dermatologists is necessary to find solutions to bridge the gap.

Learning objectives:

- To identify factors associated with research output in academic dermatology using the H-Index.
- To investigate sex differences in research output in dermatology.
- To provide results within a Canadian context.

Takeaway Message: Research productivity in academic dermatology in Canada is associated with years dermatology certification, attainment of a graduate degree and recent CIHR funding. Female dermatologists show significantly less academic productivity then their male colleagues despite making up half of the profession.

Clinical Skin Research

Nadia Kashetsky | **CSR05**

Syphilis Masquerading as CD4/CD8 Double-Negative Mycosis Fungoides: A Case Report

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Introduction: Syphilis is known as "the great mimicker" as it imitates a variety of conditions both clinically and histopathologically.

Methods: Here we report a case of a 54-year-old female with syphilis, initially diagnosed as CD4/CD8 double-negative mycosis fungoides. Patient informed consent was obtained to report this case.

Results: A 54-year-old female presented to the emergency department with acute onset of severe headaches, night sweats, fevers, chills, a 45-pound weight loss, malaise, diffuse muscle aches, difficulty breathing, a painful lesion on the tongue, diarrhea, and rapidly progressive erythematous and scaly plaques on her face and upper trunk. She was subsequently seen by an internal medicine specialist, who, amongst other investigations, undertook skin biopsies from representative lesions on the back. The patient was initially diagnosed with CD4/CD8 double-negative mycosis fungoides based skin biopsies. However, the morphology of individual lesions, their rapid evolution, and the patient's constellation of symptoms was difficult to reconcile based on a diagnosis of mycosis fungoides which tends to run an indolent course, with an average delay to diagnosis of about 8 years. Therefore, the differential diagnosis, based primarily on morphology, as well as systemic features was broadened to include syphilis. Syphilis serologies were ordered and came back positive, confirming a diagnosis of latent syphilis. The patient was treated with 2.4 mln units of IM penicillin, with complete resolution of cutaneous lesions as well as systemic symptoms.

Conclusions: Syphilis and its innumerable cutaneous manifestations laid the foundation for dermatology as a separate medical discipline and it behoves us to know and be able to recognize its systemic and cutaneous manifestations, particularly given that syphilis cases are on the rise. Thus, it is important for physicians to hold a high index of suspicion for syphilis and consider it in their differential diagnosis.

Learning objectives:

- Discuss syphilis as "the great imitator" in the context of mycosis fungoides,
- the importance of a differential diagnosis for infectious etiology,
- and review primary, secondary and tertiary manifestations of syphilis

Takeaway Message:

Although UVB/nbUVB appeared slightly less effective than other therapies, in light of widespread availability and a favourable long-term safety profile, we recommend that UVB/nbUVB can be considered an appropriate first-line treatment for patients with GA.

Inflammatory Skin Diseases

Harshita Patel | **INFL01**

Investigating Type 2 Immune Responses in Adult Atopic Dermatitis Patients Using An In Vitro Model for TH2 Expansion

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Introduction: Atopic dermatitis (AD) is a chronic inflammatory skin disorder dominated by TH2 cytokines. There are few adequate models to study AD, and these do not effectively recapitulate disease heterogeneity. We developed a human *in vitro* model for generating robust type 2 cells. Here we demonstrate how exposure to *Staphylococcus* enterotoxin B (SEB) alone can lead to expansion of type 2 cells from AD blood.

Methods: PBMCs isolated from adult AD patients were cultured for 7 days in the presence of *S. aureus*-derived superantigen (SEB) +/- thymic stromal lymphopoietin (TSLP) to replicate the AD inflammatory cutaneous environment. Cellular immunophenotyping was performed on harvested cells to detect canonical TH2 markers as well as intracellular cytokine production.

Results: Exposure to TSLP+SEB sustains high numbers of AD patient memory CD4+ CD45RO+ T cells *in vitro* compared to control or SEB alone; CD4+ T cells expressed high levels of activation (CD69, HLA-DR) and costimulatory (ICOS, OX40) markers and Th2-transcription factors (GATA3, pSTAT6). Discreet populations of IL-13+ IFN-y and IL-13- IFN-y+ cells were found along with a small number of double-positive cells. CD8+ T cells produced higher levels of IFN-y compared to CD4+ T cells. Notably, SEB alone was also sufficient to generate these Th1 and Th2 cytokines from patient blood.

Conclusions: Our *in vitro* AD model allows for the robust expansion of circulating IL-13+ Th2 cells from AD patient blood, thought to be key to disease pathogenesis, and facilitates investigation of various skin-derived AD-associated factors such as *S.aureus*-derived SEB.

Learning objectives:

- To understand Th2 immunity associated with atopic dermatitis
- To understand key cytokines mediating inflammatory responses in atopic dermatitis
- To learn and familiarize with techniques used in translational research such as flow cytometry.

Takeaway Message: Our in vitro model may be used to examine heterogeneity and endotypes of T cell polarization responses in atopic dermatitis patients, as well as their response to S. aureus as a key environmental factor.

Inflammatory Skin Diseases

Sarah Bélanger | **INFL02**

Investigation of the Interindividual Variability between Tissue-engineered Skin Substitutes from Different Psoriatic Patients' Cells

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Introduction: Psoriasis is a chronic inflammatory disorder of the skin characterized by excessive growth and aberrant differentiation of keratinocytes. There is a great variability in the manifestation of symptoms and the response to different treatments in patients with psoriasis. This interindividual variability is therefore a major issue during the development of new therapies to treat psoriasis. The aim of this study is to better understand the interindividual variability between skin substitutes reconstructed with cells from different psoriatic donors and their responses to an alpha-linolenic acid (ALA) treatment.

Methods: Healthy and psoriatic skin substitutes were produced according to the self-assembly method. The culture media were supplemented with 10 uM of ALA and the supplemented substitutes were compared with the unsupplemented control substitutes.

Results: A marked interindividual variability of the psoriatic phenotype was observed between the different substitutes. In fact, substitutes produced with psoriatic cells from a 46-year-old male patient (Y46) and a 64-year-old female patient (X64) had thicker and less organized epidermis than those produced with the cells of a 49-year-old male patient (Y49). Moreover, unlike the substitutes produced with cells from donors Y46 and X64, substitutes produced with cells from donor Y46 appeared to respond less strongly to ALA treatment.

Conclusions: Interindividual variability in divergent metabolic responses to omega-3 supplementation could be caused by genetic factors such as single nucleotide polymorphisms (SNPs). Therefore, characterization of the genome of psoriatic cell populations will allow the identification of SNPs associated with responses to omega-3 therapy.

Learning objectives:

- Highlight the major histological differences between substitutes produced
- Report the effects of ALA on keratinocytes' growth and differentiation
- Introduce SNPs as part of the explanation to interindividual variability in metabolic responses to omega-3 treatment

Takeaway Message: The interindividual variability in divergent metabolic responses to omega-3 treatments observed between psoriatic patients could be caused by genetic factors such as SNPs.

Skin Cancer

Amelia Martínez Villarreal | **SC01**

Gametocyte Specific Factor 1 Expression in Cutaneous T-Cell Lymphomas and Its Impact on Carcinogenesis

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Introduction: Gametocyte Specific Factor 1 (GTSF1) is a germline-cell specific gene with ectopic expression in Cutaneous T-Cell Lymphoma (CTCL) patients and has been previously shown to be associated with a worse prognosis. During germ-cell development, GTSF1 partners with the PIWI proteins to identify active retrotransposons on the genome and silence them by recruiting the DNA methylation machinery. Nonetheless, the role of GTSF1 in carcinogenesis and in retrotransposon control remains unknown.

Methods: Applying a Bayesian Analysis and Markov Chain Monte Carlo Method to the expression levels of GTSF1 across The Cancer Genome Atlas (TCGA) we analyzed the possibility of a cancer type predominance. To investigate the role of GTSF1 on CTCL, we performed shRNA mediated knockdown on cell lines. The impact of the knockdown in cancer cell biology was assessed with several methodologies such as Western Blot, immunofluorescence, a luciferase-based retrotransposition assay and qRT-PCR.

Results: Results from the TCGA data analysis showed a trend of GTSF1 ectopic expression in lymphomas and leukemias. Interestingly, knockdown of GTSF1 in the CTCL cell lines does not seem to affect retrotransposon protein expression and function. However, preliminary data does suggest that GTSF1 influences cell proliferation.

Conclusions: In conclusion, preliminary data suggests a previously unreported role of GTSF1 on cell biology, particularly on lymphomas and leukemias. The germline-cell specific expression of GTSF1 represents an excellent clinical opportunity for targeted therapy development.

Learning objectives:

- Evaluate the ectopic expression of GTSF1 on TCGA data to identify possible cancer type trends.
- Assess the impact of GTSF1 expression on retrotransposon control in CTCL cell lines.
- Evaluate a previously unreported role of GTSF1 on cell proliferation.

Takeaway Message: Ectopic expression of GTSF1 on cutaneous T-Cell Lymphoma patients has been previously associated with a worse prognosis. In germline-cell development, GTSF1 participates on the silencing of retrotransposons, however, GTSF1 in lymphomas and leukemias, particularly on CTCL, seems to play a different role.

Skin Cancer

François Lagacé | **SC02**

Investigating Sun Safety Behaviors, Beliefs, And Skin Cancer-Related Knowledge and Risk Factors in The Canadian Population

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Introduction: In Canada, Cutaneous melanoma (CM) is the 8th most diagnosed malignancy and incidence rates for CM has increased steadily over the past years. However, despite this increase, there are only limited CM public health awareness campaigns when compared to other countries, such as Australia. This translated into a decreased awareness of the seriousness of CM and its impact on people's health.

Methods: Using a validated patient survey, the Sun Exposure and Behaviour Inventory (SEBI), Canadians are asked about their personal melanoma risk, knowledge, level of concern, protective behaviors, and intentions. Participants are recruited in-person, via our website, and through pre-existing patient cohorts. Categorical variables are presented as numbers and percentages, and continuous variables as means with standard deviations.

Results: 1468 completed surveys were collected and analyzed (72% female, 86% Caucasian, average age 47.6). 55% agreed with the statement "I look better/ healthier with a tan". 59% reported having > 10 sunburns and 57% at least 1 blistering sunburn in their lifetime. 44% reported ever using a tanning bed and 78% had a tan within the last 12 months. On a typical weekend summer day, the average Canadian spends 3.4 hours outside between 10 AM and 4 PM. Only 54% of respondents reported that they wear sunscreen, 55% wear long sleeved shirts, 43% seek shade, and 29% wear a hat. ≥ 96% of respondents were aware that sun exposure is a risk factor for CM.

Conclusions: Our results show that many Canadians are subject to significant UV exposure and that many prefer their appearance with a tan. In addition, sun protective measures practiced by Canadians are sub-optimal. We hope that our results will help guide CM awareness campaigns that are tailored to the Canadian population.

Learning objectives:

- Gain a better understanding of cutaneous melanoma risk factors in Canada
- Investigate sun protective attitudes and behaviours in Canada
- Understand the Canadian population's level of worry for cutaneous melanoma

Takeaway Message: Canadians are still exposed to significant sun exposure and sun protective practices can be improved in Canada. Targeted public health awareness campaigns to prevent cutaneous melanoma have been successful in other countries, such as Australia.

Skin Cancer

Melika Motamed | **SC03**

Patterns of Gene Expression in Cutaneous T-Cell Lymphoma: Systematic Review of Transcriptomic Studies in Mycosis Fungoides

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Introduction: Mycosis fungoides (MF) is the most prevalent type of T-cell lymphoma that primarily affects the skin and presents as red, scaly patches or plaques, which may progress into tumors. Tumor development is a hallmark of progression from stage I (early) to stage II (late) and is associated with significantly worse outcomes and mortality. An analysis of the literature reveals that certain clusters of genes are associated with early and late-stage disease; however, it is exceedingly difficult to compare different studies due to methodological discrepancies, including lack of consensus in terms of controls.

Methods: This work was designed as a systematic review to examine gene expression profiles involved in MF pathogenesis and progression. Using the electronic database PubMed and our predetermined exclusion criteria, 10 of 189 publications relating to MF transcripts were selected for data extraction. From the selected publications, 2245 genes were obtained at which they were further refined to include only those genes that appeared in two or more publications, yielding 150 recurrent genes.

Results: Categorization of these genes identified activated pathways involved in pathways such as cell cycle and proliferation, chromosomal instability, and leukocyte migration. We identified 15 genes implicated in MF progression, which were involved in cell proliferation, immune checkpoints, resistance to apoptosis, and immune response.

Conclusions: In highlighting the discrepancies in the way MF transcriptomic data is obtained, further research can focus on not only unifying their approach but also focus on the 150 pertinent genes identified in this review

Learning objectives:

- Understand the limitations of currently available date that impedes progress in biomarker development in Mycosis fungoides
- Understand the categories of differentially expressed genes in Mycosis fungoides
- Understand the categories of genes implicated in Mycosis fungoides disease progression

Takeaway Message: In our systematic review we found that out of 2245 differentially expressed genes,150 recurrent genes were identified which were involved in pathways such as chromosome instability and leukocyte migration. Of those 150 genes, 15 were implicated in disease progression.

Skin Cancer

Melissa Berman-Rosa | **SC04**

Geographic and Environmental Factors and Their Association with Melanoma Incidence in Canada: A National Population-Based Study

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Introduction: In order to elucidate potential contributors to the cutaneous melanoma (CM) rising trend and identify potential areas for intervention, in the following ecological study we wished to determine if large-scale patterns of associations exist between environmental factors and melanoma incidence across Canada.

Methods: Incidence rates of CM across Canada for the 1992-2010 period were obtained from previous publications and are presented as crude incidence rates per 100 000 individuals per year. For the same period, we retrieved data from the Canadian Urban Environmental Health Research Consortium on environmental factors: UVR; greenspace, as measured by the normalized difference vegetation index (NDVI); annual highest temperature; absolute number and average length of yearly heat events; annual total precipitation (rain and snow); and the absolute number and average length of events with precipitation (rain and snow). We used the negative binomial regression model in R (version 4.0.3) to analyze patterns of CM cases aggregated by Canadian FSAs. Selection between collinear independent variables was determined by pairwise comparison of p-values from univariate negative binomial regression analyses, and stepwise model selection was performed on the subset of non-collinear risk factors.

Results: See table (missing- not included in submission)

Conclusions: Higher general annual temperature (i.e., more pleasant ambient temperature), availability of green spaces, and UVR were identified as factors associated with greatest predicted increase in melanoma cases. We hypothesize these factors exert their effects on melanoma incidence by modulating behaviour and incentivizing individuals to spend time outdoors in more pleasant ambient temperature, or indoors with more clothing to protect from the high temperatures, heat waves, and rainfall.

Learning objectives:

- Elucidating environmental effects on the rising incidence of cutaneous melanoma are important for identifying potential areas for public health interventions.
- Lower temperatures, availability of green spaces, and UVR predicted the greatest increase in melanoma cases. Rainfall, number of heat events, and highest annual average temperature predicted decreases in melanoma incidence.
- We hypothesize these factors affect melanoma incidence via modulating behaviour.

Takeaway Message: Environmental factors such as temperature, rainfall, green spaces and UVR predict affect melanoma incidence in Canada. Geographic areas with greater exposure to these factors should be targets for public health interventions seeking to curve the rising incidence of cutaneous melanoma.

Skin Cancer

Philippe Lefrançois | **SC05**

In Silico Analyses of The Tumor Microenvironment in Basal Cell Carcinoma Highlight Tumoral Inflammation, A Th2 Cytokine Shift and A Mesenchymal Stem Cell-Like Phenotype in Advanced Tumors

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Introduction: Basal Cell Carcinoma (BCC) represents the most common form of all cancers. BCC is characteristically surrounded by a fibromyxoid stroma. Previous studies have suggested a shift towards a Th2 response, an increase in T regulatory lymphocytes and the presence of cancer-associated fibroblasts in the BCC tumor microenvironment.

Methods: In this study, we aimed to further characterize the BCC tumor microenvironment in detail by analyzing BCC RNA-Sequencing data and correlating it with clinically-relevant features, using *in silico* RNA deconvolution.

Results: Using immune cell type deconvolution by CIBERSORT, we have identified a brisk lymphocytic infiltration, and more abundant macrophages in BCC tumors compared to normal skin. Using cell type enrichment by xCell, we confirmed the observed immune infiltration in BCC tumors compared to normal skin. We observed a shift towards Th2 immunity in advanced tumors and vismodegib-resistant tumors. Tumoral inflammation induced by macrophage activity was associated with advanced BCC, while lymphocytic infiltration was greatest in non-advanced tumors, likely related to an adaptive anti-tumoral response. In advanced and vismodegib-resistant BCC, mesenchymal stem cell-like properties were observed. Particularly in vismodegib-resistant BCC, fibroblasts and adipocytes were found at high number, which ultimately may contribute to the decreased drug delivery to the tumor.

Conclusions: This study has revealed notable BCC tumor microenvironment findings associated with important clinical features. Microenvironment-altering agents may be used locally for "routine" BCC and systematically for advanced or resistant BCC.

Learning objectives:

- Discover immune microenvironment hallmarks of BCC according to clinically-relevant features
- Understand RNA deconvolution for microenvironment characterization
- Learn how stromal and immune elements interact for BCC pathogenesis

Takeaway Message: Aggressive BCC tumors have more stromal elements and mesenchymal stem cell-like features. They display a Th2 shift along with macrophage-predominant inflammation.

Skin Cancer

Pingxing Xie | **SC06**

Gene-Environment Interaction Analysis of Skin Cancers in UK Biobank

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Introduction: Lifetime ultraviolet (UV) exposure is a well-established risk factor for the development of basal and cutaneous squamous cell carcinomas (BCC and cSCC), and melanoma. Genetic predisposition also play a contributory role in the increased risk of these skin cancers. Thus, investigating the interaction between inherited genetic markers and environmental risk factors is crucial to elucidate the pathophysiology of these diseases.

Methods: In this project, we used data from the UK Biobank, which contains approximately 500,000 participants with genome-wide genotyping data generated by the Affymetrix UK Biobank Axiom microarray. All participants are also included in the UK national cancer registries. We identified individuals who have received diagnoses of BCC (n=15,638), cSCC (n=2,111), invasive melanoma (n=3,422) and melanoma *in situ* (n=1,052). For each individual, we obtained general information (ethnic background, self-reported skin color and hair color), as well as self-reported data related to sun exposure from the UK Biobank. We assessed the association between sun exposure factors and risk of developing the above skin cancers. Then, we extracted single nucleotide polymorphisms (SNPs) from 193 genes directly and indirectly involved in DNA repair pathways, and performed gene-by-environment interaction analysis to explore the synergistic effects of sun exposure and DNA repair genes on the above cancers.

Results: Our analyses have revealed several factors (skin color, hair color, use of sun protection, solarium use, time spent outdoors) that are significantly associated with BCC, cSCC and melanoma. These behavioral factors further interact with variations in DNA repair genes leading to a greater incidence of these malignancies, suggesting a synergistic contribution of sun exposure and inherited predisposition.

Conclusions: Our preliminary results have yielded associations between sun exposure factors, genotype and the development of skin cancers. The results support programs to identify individuals at highest risk for developing cutaneous cancers based on behaviors and inherited factors.

Learning objectives:

- Elucidate interplay between genetic and environmental factors in skin cancer pathogenesis
- Quantify risk from sun exposure factors and DNA repair gene variants on skin cancers
- Identify high-risk behaviors and genotypes associated with skin cancers

Takeaway Message: Combining demographic, environmental and genetic data improves understanding of the pathophysiological landscape of skin cancers.

Skin Cancer

Santina Conte | **SC07**

Cutaneous Melanoma Incidence and Mortality Trends in Canada from 2011-2017

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Introduction: As the most serious type of skin cancer, cutaneous melanoma (CM) causes more deaths than any other cutaneous cancer, accounting for approximately 1.9% and 1.2% of all cancer deaths in men and women, respectively, in Canada, while being one of the most common cancers diagnosed in young adults. Despite extensive knowledge regarding the danger of melanoma, little is known regarding its epidemiology in Canada.

Methods: We extracted data for Canadian CM patients from all provinces and territories, with the exception of Québec, from the Canadian Cancer Registry and Canadian Vital Statistics databases, and analysed such data based on clinical and pathological characteristics, such as morphology, topography, age, sex and geographical location, for years between 2011 and 2017.

Results: Between 2011 and 2017, there were 39,615 new CM diagnoses and 5,890 mortality cases across the country. Of these, 45.8% of incidence cases and 37.1% of mortality cases were women. We observed an incidence rate of 20.75 cases per 100,000 individuals per year, which had increased from 12.29 cases per 100,000 individuals per year in 1992-2010. The mean age at diagnosis was 63.26 years (males: 65.3, females: 60.8). Overall, the incidence rate in both sexes continues to rise, while the mortality rate has begun to decline in women in recent years. Analysis at the provincial and forward sortation area (FSA) levels corroborated the aforementioned incidence findings.

Conclusions: Such an analysis of longitudinal, spatiotemporal trends of CM in Canada has allowed us to better comprehend the disease burden of CM across the country.

Learning objectives:

- To better understand the epidemiology of CM in Canada.
- To compare the aforementioned results to those of the previous two decades.
- To use this data to create and promote prevention campaigns in hopes of reducing melanoma incidence and mortality rates in the near future.

Takeaway Message: This study highlights the reality of CM across Canada, and such epidemiological trends will allow us to better target at-risk populations in order to decrease CM incidence and mortality rates in the future.

Basic Sciences

Alexe Grenier | **BS01**

Impact of Cigarette Smoke and Sun Rays on Skin Aging Using Tissue-Engineered Skin Substitutes

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Introduction: Skin aging is the most visible element of the aging process, giving rise to a major concern for anyone. This phenomenon is influenced by two distinct processes: intrinsic and extrinsic aging. The latter regroups all the external factors that influence skin aging, including cigarette smoke and sun rays. While these factors, studied separately, are known to cause premature skin aging, the effects of their synergy have been poorly characterized. The main objective of this project is therefore to assess the harmful impact of this synergy on skin aging.

Methods: For this project, healthy skin substitutes were produced according to the self-assembly method and then exposed to cigarette smoke extract (CSE), followed by irradiations at different doses of UVA (5, 10 and 20 kJ/m2). CSE was obtained by capturing the soluble fraction of cigarette (3R4F) smoke in PBS using an AGI-30 impinger. The skin substitutes were subsequently analyzed by histology, immunofluorescence and dot blot (collagen-I, collagen-III, collagen-IV, elastin).

Results: Histological analyses revealed a decrease in living epidermis thickness following exposure to CSE combined with 20 kJ/m2 of UVA compared to the control. A decreased in the expression of collagen-III (significant) and collagen-IV was observed with the immunostainings when the skin substitutes were exposed to CSE combined with a UVA dose, and this observation was even more accentuated with the dose of 20 kJ/m2 UVA.

Conclusions: This work demonstrates a synergistic effect between cigarette smoke and sunlight on the expression of proteins altered during the aging process, suggesting their involvement in premature skin aging. We are now trying to demystify and further investigate the mechanisms involved in this synergy.

Learning objectives:

- Demystify the interaction between cigarette smoke and sun rays
- Explain the impact of the synergy on skin aging
- Understand the complexity of the synergy between cigarette smoke and sun rays

Takeaway Message: Skin aging is a complex multifactorial phenomenon that needs to be investigate further in order to better understand how to control its clinical signs. Multiple factors can interact with one another and aggravate the process.

Basic Sciences

Andréa Tremblay | **BS02**

Docosahexaenoic Acid Supplementation of Cell Culture Media Leads to Optimized Barrier Function in Tissue-Engineered Reconstructed Skin

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Introduction: Skin models currently used in dermopharmaceutical studies are more permeable than normal human skin (NHS). This observation could be explained by the low levels of polyunsaturated fatty acids (PUFAs) found in the lipid profile of skin substitutes compared to NHS. The use of docosahexaenoic acid (DHA) could optimize the barrier function of skin substitutes by modulating their lipid profile. The aim of this study was to evaluate the impact of DHA supplementation on the skin barrier function of reconstructed human skin.

Methods: To this end, DHA supplemented skin substitutes (substituteDHA+) were produced in parallel to unsupplemented substitutes (substitute-), used as controls, according to the self-assembly method. SubstitutesDHA+ were cultured in a DHA concentration of 10 uM starting from fibroblasts seeding until biopsies were sampled from skin substitutes for analysis. The testosterone permeability assay was performed on a Franz cell diffusion system and testosterone was quantified in samples using ultra-performance liquid chromatography. The fatty acids contained in epidermal phospholipids of skin substitutes were analyzed by gas chromatography coupled with mass spectrometry. Indirect immunofluorescence and western blot analysis were conducted for claudin-1 marker in both skin substitute conditions.

Results: Skin morphology and epidermal differentiation were similar for both conditions and substitutesDHA+. Testosterone permeability was significantly reduced in substitutesDHA+ while lipid profile analysis showed that DHA was successfully incorporated in epidermal phospholipids. Expression of claudin-1 appeared to be increased in substitutesDHA+ compared to controls.

Conclusions: In conclusion, DHA supplementation led to optimized lipid profile, which in turn decreased testosterone permeability.

Learning objectives:

This study provides a better understanding of the skin barrier function, highlights the importance of lipid metabolism in the skin and contributes to fundamental knowledge concerning tissue-engineering applications.

Takeaway Message: Overall, the skin barrier function of reconstructed human skin is improved by the addition of DHA to the cell culture media.

Basic Sciences

Vincent Clément | **BS03**

Tridimensional Cell Culture of Dermal Fibroblasts Promotes Exosome-Mediated Secretion of Extracellular Matrix Proteins

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Introduction: Extracellular matrix (ECM) secretion, deposition and assembly are part of whole more complex biological process influencing many other cellular behaviors. Emerging evidences are attributing a significant role to fibroblast-derived extracellular vesicles (EVs) in a plethora of ECM-associated functions, but those effects still remain largely unknown. Here we report that tri-dimensional (3D) cell culture of dermal fibroblasts promotes secretion of exosomes carrying a large quantity of proteins involve in the formation, organization and remodeling of ECM

Methods: 2D and 3D cell culture models we generated using fibroblasts isolated from healthy individuals. Exosomes were isolated from the conditioned media and characterized by western blot, NTA and TEM. The exosomal cargo was analyzed by RNAseq and mass spectrometry MS/MS. We also tested the proliferation and migration profiles competencies of derived exosomes following proper uptake by fibroblasts.

Results: In the 3D model, genes expression was highly modulated and linked to ECM, cellular migration and proliferation, and inflammatory response. Mass spectrometry in-depth analysis of exosomal cargo reveal 105 significantly upregulated and 112 downregulated proteins in fibroblasts cultured in 3D compared to a standard 2D culture method. We also provide evidences that the interleukin 6 (IL-6) cytokine is central to the signaling pathways related with ECM formation and is contributing to cell migration and proliferation.

Conclusions: Overall, our data suggest that fibroblast-derived exosomes might participate to many steps of the establishment of ECM of the dermis.

Learning objectives:

- To characterize the differences in exosomal cargo between bi- and tri-dimensional fibroblast cultures,
- To analyze exosomal cargo linked to extracellular matrix processing,
- To confirm exosomal uptake and determine the effect of 2D and 3D exosomes on proliferation and migration properties

Takeaway Message: Exosomes derived from 3D cultured dermis fibroblasts play an important role in ECM processing and are involved in migration and proliferation processes

Basic Sciences

Vincent Roy | **BS04**

Increased Extracellular-Matrix Deposition in a Tissue-Engineered Skin Model Derived from NF1 Patients

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Introduction: Neurofibromatosis type 1 (NF1) is a common multisystemic genetic disorder characterized by cutaneous manifestations and the development of multiple benign skin tumors, called neurofibromas. Cutaneous neurofibromas are mainly composed of Schwann cells, fibroblasts, perineural cells and endothelial cells all embedded in an abundant extracellular matrix (ECM). Hyperproliferating Schwann cells, deficient in neurofibromin (NF1-/-), are known to secrete factors promoting matrix remodeling and collagen deposition by fibroblasts and actively participate to the establishment of the tumor microenvironment. However, still very little is known about the actual role of haploinsufficient (NF1+/-) skin fibroblast in the initiation, formation and growth of cutaneous neurofibromas. Hence, the purpose of this study is to characterize in vitro the ECM proteins content produced by patient derived NF1+/- dermal fibroblasts using tissue engineering and 3D cell culture.

Methods: Tissue-engineered skins were generated using fibroblasts and keratinocytes, isolated from NF1 patients and healthy control individuals. ECM proteins produced by dermal fibroblasts were assessed by immunofluorescence and quantified using dot blot analysis. Thickness and mechanical properties of the reconstructed dermis were also evaluated.

Results: NF1-derived dermis were significantly thicker and have a higher maximum force to failure in comparison to the control-derived ones. Moreover, fibronectin was significantly more expressed in NF1+/- fibroblasts when cultured in 3D.

Conclusions: NF1+/- skin fibroblasts could more actively participate in matrix remodeling and tumor microenvironment modification of cutaneous neurofibromas by secreting more fibronectin. More investigations are needed to determine by which mechanisms ECM secretion is enhanced in vitro.

Learning objectives:

- To characterize the role of skin fibroblasts in the NF1 pathogenesis,
- To get a deepen knowledge of the tumor microenvironment in the pathogenesis of cutaneous neurofibromas,
- To learn about extracellular matrix processing and
- To develop an innovative NF1 in vitro model.

Takeaway Message: Dermal fibroblasts have a significant impact on the formation of tumor microenvironment and cutaneous neurofibromas.

Virtual Posters

Amanda Wurz | **V01**

Exploring Participants' and Staff's Experiences Within A Multi-Faceted COVID-19 Psychological Health Intervention: A Follow-Up to the SPIN-CHAT Trial

Amanda Wurz, *University of Calgary;*
Brett Thombs, *Jewish General Hospital and McGill University;*
Delaney Duchek, *University of Calgary;* ***Mannat Bansal,*** *University of Calgary;*
Kelsey Ellis, *University of Calgary;* ***S. Nicole Culos-Reed,*** *University of Calgary*

Introduction: COVID-19 is exerting a tremendous toll on psychological health, which may be heightened for individuals with pre-existing medical conditions who are at elevated risk of medical complications or mortality from the virus. The virtually delivered, multi-faceted SPIN-CHAT program was developed to enhance psychological health amongst individuals with systemic sclerosis (SSc; commonly known as scleroderma) during COVID-19. The program was initially evaluated using a partially-nested randomized controlled trial (RCT). No significant changes in psychological health were observed post-program, however anxiety and depression improved 6 weeks post-program. To better understand the potential benefits of the SPIN-CHAT program and to identify aspects of the program design and development that were/were not beneficial, this study explored participants' and staff's experiences within the SPIN-CHAT program.

Methods: Thirty adults with SSc (*M*age=54.9±SD=13.0 years) who participated in the SPIN-CHAT program and 22 staff (i.e., patient facilitators, professional educators, trial management) participated in one-on-one, virtual, semi-structured interviews post-program. Data were analyzed using thematic analysis.

Results: Participants described how the SPIN-CHAT program enhanced their psychological health by providing social support, structure and self-management knowledge, confidence, and skills. Participants and staff described useful supportive strategies (e.g., sharing/accessing resources/information) and commented that critical to promoting psychological health was the participant-centred nature of the SPIN-CHAT program and interpersonal qualities of the staff. In addition, participants described being satisfied with the SPIN-CHAT program and (along with staff) identified aspects of the program that worked well (e.g., structure, flexibility) and others to consider for improvement (e.g., educational topics, group size).

Conclusions: Participants' and staff's perspectives highlight how the SPIN-CHAT program helped individuals with SSc experience enhanced psychological health. The feedback gained can be used to inform the design and development of future programs and may offer guidance to others working within and beyond SSc to find ways to promote psychological health during COVID-19.

Learning objectives: After this presentation, you will be able to:

- Describe the SPIN-CHAT program
- Understand the psychological impact of the program and name factors influencing the benefits accrued
- Explain aspects of the program that should be considered for refinement and future program design
- Discuss strategies to scale the SPIN-CHAT program

Takeaway Message: Acquiring insights from participants and staff enabled a deeper understanding into how the SPIN-CHAT program helped individuals with systemic sclerosis experience enhanced psychological health. Participants' and staff's insights also provided important information to guide future program design and implementation.

Virtual Poster Session:

Amy X. Du | **V02**

Machine Learning Model for Predicting Outcomes of Biologic Therapy in Psoriasis

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Introduction: Biological agents used for the therapy of psoriasis lose efficacy over time, leading to discontinuation of the drug. Optimization of long-term biologic treatment is an area of medical need but there are no prediction tools for biologic drug discontinuation. We compare the classic, risk-factor based prediction of drug persistence to a machine learning-based model to predict the 5-year rate of biologic drug discontinuation.

Methods: The Danish national biologic therapy registry, Dermbio, comprising 6,172 treatment series with anti-TNF (etanercept, infliximab, adalimumab), ustekinumab, guselkumab and anti-IL17 (secukinumab and ixekizumab) in 3,388 unique patients, was used as data source. Hazard ratios (HR) were computed for all available predictive factors using Cox regression analysis. Different machine learning (ML) models for the prediction of 5-year risk of drug discontinuation were trained using the 5-fold cross validation technique and using 10 clinical features routinely assessed in psoriasis patients as input variables. Model performance was assessed using the area under the receiver operating characteristic curve (AUC).

Results: In concordance with previous studies, the lowest 5-year risk of discontinuation was associated with therapy with ustekinumab or ixekizumab, male sex and no previous exposure to biologic therapy. The predictive model based on those risk factors had an AUC of 0.61. The best ML model (gradient boosted trees) had an AUC of 0.85.

Conclusions: A machine learning-based approach accurately predicts the risk of discontinuation of biologic therapy based on simple clinical variables available in clinical practice. ML could be incorporated into clinical decision making in the future.

Learning objectives:

- Recognize the need for biologic discontinuation prediction tools in the context of therapy optimization.
- Compare the classic, risk-factor based prediction of drug persistence to a machine learning-based model to predict the 5-year rate of biologic drug discontinuation.
- Appreciate the benefits and accuracy of ML prediction and prognostication when compared to a traditional statistical model.

Takeaway Message: ML shows potential in accurately predicting the risk of discontinuation of biologic therapy based on simple and clinically relevant patient variables. It is a tool and that can be considered in clinical practice in the near future.

Virtual Poster Session:

Anastasiya Muntyanu | **V03**

Association of Occupational Exposures to Development of Systemic Sclerosis: A Canadian Scleroderma Research Group Study

***Anastasiya Muntyanu* 1, MD, Raymond Milan 2, Elham Rahme 3,4, Murray Baron 5 MD , FRCPC, Elena Netchiporouk 1 MD, MSc, FRCPC, The Canadian Scleroderma Research Group**

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Introduction: Systemic sclerosis (SSc) is an autoimmune disease with significant morbidity and mortality and is thought to be induced by an environmental trigger in a genetically predisposed individual. The aim of this study was to determine effect of occupational exposure on disease manifestations and severity.

Methods: Data was obtained from the Canadian Scleroderma Research Group (CSRG) cohort, containing 1525 patients, over the years 2004-2019. Demographics, occupational exposure history, disease features, and mortality data were collected. Multinomial logistic regression was performed, stratified by sex, to determine characteristics associated with occupational exposure to silica as compared to exposure to other substances and unexposed controls. Survival analysis using Kaplan-Meier curve was performed.

Results: Among 1525 patients (86.4% females), 494 patients (32.4%) had one or more self-reported exposures (e.g. silica, solvents, asbestos, welding fumes), with 6.7% exposed to silica. Female to male ratio was reduced in patients with occupational exposures compared to the entire CSRG cohort (1.5:1 F:M vs. 6:1; OR 2.16, 95% CI 1.68-2.77; $p<0.0001$). Multinomial logistic regression adjusted for age and stratified by sex revealed that males exposed to silica were more likely to be smokers (OR 3.92; 95% CI 1.24-12.25) and have lung fibrosis (OR 2.20; 95% CI 1.01-4.79) when compared to those not exposed. Females were more likely to have diffuse disease (OR 2.25; 95% CI 1.25-4.05) compared to the unexposed group. Survival analysis showed a general trend in mortality for the silica exposed group was higher than the other exposures group and no exposures group, but this did not reach statistical significance ($p= 0.1843$).

Conclusions: A higher proportion of SSc patients with occupational exposure were males and more severe disease phenotype was observed in the exposed group. In addition to effective workplace protection strategies, taking a detailed occupational history and prevention education are critical.

Learning objectives:

- Identify occupational exposures which may be associated with SSc development
- Determine differences in disease manifestation in patients with occupational exposure to silica as compared to unexposed controls.
- Optimize history taking and counselling of patients to consider occupational factors.

Takeaway Message: Occupational exposures to silica and other substances may affect disease manifestations including interstitial lung disease and development of diffuse cutaneous subtype of SSc. Hence asking a detailed occupational history and counselling patients is an important aspect to consider.

Virtual Poster Session:

Anastasiya Muntyanu | **V04**

Evaluating the Association of Neighborhood Environmental Characteristics and Psoriasis Incidence

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Introduction: Greenness has been previously associated with improved health outcomes in many diseases and better surgical recovery. Among putative mechanisms "fresh air" is thought to benefit health by mitigating exposure to heat, noise, air pollution, relieving mental and physiological stress, and promoting healthful activities. GoodScore.City initiative highlights the importance of a healthy neighborhood for human health. In this study, we aimed to determine the correlation between neighborhood characteristics and psoriasis incidence.

Methods: Incident cases of adult onset psoriasis (≥20 years old) were obtained from provincial health administrative databases (Régie de l'Assurance Maladie du Québec (RAMQ) and MED-ECHO) using International Classification of Diseases (ICD)-9 and 10 codes for psoriasis (696.1, L40.x) for years 1999-2014 (1997-8 and 2015 were excluded to account for prevalent cases). Incidence was determined per Forward Sortation Area (FSA) and geographically mapped using ArcGIS software. Average population ≥20 years-old per FSA (census years 2001, 2006, and 2011) was used as the denominator. Data on neighborhood risk factors including intersection and dwelling density, annual average normalized difference vegetation index (NDVI) (greenness index), as well as nighttime light was obtained from Canadian Urban Environmental Health Research Consortium (CANUE).

Results: Pearson correlation was performed by FSA to determine correlation of risk factors with psoriasis incidence and $p<0.05$ was accepted as significant. Increased intersection density ($p<0.0001$), increased dwelling density ($p=0.0002$), and decreased greenness index ($p<0.0001$) corresponded to increased psoriasis incidence. Additionally, a weaker correlation of increased nighttime light brightness to psoriasis incidence was also observed ($p=0.0438$).

Conclusions: Similar to systemic metabolic diseases, environmental factors such as higher density of intersections, high dwelling density, decreased greenness and increased nighttime brightness could be important environmental contributors to psoriasis development. Future studies focusing on psoriasis outcomes are ongoing.

Learning objectives:

- Identify variables which could be used to evaluate neighborhood quality and greenness.
- Determine the association between neighborhood characteristics and psoriasis incidence.
- Evaluate possible reasons for uneven geographic distribution of psoriasis cases in Quebec.

Takeaway Message: Environmental factors such as higher density of intersections, high dwelling density, decreased greenness and increased nighttime brightness could be important contributors to psoriasis development.

Virtual Poster Session:

Anastasiya Muntyanu | **V05**

The Relationship Between Socioeconomic Status and Psoriasis Incidence

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Introduction: Area-based measures of socio-economic status (SES) are frequently utilized in population-based research. Social deprivation represents deprivation of relationships between individuals in the family, workplace, and community and material deprivation represents deprivation of goods and conveniences. Both indexes correlate with metabolic diseases (e.g. hypertension, obesity), mood disorders (e.g. depression) and substance overuse (e.g. alcohol, smoking). Psoriasis is one of the most common skin diseases and is known to have a higher incidence/severity in patients with above-mentioned comorbidities. We sought to conduct the first population-based study in Quebec, evaluating the relationship between SES and psoriasis incidence.

Methods: Incident cases of adult onset psoriasis (≥20-years-old) were obtained from provincial administrative databases (Régie de l'Assurance Maladie du Québec (RAMQ) and MED-ECHO) using International Classification of Diseases (ICD)-9/10 codes for psoriasis(696.1, L40.x) for years 1999-2014 (1997-8 and 2015 were excluded to account for prevalent cases). Incidence was determined per Forward Sortation Area (FSA) and mapped using ArcGIS software. Average population ≥20-years-old per FSA (census years 2001, 2006, and 2011) was used as denominator. Data on SES indicators including marginalization index composed of four separate categories each evaluated by quintiles (1 = best, 5 = worst SES) and deprivation index measured by the material and social factor scores (<0 less deprivation; >0 more deprivation) was obtained from Canadian Urban Environmental Health Research Consortium (CANUE).

Results: Pearson correlation was performed by FSA to determine correlation of risk factors with psoriasis incidence. Marginalization indexes such as instability ($p<0.0001$), deprivation (<0.0001), dependency (<0.0001), and ethnic composition ($p=0.0331$) were found to have a significantly positive correlation with psoriasis incidence. Social factor score ($p=0.0061$) and material factor score ($p=0.0297$) were also positively correlated.

Conclusions: Worse area-based SES strongly correlates with psoriasis incidence. Understanding health inequity in psoriasis is an important first step toward patients' advocacy and resource allocation.

Learning objectives:

- Identify the variables which can be used to study socioeconomic status in population-based studies.
- Determine the association between socioeconomic status and psoriasis incidence.
- Evaluate possible reasons for uneven geographic distribution of psoriasis cases in Quebec.

Takeaway Message: Worse area-based socioeconomic status is strongly correlated with psoriasis incidence.

Virtual Poster Session:

Augustin Barolet | **V06**

Photobiomodulation In the Near-Infrared and Red Spectra Induces Nitric Oxide Release in Ex-Vivo Human Skin Homogenate Via Enzymatic Pathways

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Introduction: Solar visible (400 – 700 nm) and near-infrared (IR-A: 700-1200 nm) spectra are known to be absorbed by human skin and modulate beneficial cell signalling pathways. Nowadays, these spectra can be artificially reproduced using non-ionizing low-intensity light. Our group thinks that visible and near-infrared light absorption may modulate nitric oxide (NO) metabolism at the cellular level. NO is a biomolecule omnipresent in the body that can be released enzymatically or photolytically in the skin. NO is identified as a very useful biomolecule; it protects cells from oxidative stress, promotes wound healing, acts as a vasodilating-signalling molecule, etc.

Methods: The Griess colorimetric nitrite assay was used for the indirect quantitative determination of NO in ex-vivo human skin homogenates. IR-A (850 nm) and red (660 nm) were compared to narrowband UVA (365 nm), our positive control.

Results: IR-A and red can release a significant amount of NO when compared to sham group. As expected, our benchmark UVA released the highest amount of NO. The non-selective NOS inhibitor NG-monomethyl L-arginine (L-NMMA) abrogated most of the NIR-related NO release in our ex-vivo human skin model. In addition, the selective NO scavenger carboxyl-PTIO decreased the amount of NO released by all wavelengths.

Conclusions: Non-ionizing wavelengths, like NIR and red spectra, can release NO in skin cells. Further studies are needed to elucidate the molecular pathways related to light-based NO modulation in the skin.

Learning objectives:

- To evaluate the capacity of non-ionizing wavelengths to release NO in our ex-vivo skin model. To assess the molecular mechanisms involved in the photorelease of NO.
- To test Griess assay sensitivity in our ex-vivo skin model.

Takeaway Message: NIR and red spectra can release significant amounts of NO in human skin. Moreover, NIR and red cellular impacts on NO metabolism seem to be related to enzymatic NO synthase modulation unlike UVA-triggered photolytic effects.

Virtual Poster Session:

Connor Prosty | **V07**

In Silico Identification of Immune Cell-Types and Pathways Involved in Chronic Spontaneous Urticaria

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Introduction: Chronic spontaneous urticaria (CSU) is defined by the presence of cutaneous wheals and/or angioedema occurring in the absence of an identifiable external stimulus and persist for ≥6 weeks. Current evidence suggests that half of CSU cases have an autoimmune etiology; however, the immune pathogenesis of CSU is poorly understood. Therefore, we sought to investigate the transcriptional landscape of CSU to characterize the immunological response.

Methods: Transcriptomic data acquired by microarray of 15 CSU lesional and non-lesional skin biopsies and 12 healthy control skin biopsies were obtained from the Gene Expression Omnibus (GSE72542 and GSE57178). Differentially expressed genes were identified using GEO2R (Q-value <0.05, logFc>1). Pathway analyses were conducted using ToppFun and KEGG databases. RNA deconvolution was performed by CIBERSORT and cell type abundance scores were determined by xCell.

Results: In CSU lesional skin biopsies versus healthy control skin, upregulated pathways include IL-4 and IL-13 signaling (Q-value=1.03x10-13), IL-17 signaling (Q-value=3.75x10-8) and Th17 cell differentiation (Q-value = 0.017). RNA deconvolution by CIBERSORT revealed increased CD4+ resting memory T-cells (Q-value=0.0081) in lesional versus control skin. Further, regulatory T-cells (Treg) (Q-value=0.014) and resting mast cells (Q=0.014) were increased in non-lesional CSU compared to lesional CSU samples. xCell analysis found increased cell abundance scores for class-switched memory B-cells (Q-value=0.015) in lesional CSU versus healthy control skin but Th1 (Q-value=0.30) and Th2 (Q-value=0.55) scores were not significantly different.

Conclusions: Our results suggest that Th2 and Th17 pathways may be important in CSU; however, Th2/Th17 cell abundance scores were not increased. The increased cell abundance score of class-switched memory B-cells in lesional samples may indicate increased IgE-secreting B-cells driven by the Th2 response. Increased resting mast cells and Treg abundance scores in non-lesional samples may suggest local suppression of wheal formation. Larger studies with phenotyping of CSU patients into autoallergic and autoimmune subsets will be helpful to confirm these results.

Learning objectives:

- Understand the immune cells involved in CSU.
- Understand the differences in immune cell composition between lesional and non-lesional CSU skin and healthy control skin.
- Understand the cytokines and immune pathways implicated in CSU.

Takeaway Message: Th2 and Th17 pathways are upregulated in lesional CSU skin which may be driving the inflammatory response and regulatory T-cells are increased in non-lesional skin suggesting suppression of wheal formation.

Virtual Poster Session:

Linda Kwakkenbos | **V08**

Pain Intensity and Interference Levels and Associated Factors in Systemic Sclerosis: A Cross-sectional Study of 2157 Participants from the Scleroderma Patient-centered Intervention Network (SPIN) Cohort

Yvonne C. Lee, MD, MMSc;1 Rina S. Fox, PhD, MPH;2 Linda Kwakkenbos, PhD;3,4 Brooke Levis, PhD;5 Marie-Eve Carrier, MSc;6 Joep Welling, RN;7,8 Maureen Sauvé, BA;9 Luc Mouthon, MD, PhD;10,11 Andrea Benedetti, PhD;,12-14 Susan J. Bartlett, PhD;12,15 John Varga, MD;16 Brett D. Thombs, PhD;6,12,13,17-20 on behalf of the Scleroderma Patient-centered Intervention Network Investigators.

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Introduction: Pain is important for people with systemic sclerosis (SSc; scleroderma) but often overlooked in research and clinical care. Objectives were to (1) assess levels of pain intensity and interference and (2) evaluate sociodemographic and disease factors associated with pain intensity and interference.

Methods: Participants in the Scleroderma Patient-centered Intervention Network Cohort who completed pain intensity and interference measures (Patient Reported Outcomes Information System-29 profile v2.0) as part of baseline assessments were included. Associations of pain intensity and pain interference with sociodemographic variables, SSc-related variables, and overlap syndromes were assessed with multiple linear regression. Continuous independent variables were standardized.

Results: Among 2157 participants, 1870 (87%) reported at least mild pain (³ 1 on 0 to 10 scale), and 815 (38%) reported moderate-to-severe pain (³ 5); 757 (35%) reported moderate-to-severe pain interference. Greater pain intensity was independently associated with female sex (0.58 points, 95% confidence interval [CI] 0.26 to 0.90), non-White race/ethnicity (0.50 points, 95% CI 0.21 to 0.79), less education (0.30 points per standard deviation [SD], 95% CI 0.19 to 0.41), country (reference=United States; Canada, 0.29 points, 95% CI 0.01 to 0.57; United Kingdom, 0.58 points, 95% CI 0.21 to 0.95), greater BMI (0.35 points per SD, 95% CI 0.24 to 0.45); joint contractures (0.67 points, 95% CI 0.39 to 0.94), digital ulcers (0.33 points, 95% CI 0.10 to 0.55), gastrointestinal involvement (0.66 points, 95% CI 0.33 to 0.98), skin involvement (0.22 points per SD, 95% CI 0.10 to 0.35), rheumatoid arthritis (0.96 points, 95% CI 0.50 to 1.43) and Sjögren's syndrome (0.42 points, 95% CI 0.01 to 0.83). Pain interference results were similar.

Conclusions: Pain is common among people with SSc and interferes with daily functioning. Research is needed to better understand patterns of pain and potential causes and to develop interventions to target pain sources and support coping.

Learning objectives:

- Participants will be able to understand levels of pain intensity and how pain interferes with daily functioning among individuals with SSc.
- Participants will be able to describe disease manifestations in SSc that are significantly associated with both pain intensity and interference.
- Participants will be able to understand how they can work with patients to address pain, which includes identifying and addressing SSc manifestations associated with their pain and supporting behavioural approaches to minimize impact on function and quality of life.

Takeaway Message: Results of our study underline the centrality of pain in the experiences of people with scleroderma, and their ability to carry out daily activities. Scleroderma disease manifestation is diverse, and many scleroderma-related factors may contribute to pain intensity and interference.

Virtual Poster Session:

Mbarka Bchetnia | **V09**

Successful Allele-Specific Inactivation of Autosomal Dominant Epidermolysis Bullosa Simplex Mutation Using CRISPR/CAS9

Mbarka Bchetnia1,2, Julie Powell3, Charles Morin1,4, Catherine McCuaig3, Audrey Dupérée4, Jacques P. Tremblay5, Catherine Laprise1,2

1Université du Québec à Chicoutimi, Département des sciences fondamentales, Saguenay, Canada;
2Université du Québec à Chicoutimi, Centre intersectoriel en santé durable, Saguenay, Canada;
3Hôpital Ste-Justine, Montréal, Canada;
4Centre intégré universitaire de santé et des services sociaux du Saguenay-Lac-St-Jean, Saguenay, Canada;
5Centre de recherche du CHU de Québec, Université Laval, Québec, Canada;

Introduction: Epidermolysis bullosa simplex (EBS) is a rare genetic disorder of the skin caused by dominant-negative mutations in either keratin 5 (*KRT5*) or keratin 14 (*KRT14*) resulting in impairment of keratin filament network and skin bubbles formation. More than 230 EBS causative mutations were described. Until now, there is no treatment for EBS and the care is primarily palliative. The discovery of the clustered regularly interspaced short palindromic repeat (CRISPR/Cas9) system, eight years ago, raised hope for the treatment of EBS by mutant allele-specific gene disruption induced by non-homologous end-joining (NHEJ).

We aim to disrupt the mutant allele for a severe heterozygous EBS missense mutation in *KRT5* that generates a novel protospacer-adjacent motif (PAM) for the endonuclease *Streptococcus pyogenes Cas9* (*SpCas9*).

Methods: We designed a guide RNA sequence (sgRNA) that should guide the SpCas9 to introduce a DNA cleavage only within the mutant allele. Then we transfected patient's keratinocytes with the ribonucleoprotein complex (SpCas9/sgRNA) by electroporation and we proceeded to single cell cloning. Obtained clones were analysed by deep sequencing at the DNA and RNA level and by immunoblotting for keratin 5 protein expression.

Results: We achieved successful stringent mutant allele specific knockout in two clones. An absence of synthesis of mutant transcript was further confirmed indicating permanent mutant allele-specific inactivation. At the protein level, results showed keratin 5 less expression in edited EBS patient keratinocytes compared to non-edited cells and the wild-type allele expression should be sufficient for normal function. The gene-repaired keratinocytes will be used to engineer skin tissue that will be transplanted to patients as autografts.

Conclusions: This study is the first description of allele specific CRISPR/Cas9 gene inactivation at a novel PAM created by one EBS causing heterozygous pathogenic variation and it highlights the potential for therapeutic utilization of DNA variation-derived PAMs for dominantly inherited diseases.

Learning objectives:

- Genome editing by CRISPR/Cas9 technology has revolutionized therapeutic research on dominant diseases by opening up the possibility of directly targeting and inactivating the mutant allele.
- CRISPR/Cas9 edition of epidermolysis bullosa simplex keratinocytes resulted in inactivation of the mutant allele and prevented the generation of mutant *KRT5* mRNA and protein.
- This study raises hope for the treatment of other dominant diseases.

Takeaway Message: Our study describes allele specific CRISPR/Cas9 gene inactivation at a novel PAM created by an epidermolysis bullosa simplex mutation and provides a model for application of such strategy to other dominantly inherited diseases

Virtual Poster Session:

Sara Mirali | **V10**

Drugs Associated with the Development of Erythema Multiforme: a Systematic Review

Sara Mirali1, Asfandyar Mufti2, Abrahim Abduelmula3, Jensen Yeung2, 4, 5, Neil H. Shear1, 2, 4

1. Faculty of Medicine, University of Toronto, Toronto, ON, Canada, 2. Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada, 3. Faculty of Medicine, University of Western Ontario, London, ON, Canada, 4. Sunnybrook Health Sciences Centre, Toronto, ON, Canada, 5. Women's College Hospital, Toronto, ON, Canada

Introduction: Erythema multiforme (EM) is an acute hypersensitivity reaction that can present with target lesions, erythematous macules or papules, and vesicles. EM can be triggered by viral infections, including COVID-19, or less commonly by drugs. Drug-induced EM can be mistaken for other adverse drug reactions (ADRs), such as Steven-Johnson syndrome. The aim of this systematic review was to critically assess all reported cases of drug-induced EM in order to characterize its clinical presentation and treatment. These data will assist dermatologists and other healthcare providers treating patients with cutaneous ADRs.

Methods: MEDLINE and Embase were searched for original articles describing drug-induced EM. Subject demographics, details of drug-induced EM, and treatment were extracted from 37 articles representing 45 patients.

Results: The mean latency period between starting the suspected drug and the appearance of EM lesions was 10.9 days (range: 0.5-60 days). Lesions were commonly described as target lesions (31.1%, n=14/45), papules (15.6%, n=7/45), or macules (8.9%, n=4/45). Histopathological findings included perivascular inflammatory infiltrates (28.9%, n=13/45), necrotic keratinocytes (20.2%, n=9/45), and spongiosis (8.9%, n=4/45). EM was most commonly associated with kinase inhibitors (28.9%, n=13/45), biologics (11.1%, 5/45), and nonsteroidal anti-inflammatory drugs (6.7%, n=3/45). Of the 35 cases that reported improvement of EM, 80.0% (n=28/35) had complete resolution with a mean resolution period of 10.5 days. Lesions were treated in 80.0% (n=36/45) of cases and treatment options consisted primarily of different corticosteroid formulations with similar resolution periods. Overall, the mean Naranjo ADR score was 5 and the mean Koh ADR score was 83, suggesting probable causality.

Conclusions: Drug-induced EM was most frequently associated with kinase inhibitors, particularly sorafenib. EM is frequently treated with oral and topical corticosteroids.

Learning objectives:

- Understand the clinical presentation of drug-induced EM and the importance of ruling out COVID-19 even when the suspected etiology is drug-related
- Identify which drug classes are most frequently associated with the development of EM
- Summarize the treatment options for drug-induced EM and their relative effectiveness.

Takeaway Message: Drug-induced EM typically develops within weeks and occurs most frequently with kinase inhibitors. The most common treatment is stopping the suspected drug and administering corticosteroids. Moreover, the risk of recurrence is low once the suspected drug is discontinued.

Virtual Poster Session:

Sarah Currie | **V11**

Highly Sensitive Bacteria-Responsive Membranes Consisting of Core-Shell Polyurethane Polyvinylpyrrolidone Electrospun Nanofibers for In Situ Detection of Bacterial Infections

***Sarah Currie** (a,1), Farinaz Jonidi Shariatzadeh (b,1), Hardev Singh (a,c), Sarvesh Logsetty (d) and Song Liu (a,b,*)*

a Department of Biosystems Engineering, Faculty of Agricultural and Food Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

b Biomedical Engineering, Faculty of Engineering, University of Manitoba, Winnipeg, Manitoba, Canada

c Department of Chemistry, Chandigarh University, Gharuan-140413, Mohali, Punjab, India

d Departments of Surgery and Psychiatry, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada

1: equal contribution

**: corresponding author; Dr. Song Liu; song.liu@umanitoba.ca; +1) 204-474-9616*

Introduction: Bacteria responsive color-changing wound dressings offer a valuable platform for continuous monitoring of the wound bed facilitating early detection of bacterial infection. In this study, we present a highly sensitive electrospun nanofibrous polyurethane wound dressing, incorporating a hemicyanine-based chromogenic probe with a labile ester linkage that can be enzymatically cleaved by bacterial lipase released from clinically relevant strains such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods: A rapid chromogenic response was achieved by localizing the dye at the surface of core-shell fibers, resulting in a 5x faster response relative to conventional nanofibers.

Results: By incorporating polyvinylpyrrolidone (PVP) dopant in the shell, the sensitivity was boosted to enable detection of bacteria at clinically relevant concentrations after 2h exposure: 2.5 × 10^5 CFU/cm2 *P. aeruginosa* and 1.0 × 10^6 CFU/cm2MRSA. Introduction of PVP in the shell also boosted the degree of hydrolysis of the chromogenic probe by a factor of 1.2x after 3h exposure to a low concentration of *P. aeruginosa (*10^5 CFU/cm2). PVP was also found to improve the discernibility of the color change at high bacterial concentrations.

Conclusions: The co-operativity between the chromogenic probe, fiber structure and polymer composition is well-suited for timely *in situ* detection of wound infections.

Learning objectives:

Methods for *in situ* detection of skin infections, electrospun dressings for wound healing, sensitive detection of *P. aeruginosa* and MRSA.

Takeaway Message: Highly sensitive in situ detection of wound pathogens such as P. aeruginosa and MRSA was achieved at threshold concentrations of 10^5-10^6 CFU/cm^2 by incorporating a lipase-cleavable dye into various electrospun nanofibrous membranes.

Virtual Poster Session:

Sara Sheikh-Oleslami | **V12**

Evaluating the Survivability and Functionality of Cells Derived from Rat Adipose Micro Fragments Embedded Within Nutritional Liquid Scaffold.

Sara Sheikh-Oleslami *(Faculty of Medicine, University of British Columbia and International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada),* ***Nafise Amiri*** *(International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada),* ***Reza B Jalili*** *(Department of Surgery, Division of Plastic Surgery, University of British Columbia and International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada),* ***Ida Hassanpour*** *(International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada),* ***Ruhangiz T Kilani*** *(International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada),* ***Aziz Ghahary*** *(Department of Surgery, Division of Plastic Surgery, University of British Columbia and International Collaboration on Repair Discoveries (ICORD), Vancouver, Canada)*

Introduction: Abundant inflammation, lack of matrix deposition and paucity of progenitor cells delay normal healing processes in chronic wounds. One major problem with commercially available solid (sheet) scaffolds is their inability to conform to wounds of varying shapes and sizes. Our group has developed Meshfill, a liquid skin substitute which can intimately conform to wound topography and has all the necessary ingredients for skin cells to be nourished, proliferate and migrate in. As chronic wounds are deficient in active cells to migrate into wound regions, here, we combined Meshfill with adipose micro-fragments as a source of progenitor cells to develop a composite, *in situ* skin substitute for wound healing. We hypothesize that adipocytes derived from rat micro-fragmented fat survive and maintain their migratory capacity when cultured with a 3D nutritional liquid scaffold.

Methods: Fresh rat adipose micro-fragments were embedded within liquid MeshFill and cultured for either 7 or 14 days. A live/dead assay was used to evaluate the viability and migratory capacity of the adipose derived cells out of the fat fragments.

Results: The live/dead assay demonstrated a high number of green cells within the 3D MeshFill after 7 and 14 days. The number of red cells was negligent, indicating cell viability in this system, even after 14 days. Further, the migratory capacity of these cells was demonstrated through migration out from the fragments.

Conclusions: A 3D nutritional liquid skin scaffold is a rich environment for adipocyte viability and migration. As such, adipose micro-fragments combined with MeshFill could be used both as a source of cells and as a rich scaffold for treating chronic wounds.

Learning objectives:

- Adipose micro-fragments are viable and able to migrate in liquid scaffolds
- Adipose tissue is a good source of progenitor cells for wound healing
- Liquid dermal scaffolds can fill wounds of any shape or depth

Takeaway Message: Embedding adipose micro-fragments in an injectable liquid scaffold shows cell migration and can be a good source of progenitor cells to generate a three-dimensional matrix for promotion of the wound healing process.

Virtual Poster Session:

Zainab Ridha and Lina Belmesk | **V13**

Systemic Disease Association with Multiple Eruptive Dermatofibromas: A Systematic Review

Zainab Ridha1†, Lina Belmesk, M.D.2†, Abdulhadi Jfri, M.D., M.SC.3, Sofianne Gabrielli, B.Sc, M.Sc.3, Zeinah AlHalees M.D.3, Moshe Ben-Shoshan M.D., M.Sc.4, Xun Zhang, Ph.D.4,5, Elena Netchiporouk, M.D., M.Sc., FRCPC3

†These authors contributed equally to this systematic review.

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4Division of Allergy, Immunology and Dermatology, McGill University Health Centre, Montreal Children's Hospital, 1001 Decarie Boul, QC, H4A 3H9, Canada.

5Centre for Outcomes Research and Evaluation, McGill University Health Centre, Montreal Children's Hospital, 1001 Decarie Boul, QC, H4A 3H9, Canada.

Introduction: While multiple eruptive dermatofibromas (MEDF) are benign in nature, they have been associated with various medical conditions, particularly autoimmune diseases and immunosuppression. We conducted a systematic review of reported cases of MEDF to identify and summarize the associated systemic conditions while discerning the common, as opposed to more anecdotal, associations.

Methods: A search was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) with PubMed, Embase and Web of Science. Case reports and case series of MEDF reported from 1951 to 2020 were selected. To be included, patients had to have a clinical presentation concordant with MEDF confirmed by the authors or meet the definition of MEDF: ≥ 15 dermatofibromas (DF), or an eruptive appearance of five to eight DFs over a period of four months or less. Articles were screened for patients' demographics, clinical manifestations and characteristics, as well as concomitant medical conditions and medications.

Results: In this systematic review, 148 published articles were included, yielding 181 cases. Among 166 patients with known underlying medical condition, 86 (51.8%) had either an acquired immunosuppression (disease or drug-induced) or an autoimmune disorder, 33 (19.9%) were completely healthy without any pre-existing disease nor taking any systemic medication, and 11 (6.6%) were familial. The 3 most common medical conditions associated with MEDF were lupus erythematosus (LE) in 32 (19.3%) cases, human immunodeficiency virus (HIV) infection in 21 (12.7%) and hematologic malignancies in 10 (6.0%).

Conclusions: MEDF is rare and benign but may represent a cutaneous sign of important underlying autoimmune disease, HIV or other cause of immunosuppression. Patients with MEDF should be carefully questioned and examined to identify patients at risk for identified associations and limited screening including ANA, HIV and complete blood count may be performed if clinically warranted. Larger studies are required to assess the nature of underlying systemic associations.

Learning objectives:

- Recognize the medical conditions associated with multiple eruptive dermatofibromas.
- Evaluate the frequency and the nature of underlying disease associations with multiple eruptive dermatofibromas.
- Recognize the multiple eruptive dermatofibromas characteristics according to underlying diseases.

Takeaway Message: Although not dangerous, clinicians must recognize that MEDF may represent a cutaneous sign of immunosuppression and/or autoimmune diseases. Dermatologists should consider screening for SLE, HIV, hematologic malignancy or immunosuppression of other cases.

SkIN Canada Trainee Workshop
Industry Career Path

Thursday
November 11, 2021
(1:00 – 2:50 PM)

"Industry partners will engage trainees about opportunities and paths for a career in pharmaceutical industry with the goal of treating skin diseases"

SkIN Canada Trainee Workshop
Patient Engagement in Research

Friday
November 12, 2021
(1:00 – 2:50 PM)

"Patient engagement in research: top tips for working with patient organizations" "clinical trials Ontario - patient decision aid "

"PATIENT ENGAGEMENT IN RESEARCH: TOP TIPS FOR WORKING WITH PATIENT ORGANIZATIONS"

Rachael Manion

Executive Director; Canadian Skin Patient Alliance, Canadian Association of Psoriasis Patients Co-director; Skin Investigation Network of Canada

Rachael Manion is the Chair of the Patient Advisory Council of the Skin Investigation Network of Canada (SkIN Canada) and the Executive Director of the Canadian Skin Patient Alliance and the Canadian Association of Psoriasis Patients. Drawing on her background as a lawyer and consultant, Rachael brings a strategic and creative approach to advocating for better patient care and is committed to enhancing patient engagement in research.

"CLINICAL TRIALS ONTARIO - PATIENT DECISION AID"

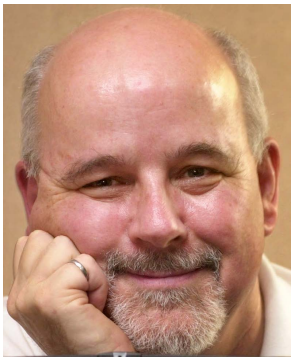
An Introduction to Patient-Oriented Research: A Case Study and Resources to Help You.

Dawn Richards, David Wells and Monica Parry

Join us to learn about patient-oriented research: what it is, common terms, and how you might consider this within the context of your own research project. The session will be hosted by members of a patient-oriented research team, and includes a clinician-researcher, a person who lives with diabetes, and a person who works to engage patients in projects at a not for profit clinical trials organization. The team will help you learn about patient-oriented research through sharing a case study of a research project that has resulted in tools to help you carry out research this way. There will be lots of time to reflect on your own work and ask plenty of questions.

Dawn Richards, PhD
Director, Patient and Public Engagement
Clinical Trials Ontario

Dr. Dawn Richards is the founder of Five02 Labs Inc., and Director of Patient and Public Engagement at Clinical Trials Ontario. With a PhD (Analytical Chemistry) from the University of Alberta, and experience in a variety of roles during the past 20 years, it is her diagnosis with rheumatoid arthritis ten years ago that instigated a journey to combine her passion for science with making the most of her diagnosis. In her role at CTO, Dawn is charged with executing on CTO's strategic pillar of patient and public engagement.



David Ernest Wells

David is a patient partner with Diabetes Action Canada, the Maritime SPOR Support Unit , and Patients for Patient Safety Canada (associated with Healthcare Excellence Canada). He lives in Fredericton, New Brunswick, and turned 82 years old on 2021-06-29. From 2005-2011 Dave chaired the New Brunswick Surgical Care Network Advisory Committee, which designed and implemented new procedures that reduced surgical wait times in New Brunswick 50% to 70%. During 2012-2015 Dave was the patient representative on the New Brunswick Primary Health Care Steering Committee, which changed the delivery of primary health care in New Brunswick by producing an extensive Guidelines document adopted for Family Medicine New Brunswick in 2017. In 2019 he qualified as a Certified Professional in Healthcare Information and Management Systems (CPHIMS-CA) with Digital Health Canada.

Monica Parry, MEd, MSc, NP-Adult, PhD, CCN(C)
Visiting Associate Professor, Central South University, China
Associate Professor, Lawrence S. Bloomberg Faculty of Nursing

Dr. Parry is an Associate Professor at the Lawrence S. Bloomberg Faculty of Nursing and a Nurse Practitioner in the cardiac program at Kingston Health Sciences Centre. Monica's program of research focuses on patient engagement and the sex/gendered factors that impact the burden of cardiovascular disease. Current funded studies are focused on developing and systematically evaluating a digital health intervention (at heart) for women with heart disease. Monica is a Co-I in the SPOR Network focused on Diabetes and its Complications (Diabetes Action Canada), CIHR's e-Health Innovation Project focused on Technology-Enabled Remote Monitoring and Self-Management, and in GOING-FWD: Gender Outcomes International Group: to Further Well-being Development. In collaboration with Clinical Trials Ontario, Monica has also been co-leading CIHR and OSSU-funded studies to systematically develop and test digital patient partner and investigator decision aids designed to increase patient-investigator partnerships in research. She is a member of CIHR's College of Reviewers, the Banting & Best Diabetes Centre, and the Toronto Health Economics and Technology Assessment Collaborative.

SkIN Canada Trainee Workshop
Academic Career Path

Saturday
November 13, 2021
(12:00 – 1:50 PM)

"Academic career path from the perspectives of established and early career investigators"

12:00 to 12:10PM
Welcome remarks & Introductions.

12:10 to 12:35PM
"Career Path of a University Professor in a Life Sciences Department: Challenges and Rewards"
The requirements to get hired, getting tenure, the art of balancing teaching with research including grant writing, publishing, handling rejections from granting agencies and editors, etc. - from hiring until retirement.

John H. White, PhD, McGill University

12:35 to 1:00PM
"Career Path of an Academic Clinician-Scientist: Challenges and Rewards"
The clinician-scientist, once a popular career trajectory in dermatology, is threatened by extinction. Dermatology training programs increasingly focus on the practical aspects of medicine. Many would consider research as an esoteric activity, detached from real-world medicine and thus not worth serious investment of time and effort.
However, the research, with all its current limitations, remains the main source of invigorating energy without which the dermatology will wither and decline.
We will discuss how incorporating research in the career can benefit the physician, by advancing career possibilities, as an antidote to fragility, as a remedy to the cognitive filter bubble, and as a meaningful activity providing purpose in the professional life.

Robert Gniadecki, MD, PhD, DMSci, FCDA, University of Alberta

1:00 to 1:25PM
"Academic Career Path from the Perspective of an Early Career Investigator"
The path to an academic research career can be remarkably diverse. In this talk, I will discuss the training experiences that lead to my success in obtaining a position as a veterinary clinician scientist in regenerative medicine. I will discuss the skills and accomplishments that I think helped to make me more marketable, the many challenges along the way, and the realities of starting a new research laboratory as a New Investigator.

Holly Sparks, DVM, PhD, University of Calgary

1:25 to 1:50PM Panel Discussions and Q&A

Dr. John White did his undergraduate and master's level training in biochemistry and chemistry at Carleton University in Ottawa, which was followed by a Ph.D. in biochemistry at Harvard University in Cambridge Massachusetts. He then did 4 years of postdoctoral work in the laboratory of Professor Pierre Chambon in Strasbourg France where he studied how steroid receptors regulate gene transcription. He was hired as an Assistant Professor in the Department of Physiology at McGill in 1991.

He is now the Joseph Morley Drake Professor and Chair of the Department of Physiology. For more than 20 years he has used his training in molecular genetics and biochemistry to study the biology of vitamin D and how it regulates immune system function and cell growth and differentiation.

Dr. Robert Gniadecki received his MD degree from Warsaw Medical School (Poland) in 1991 and three years later he obtained his PhD from the Faculty of Health Sciences at Copenhagen University (Denmark) and became a specialist in dermatology in 2001 (certified in Denmark and Canada). In 2010 he was appointed as a full clinical professor at the University of Copenhagen and in 2015 at the University of Alberta, Canada. Dr. Gniadecki has served as a president of the Danish Dermatological Society, treasurer of the Canadian Dermatology Foundation and board members of the ESDR (European Society of Dermatological Research) and ISCL (International Society of Cutaneous Lymphomas).

Dr. Holly Sparks earned her DVM from Michigan State University in 2008. After pursuing advanced clinical training, she became Board Certified in Veterinary Surgery in 2015. In 2019, she earned her PhD in stem cell biology and regenerative medicine from the University of Calgary under the supervision of Dr. Jeff Biernaskie. Dr. Sparks then joined the Faculty of Veterinary Medicine at the University of Calgary in 2020 where she is currently an assistant professor of Large Animal Surgery and a member of the McCaig Institute for Bone & Joint Health. Her research program is focused on understanding how resident cells regulate tissue function across the span of musculoskeletal health. In doing so, her team seeks to develop approaches to both prevent and treat athletic injuries as well as improve function after severe skin wounds in patients across species.

Skin Research Group *of* Canada 2021

Travel Award Winners

Layla Nabai, *University of British Columbia*
Extracellular Granzyme B in cutaneous leishmaniasis

Martin Barbier, *Centre de recherche en organogénèse expérimentale de l'Université Laval / LOEX*
Ex vivo gene therapy of skin cells and autologous bilayered skin susbtitutes as a potential treatment for Recessive Dystrophic Epidermolysis Bullosa skin wounds.

Nadia Kashetsky, *Memorial University of Newfoundland*
Light and Laser-based Treatments for Granuloma Annulare: A Systematic Review.

Sarthak Sinha, *University of Calgary*
Single-cell multi-omics reveals skin regeneration is enabled in the absence of fibroblast inflammatory priming.

Wisoo Shin, *University of Calgary*
A shift in fibroblast heterogeneity in aging mice inhibits wound induced hair neogenesis (WIHN).

Serena Mandla, *University of Toronto*
Filling the wound gap: Clinical translation of an instructional peptide-modified hydrogel in xenografted human skin wounds.

Carla Spina, *Exciton Pharma Corp.*
Hypervalent Complexes in Wound Infection and Healing.

Katlyn Richardson, *University of British Columbia*
Granzyme K: A Novel Therapeutic Target for Psoriasis.

Megan Pawluk, *University of British Columbia*
Granzyme B Contributes to Radiation Dermatitis through E-Cadherin Cleavage and Loss of Epithelial Barrier Function.

Geneviève Rioux, *Université Laval*
Study of the role of pathological keratinocytes and their communication with T cells using tissue engineered psoriatic skin.

Sara Mirali, *University of Toronto*
Light and Laser-based Treatments for Hidradenitis Suppurativa: a Systematic Review.

Jordanna Roesler, *University of British Columbia*
Dermatological Conditions in Rural and Remote Indigenous Communities of North America: A Systematic Review.

Sophie Morin, *Université Laval*
Investigation of the influence of alpha-linolenic acid in a 3-D engineered immunocompetent psoriatic skin model.

Shu Feng Zhou, *Harvard medical school*
Unraveling the contribution of ACTL6A, a chromatin remodeling factor, to immune evasion in head and neck squamous cell carcinoma.

Brice Magne, *Université Laval*
Exploring the role of autophagy in skin pigmentation.

Emilie Attiogbe, *Centre de recherche en organogénèse expérimentale de l'Université Laval / LOEX*
Immunocompetent, vascularized, autologous 3D skin model reconstructed by tissue engineering for wound healing studies.

Karel Ferland, *Centre de recherche en organogénèse expérimentale de l'Université Laval / LOEX*
Using physiological factors to improve self-assembled skin substitutes pigmentation.

Melanie Laurin, *Université Laval*
Deciphering the functions of FGD RhoGEFs during skin development.

Skin Research Group *of* Canada 2021

Participants

Ahmad Chehade	*University of Alberta*
Al DaSilva	*Bausch Health Canada*
Alexe Grenier	*Centre de recherche en organogénèse expérimentale de l'Université Laval/LOEX*
Alvaro Sierra Sanchez	*CHU de Québec – Université Laval Research Center, LOEX-Hôpital de l'Enfant-Jésus, Université Laval*
Amanda Wurz	*University of the Fraser Valley*
Amani Hassan	*McGill University*
Amelia Martinez Villarreal	*McGill University*
An-Wen Chan	*Women's College Research Institute, University of Toronto*
Anabelle Demers	*Chu de Québec université Laval, LOEX*
Anastasiya Muntyanu	*McGill University*
Andréa Tremblay	*Centre de Recherche en Organogénèse Expérimentale de l'Université Laval/LOEX*
Andrew Leask	*University of Saskatchewan*
Anie Philip	*McGill University*
Anindyo Chakraborty	*McGill University*
Arzina Jaffer	*University of Calgary*
Augustin Barolet	*Laboratoire en organogénèse du CHU de Québec/LOEX*
Aziz Ghahary	*University of British Columbia*
Benoît Deslauriers	*Amgen Canada*
Brandon Ramchatesingh	*RI- MUHC*
Brice Magne	*LOEX , Université Laval, CHU de Québec-Université Laval Research Centre*
Cameron Wong	*University of Calgary*
Carla Spina	*Exciton Pharma Corp.*
Carolyn Jack	*RI-MUHC*
Connor Prosty	*McGill University*
Cori Lau	*McGill University*
Daniele Raymond	*Sun Pharmaceuticals*
David Wells	*Clinical Trials Ontario*
Dawn Richards	*Clinical Trials Ontario*
Diana Bolano Del Vecchio	*Kyowa Kirin*
Dieter Reinhardt	*McGill University*
Elahe Mirzarazi	*McGill University*

Elodie Labit	*University of Calgary*
Emilie Attiogbe	*LOEX, Laval University*
Emilie Doucet	*LOEX, Université Laval; CRCHU de Québec – Université Laval*
Eren Kutluberk	*University of British Columbia & University of Calgary*
Etienne Patenaude	*Lilly*
Étienne Savard	*LOEX, Université Laval*
Feras Ghazawi	*University of Ottawa*
François Lagacé	*Division of Dermatology, McGill University*
François Berthod	*Université Laval*
Gaurav Isola	*McGill University Health Centre*
Geneviève Rioux	*Centre de Recherche en Organogénèse Expérimentale de l'Université Laval*
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