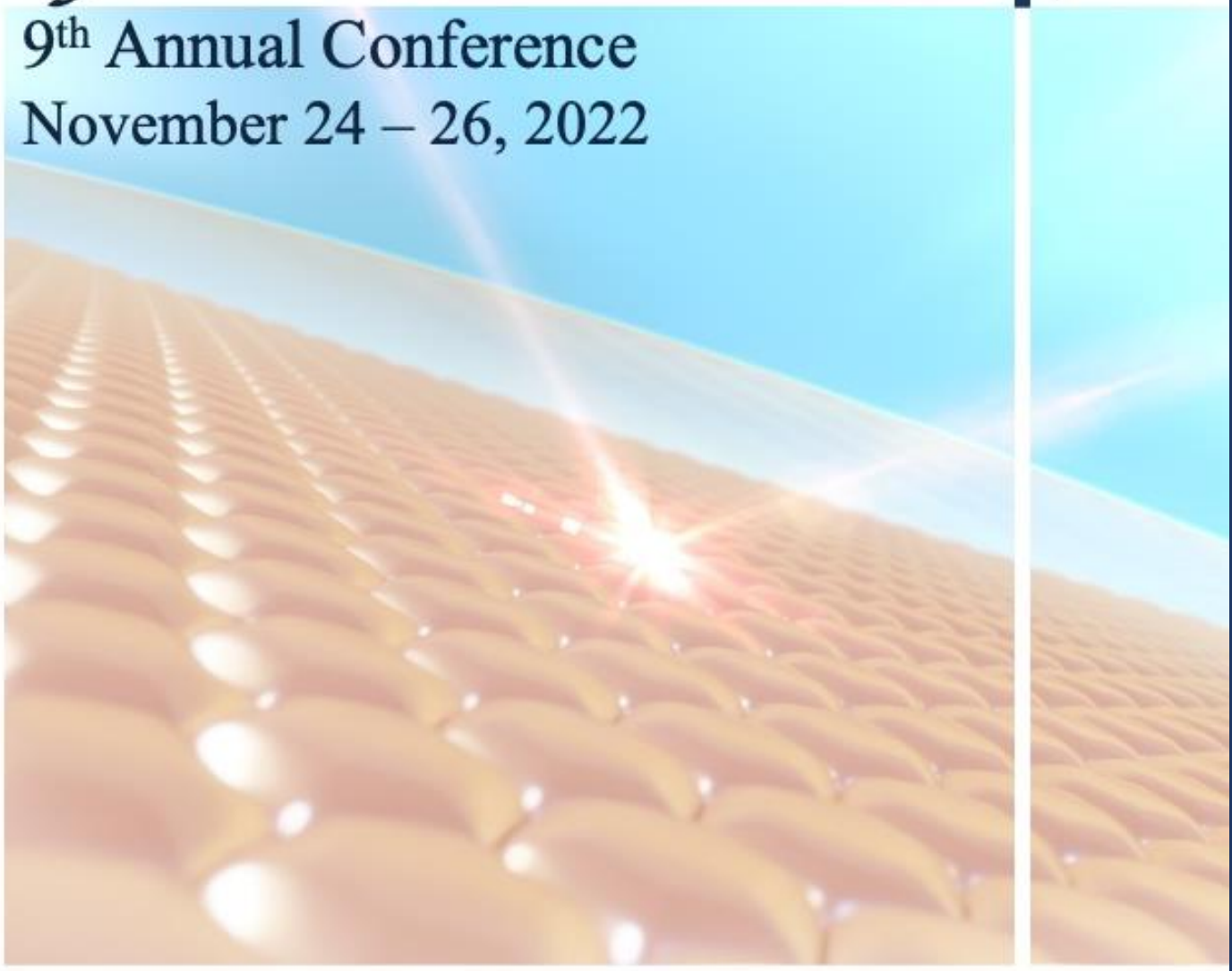
TORONTO 2022

Skin Research Group *of* Canada

9th Annual Conference

November 24 – 26, 2022



Researchers and Clinicians Dedicated to Improving Skin Health

PROGRAM & ABSTRACTS

Skin Research Group *of* Canada 2022

Dear Colleagues and Friends,

It is my great pleasure to welcome you to the 9th Annual Skin Research Group of Canada (SRGC) Conference. The SRGC annual meeting is a Canadian national conference focused exclusively on skin research and has been held since 2014. The SRGC conference presents an important platform for all skin researchers in Canada to come together to advance skin science, promote collaboration, networking, interact with skin disease patients and to support the next generation of skin scientists. We are grateful to our industry sponsors and the CIHR for their generous support of this event.

The SRGC 2022 conference is held in the dynamic metropolis city of Toronto, Ontario. The tremendous response and participation to our meeting is an indication of its high quality and impact. This year's meeting is co-chaired by ***Dr. Véronique Moulin*** *from the* ***Laval University****,* ***Dr. Andrew Leask*** *from the* ***University of Saskatchewan*** *and* ***Dr. Joel Fish from the University of Toronto****. We have more than 150 registered attendees including researchers, clinicians, trainees and industry partners from across Canada and also a number of international participants. The organizers have invited distinguished scholars from across the globe as keynote speakers, including* ***Dr. Tanya Shaw from King's College London, UK, Dr. Maria Da Graca Raposo from the CNRS, Paris, France and Dr. David O'Gorman from the Western University, Canada.***

The SRGC conference was established with an aim to bridge the gaps in basic and clinical skin research. The primary focus of the conference is to encourage and motivate future skin scientists by giving them a platform to showcase their results, share ideas, as well as to network with established scientists in the field of skin research. Multiple workshops will be held during the annual meeting to help achieve these objectives. Excellent work of basic- and clinician-scientists was recognized through 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, patients, industry, decision makers and disease support/advocacy groups;*
- *To foster novel research collaborations and help develop networking on skin research in Canada.*

Again, welcome to SRGC 2022. I hope you will find the meeting to be both stimulating and rewarding. Thank you.

President, Skin Research Group of Canada
Ivan V. Litvinov, MD, Ph.D., FRCPC
Director, Division of Dermatology, McGill University
Director, Division of Dermatology, McGill University Health Centre / Department of Medicine

Skin Research Group *of* Canada 2022

SRGC LOGO
2014 - 2022

www.skinresearchgroup.org

website

Padma Madiraju MSc

Administrative coordinator
2014 - 2022

Skin Research Group *of* Canada 2022

On behalf of the Scientific Organizing Committee, we would like to welcome you to the 2022 Skin Research Group of Canada 9th Annual Scientific Meeting. As in the years past, SRGC2022 will serve to showcase the very best in Canadian basic science, translational and clinical skin research.

This year SRGC 2022 will be held in parallel with Dermatology Update fall meeting at the Hotel Hilton Toronto from NOV 24 to 26, 2022. Along with presentations from outstanding faculty and trainees from across Canada, we have an incredible array of invited keynote speakers who will provide state-of-the-art lectures pertaining to different aspects of skin disease and innovative therapeutics.

We are extremely fortunate to have Dr. Tanya Shaw from King's College London, UK, who will share her pioneering work on anatomical diversity of skin and its implications in treatment of skin conditions. Dr. Maria Da Graca Raposo from the CNRS, Paris, France will share new insights from her laboratory on the physiopathology of human skin pigmentation. Dr. David O'Gorman from the Western University, Canada will speak on behalf of Dupuytren's Canada, our final keynote lecture will be delivered by SRGC President Dr. Ivan V Litvinov of McGill University Health Center.

We look forward to share our programming with you as we celebrate leading-edge skin research here in Canada.

Sincerely,

SRGC2022 Scientific Organizing Committee Co-chairs

Véronique Moulin Ph.D.
Professor, Department of Surgery; Director, Regenerative Medicine Axis, Faculty of Medicine
Laval University

Joel Fish MD, MSc, FRCS(C)
Medical Director – Burn Program, Division of Plastic and Reconstructive Surgery, SickKids;
Professor of Surgery, University of Toronto

Andrew Leask, Ph.D.
Professor, Precision Oral and Systemic Health College of Dentistry
University of Saskatchewan

Skin Research Group *of* Canada 2022
Scientific Review Committee

Andrew Leask, BSc, PhD

University of Saskatchewan

Anie Philip, PhD

McGill University

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

McGill University, Royal Victoria Hospital

Julie Fradette, PhD

LOEX/ Université Laval

Lucie Germain, PhD

CHU de Québec-Université Laval Research Center/LOEX

Mélanie Laurin, PhD

Centre de recherche du CHU de Québec - Université Laval

Robert Gniadecki, MD, PhD, DMSci

University of Alberta

Veronique Moulin, PhD

LOEX/ Université Laval

Skin Research Group *of* Canada 2022 Program

THURSDAY, 24 NOVEMBER

7:30 - 8:00am	**Registration & Poster Set Up**
8:00 - 10:00am	**Plenary Session I** **Clinical Skin Research** **Moderators: Robert Gniadecki & Brice Valentin Magne**
8:00 – 8:20am	Treatment of Ocular Rosacea: A Systematic Review. **Ilya Mukovozov, University of British Columbia**
8:20am	Reddit Analysis of Eczema Posts Uncovers Patient Needs. **Maxine Joly-Chevrier, Université de Montréal**
8:30am	Pneumocystis Pneumonia (PCP) Prophylaxis in Chronic Inflammatory Skin Disease Patients: Systematic Review and Meta-analysis. **Samia Rahman, University of Alberta**
8:40am	Perspectives and Knowledge of Acne Vulgaris Amongst Pre-Pubescent Youth: Preliminary Results from a New Educational Intervention. **Vincent Wan, University of British Columbia**
8:50am	Comparison of Clinical Presentations and Treatment Outcomes of Pityrosporum Folliculitis in Immunocompetent versus Immunocompromised Patients. **Maxwell Green, Tulane University School of Medicine**
9:00am	Coffee Break
9:10am	Clinical Course and Treatment Outcomes of IgA Vasculitis in Adults: A Systematic Review **Samantha Starkey, University of British Columbia**
9:20am	Interventions for post-burn pruritus: a Cochrane systematic review and meta-analysis. **Sarthak Sinha, Cumming School of Medicine, University of Calgary**
9:30am	The relevance of skin biopsies in the diagnosis of Stevens-Johnson syndrome and/or toxic epidermal necrolysis. **Farhan Mahmood, University of Ottawa**
9:40am	Internal Medicine Meets External Medicine: Survey of Dermatology Education for Internal Medicine Residents. **Valerie Doyon, University of British Columbia**

9:50am	Barriers to Healthcare Access for Patients with Psoriasis. **Jeffrey Toy, University of British Columbia**
10:00 - 12:00pm	**Come See My Poster (Moderated Poster Walks)** **Visit Our Sponsor Booths** **Lunch Break**
12:00 - 2:00pm	**SKiN Canada Workshop**
2:00 - 3:00pm	**SRGC Keynote Lecture | Frontiers in Clinical Research** "**Dupuytren's Disease – a riddle inside a mystery, wrapped in…skin?**" ***David O'Gorman, MSc PhD Western University*** *Moderated by Andrew Leask*
3:00 - 5:00pm	**Plenary Session II** **Wound Healing and Regeneration** **Moderators: Andrew Leask & Sophie Morin**
3:00pm	Skin regeneration is enabled in the absence of fibroblast inflammatory priming. **Sarthak Sinha, Cumming School of Medicine, University of Calgary**
3:10pm	Mast cell degranulation contributes to fibrogenesis and resolution of dermal fibrosis. **Edwin Leong, Dalhousie University**
3:20pm	Baseline fibroblast states driving differences in scar formation in young and aged healing skin. **ArzinaJaffer, Cumming School of Medicine, University of Calgary**
3:30pm	TGF-β receptor internalization is impaired in scleroderma fibroblasts and is associated with reduced TGF-β receptor-caveolin-1 interaction. **Shikha Chawla, McGill University Health Centre**
3:40pm	Is the YAP inhibitor celastrol a novel treatment for scleroderma fibrosis? **Pratyusha Chitturi, University of Saskatchewan**
3:50pm	Investigating angiotensin II type 2 receptor signaling in cutaneous wound healing. **Julia Harrison, IWK Health Centre**
4:00pm	Coffee Break
4:20pm	Antibacterial Thermo-Sensitive Silver Hydrogel Nanocomposite Improves Wound Healing. **Nafise Amiri, University of British Columbia**

4:30pm	Comparison of split thickness skin graft (STSG) and self-assembled skin substitute (SASS) following burn trauma using three modalities. **Charles Arcand, Université Laval**
4:40pm	Ice-recrystallization inhibitors from the gluconamide family act as effective cryoprotectants for the long-term storage of dermal constructs. **Jason Dagher, LOEX – CRCHUQ**
4:50pm	Targeting scar formation window for potential anti-scar drug delivery through smart solid lipid nanoparticles. **Farinaz Jonidi Shariatzadeh, University of Manitoba**
5:00 – 6:00pm	**SRGC Keynote Lecture | Frontiers in Translational Research**
	"Anatomical Diversity of Skin in Development, Health & Disease" ***Tanya Shaw, PhD King's College London***
	Moderated by Ivan Litvinov
6:00pm	**Welcome Reception (Space Limited)**
	END OF DAY ONE

FRIDAY, 25 NOVEMBER		
8:00 - 8:30am	**Registration**	
8:30 - 10:00am	**Plenary Session III**	**Inflammatory Skin Diseases**
	Moderators: Philippe Lefrançois & Amani Hassan	
8:30 – 8:50am	In silico profiling of skin cellular infiltrates reveals divergent patterns of macrophage dysregulation in vitiligo and eczema. **Youwen Zhou, University of British Columbia**	
8:50am	Granzyme K-Mediated IL-23 Induction Exacerbates Psoriasis Severity. **Katlyn Richardson, University of British Columbia**	
9:00am	Granzyme B: A novel therapeutic target for radiation dermatitis. **Megan Pawluk, University of British Columbia**	
9:10am	Exposure to Organic Solvents and association with Systemic Sclerosis Disease Severity and Manifestations: A Canadian Scleroderma Research Group Study. **Anastasiya Muntyanu, McGill University**	
9:20am	Supplementation of the culture conditions with eicosapentaenoic acid modifies the Th17 and Treg cell balance in a tissue-engineered psoriatic skin model. **Sophie Morin, Université Laval**	

9:30am	Investigating the Effect of Biologic and Systemic Therapies on Mortality and Co-Morbidity Development. A Study of Albertan Psoriasis Patients from 2012-2020. **Saba Riaz, University of Alberta**
9:40am	Pharmacological Interventions for Primary Psychodermatologic Disorders Evaluated in Controlled Trials: A Systematic Review. **Harry Chaocheng Liu, University of British Columbia**
9:50am	Beyond Skin Deep: Case-based Online Modules to Teach Multidisciplinary Care in Dermatology among Clerkship Students. **Harry Chaocheng Liu, University of British Columbia**
10:00 - 12:00pm	**Come See My Poster**
12:00 - 2:00pm	**SKiN Canada Workshop**
2:00 - 3:00pm	**SRGC State-of-the-art Lecture** **"Physiopathology of human skin pigmentation: Biogenesis of pigment granules and functions of Extracellular Vesicles"** ***Maria Da Graca Raposo, PhD CNRS | Institut Curie*** *Moderated by Veronique Moulin*
3:00 - 5:00pm	**Plenary Session IV** **Skin Cancer** **Moderators: Melanie Laurin & Megan Pawluk**
3:00 – 3:20pm	Implication of PARP1 in repair of UV-damaged DNA to non-melanoma skin cancers. **Girish Shah, Laval University and CHU-Q Research Center**
3:20pm	The gamete specific gene, Gametocyte Specific Factor 1 (GTSF1), contributes to the Th phenotype in Cutaneous T-Cell Lymphomas. **Amelia Martinez Villarreal, McGill University**
3:30pm	Comparison of the BCC tumour microenvironment to other solid malignancies. **Eliana-Ruobing Zhang, Lady Davis Institute, McGill University**
3:40pm	CD109-IL6Rα interaction drives stemness of squamous cell carcinoma (SCC) through STAT3/Nrf2 pathway. **Amani Hassan, McGill University**
3:50pm	An Updated Systematic Review and Meta-Analysis on Efficacy and Safety of Sonic Hedgehog Inhibitors in Basal Cell Carcinomas. **Alex Nguyen, McGill University**
4:00pm	Coffee Break

4:10pm	Preferentially Expressed Antigen in Melanoma (PRAME) regulates retinoid response and cell cycle progression in basal cell carcinoma and squamous cell carcinomas. **Brandon Ramchatesingh, McGill University**
4:20pm	CD109 promotes epidermal growth factor receptor (EGFR) signaling and tumorigenicity by blocking EGFR degradation in squamous cell carcinoma cells. **Tenzin Kungyal, McGill University**
4:30pm	Early Organ Metastasis in Granulomatous Mycosis Fungoides: A Systematic Review. **Melika Motamedi, University of Alberta**
4:40pm	Follow-Up of Patients with Keratinocyte Carcinoma: Systematic Review of Clinical Practice Guidelines. **Sara Mirali, University of Toronto**
4:50pm	When Tanning is Trending: A Content Quality Study of Skin Cancer on TikTok. **Valerie Doyon, University of British Columbia**
5:00pm	**FREE NIGHT**
	END OF DAY TWO

SATURDAY, 26 NOVEMBER		
8:00 - 8:30am	**Registration**	
8:30 - 10:00am	**Plenary Session V**	**Basic Sciences**
	Moderators: Dieter Reinhardt & Sara Mirali	
8:30 – 8:50am	Understanding spatiotemporal principles of epidermal stem cell differentiation in live mice. **Katie Cockburn, McGill University**	
8:50am	Fibrillin-1 is required for the development and homeostasis of adipose tissue. **Iram Fatima Siddiqui, McGill University**	
9:00am	Ex vivo gene therapy and autologous bilayered skin substitutes as a potential treatment of Recessive Dystrophic Epidermolysis Bullosa skin wounds. **Martin A. Barbier, LOEX , Université Laval**	
9:10am	Fibulin-4 and latent transforming growth factor-β binding protein-4 interact with syndecans to regulate skin elastogenesis. **Neha Dinesh, McGill University**	

9:20am	Comparison of two extraction methods of bulge-derived keratinocytes of the hair follicle: explant method and enzymatic digestion. **Bettina Cattier, Université Laval**
9:30am	Generation of Autologous Mesenchymal Stromal Cells from an Accessible Tissue Source: The Plucked Hair Follicle. **Amatullah Fatehi, Acorn Biolabs**
9:40am	The superior angiogenic potential of nano-adipose tissue compared with stem cell-derived small extracellular vesicles to repair 3rd-degree burn injuries. **Elahe Mahdipour, Mashhad University of Medical Sciences**
9:50am	Improving Self-Assembled Skin Substitutes pigmentation with melanogenic physiological factors. **Karel Ferland, LOEX, Université Laval**
10:00 - 10:30am	**Coffee break/ Poster takedown**
10:30 - 11:30am	**SRGC Keynote Lecture** **“Studying skin cancers in patients, cell lines and mouse models”** ***Ivan V. Litvinov, MD, PhD, FRCPC McGill University Health Centre President, SRGC***
12:00 - 2:00pm	**SKiN Canada Workshop**
2:00 - 2:30pm	**AWARDS CEREMONY**
	END OF THE CONFERENCE

Skin Research Group *of* Canada 2022

SRGC Keynote Lecture

Dr. O'Gorman's keynote will describe Dupuytren's disease, current understanding of its pathophysiology and the relevance of skin involvement in this regional fibrosis, and the potential for research collaboration with a patient-driven non-for-profit organization, the Canadian Dupuytren Society.

Dr. O'Gorman graduated with a PhD from the Department of Molecular Medicine, Faculty of Medicine at the University of Sydney, Australia. From 2005, he co-directed the Roth McFarlane Hand and Upper Limb Centre (HULC) Cellular and Molecular Biology Laboratory in St. Joseph's Hospital, where his primary research focus on Dupuytren's disease was funded by the American Society of Plastic Surgeons, Canadian Society for Surgery of the Hand, and the Canadian Institutes of Health Research (CIHR).

He is currently an Associate Professor in the Fundamental Sciences and Surgical Innovation Node in the Department of Surgery, with an adjunct appointment to the Department of Biochemistry, at Western University, London, ON. Dr. O'Gorman is also a board member of the Canadian Dupuytren Society (CDS), where he serves as coordinator of the CDS Medical Advisory Board.

Frontiers in Clinical Research

Thursday 24 NOV 2:00 – 3:00PM

"Dupuytren's Disease – a riddle inside a mystery, wrapped in…skin?"

David B. O'Gorman, MSc PhD

Schulich School of Medicine and Dentistry

Western University

Skin Research Group *of* Canada 2022

SRGC Keynote Lecture

Dr. Shaw's research interests cover the areas of normal and pathological scar formation, the architecture of fibrotic extracellular matrix, cell differentiation events in skin wound healing, common molecular mediators of fibrosis and pain, and dermis development.

Dr. Shaw specializes in wound repair and scarring, with a focus on cell differentiation and extracellular matrix. She gained her PhD in Cellular and Molecular Medicine at the University of Ottawa, Canada. Dr. Shaw then moved to the UK, where she began working on wound repair as a postdoctoral fellow in the lab of Professor Paul Martin at the University of Bristol. She established her independent research group at St George's, University of London, where she worked from 2009-2014. In 2014 she joined King's, where she is now a team leader in the Centre for Inflammation Biology and Cancer Immunology, in the School of Immunology & Microbial Sciences, and is Head of the Anatomy Department.

Frontiers in Translational Research

Thursday 24 NOV 5:00 – 6:00PM

"Anatomical diversity of skin in development, health & disease"

Tanya Shaw, PhD

Centre for Inflammation Biology & Cancer Immunology
School of Immunology & Microbial Sciences
King's College London | KCL

Skin Research Group *of* Canada 2022

SRGC Keynote Lecture

Dr. Raposo received her PhD in 1989 at the Univ. Paris VII (Université de Paris). Her work focused on the intracellular trafficking of neurotransmitter receptors exploiting imaging and in particular she gained expertise in electron microscopy. From 1990 to 1995 she was a post-doc in the Immunology Center, Marseille, where she started studying the trafficking of MHC class II molecules. Because of her expertise in EM she pursued studies in immune cells in the Dept of Cell Biology, Utrecht University, The Netherlands. While in the team of Hans Geuze she showed that B lymphocytes secrete exosomes with antigen presentation capacities leading her to pursue on understanding main cell biological principles of the generation and function of Exosomes and other Extracellular Vesicles.

Since 1995 she is a team leader in the Dept of Cell Biology and Cancer. In the past 8 years she took in charge the Direction of the Training unit at Institut Curie.

Dr. Raposo research area is related to intracellular trafficking in the endocytic and exocytic pathways of eukaryotic cells. Her major research interests focus on the biogenesis and functions of exosomes and lysosome related organelles, in particular melanosomes in skin melanocytes with implications in lysosomal diseases and cancer. She combines cell biological methods from biochemistry to powerful multiscale imaging methods including cytochemistry; immunocytochemistry at the electron microscopical level, and 3D electron tomography.

Distinctions: CNRS Silver Medal, Descartes Huygens Price from Royal Dutch Academy and French Academy of Sciences, EMBO member, ISEV achievement award, Miller Professorship Award, University of California Berkeley, Grand prix Raymond Castaing and the Mrs Urmilla Agrawal Distinguished Professor “Women in Science” Indian Institute of Sciences India.

SRGC

State-of-the-art Lecture

Friday 25 NOV 2:00 – 3:00PM

"Physiopathology of human skin pigmentation: Biogenesis of pigment granules and functions of Extracellular Vesicles"

Maria Da Graca Raposo, PhD

Research Director, CNRS

Team leader, Department of Cell Biology and Cancer, CNRS UMR144 Institut Curie

Director for Advanced Training, Institut Curie

Skin Research Group *of* Canada 2022

SRGC Keynote Lecture

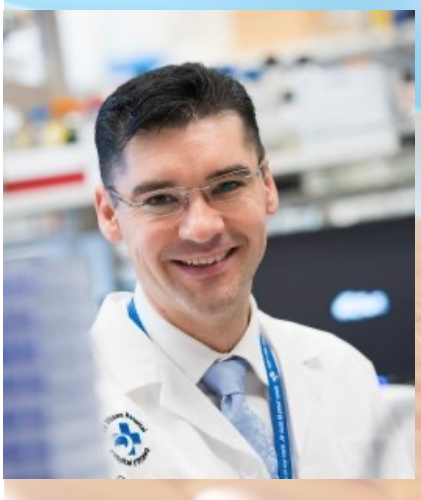
Dr. Litvinov is the Director of the Division of Dermatology of the Faculty of Medicine and Health Sciences of McGill University. He earned his Ph.D. degree in cellular and molecular medicine at the Johns Hopkins School of Medicine in Baltimore, Maryland, and his medical degree at McGill, completing dermatology residency training at McGill University Health Centre (MUHC). Prior to joining the faculty at McGill, Dr Litvinov practiced as an assistant professor and dermatology clinician-scientist at the University of Ottawa between 2015-2017.

During 2019-2021, Dr Litvinov served as regional director (Quebec) of the Canadian Dermatology Association. Currently, he serves as the president of the Skin Research Group of Canada and as a board member of the International Society for Cutaneous Lymphomas. He is also actively involved in the literature, serving as an associate editor of *Journal of Cutaneous Medicine and Surgery (JCMS)* and *Frontiers in Medicine* and as a deputy editor of *JCMS Case Reports*.

He is active in research, particularly studying cutaneous lymphomas, keratinocyte carcinomas, and melanoma, and his research is supported by various grants from the Canadian Institutes of Health Research (CIHR). Dr Litvinov directs a translational research laboratory within the cancer research program of the MUHC-Research Institute and a hematology-dermatology multidisciplinary clinic at the Glen Site of the MUHC. He also directs a skin cancer diagnosis and treatment clinic for solid organ transplant recipients, and he oversees Projet Soleil UV/SunFit Project. In 2020, Dr Litvinov received the Early Career Award in Cancer from CIHR and the 2019 President Cup Award for his contributions to dermatology and research.

SRGC
Keynote Lecture
Saturday 26 NOV 10:30–11:30AM

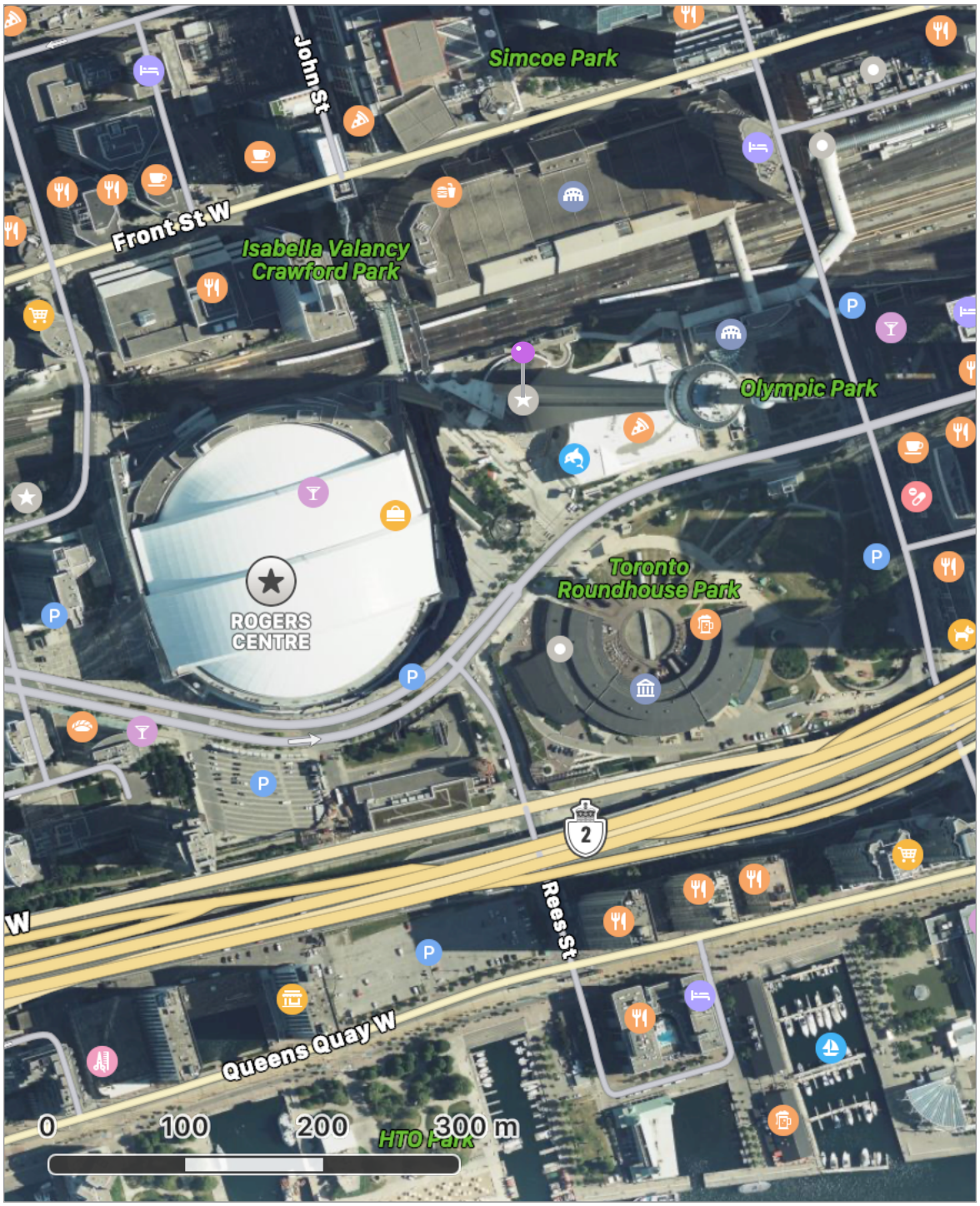
"Studying skin cancers in patients, cell lines and mouse models"



Ivan V. Litvinov, MD, Ph.D., FRCPC

Director, Division of Dermatology, McGill University
Director, Division of Dermatology, McGill University Health Centre / Department of Medicine
President, Skin Research Group of Canada

near Downtown Toronto — Toronto



SRGC
President's
Welcome Reception

To attend the reception you will need to present your SRGC registration badge with RECEPTION TAG and a government issued photo ID

Skin Research Group *of* Canada 2022
Travel Award Recipients

Ilya Mukovozov, University of British Columbia

Maxine Joly-Chevrier, Université de Montréal

Samia Rahman, University of Alberta

Vincent Wan, University of British Columbia

Maxwell Green, Tulane University School of Medicine

Samantha Starkey, University of British Columbia

Sarthak Sinha, Cumming School of Medicine, University of Calgary

Farhan Mahmood, University of Ottawa

Valerie Doyon, University of British Columbia

Jeffrey Toy, University of British Columbia

Edwin Leong, Dalhousie University

Arzina Jaffer, Cumming School of Medicine, University of Calgary

Shikha Chawla, McGill University Health Centre

Pratyusha Chitturi, University of Saskatchewan

Julia Harrison, IWK Health Centre

Nafise Amiri, University of British Columbia

Charles Arcand, Université Laval

Jason Dagher, LOEX – CRCHUQ

Farinaz Jonidi Shariatzadeh, University of Manitoba

Youwen Zhou, University of British Columbia

Katlyn Richardson, University of British Columbia

Megan Pawluk, University of British Columbia

Anastasiya Muntyanu, McGill University

Sophie Morin, Université Laval

Saba Riaz, University of Alberta

Harry Chaocheng Liu, University of British Columbia

Girish Shah, Laval University and CHU-Q Research Center

Amelia Martinez Villarreal, McGill University

Eliana-Ruobing Zhang, Lady David Institute, McGill University

Amani Hassan, McGill University

Alex Nguyen, McGill University

Brandon Ramchatesingh, McGill University

Tenzin Kungyal, McGill University

Melika Motamedi, University of Alberta

Katie Cockburn, McGill University

Iram Fatima Siddiqui, McGill University

Martin A. Barbier, LOEX, Université Laval

Neha Dinesh, McGill University

Bettina Cattier, Université Laval

Elahe Mahdipour, Mashhad University of Medical Sciences

Karel Ferland, LOEX, Université Laval

SkIN Canada

Patient Engagement Session

Thursday 24 NOV | 12:00 – 2:00PM

SkIN Canada

Translational Medicine

Friday 25 NOV | 12:00 – 2:00PM

SkIN Canada Trainee Workshops

Commercialization of University-based Discoveries
By Dr. Ernest Ho

Industry-University Collaboration in Translational Medicine
by Dr. Michael May and Dr Laurent Bozec

SkIN Canada

Knowledge Translation tools
Saturday 26 NOV | 12:00 – 2:00PM

SkIN Canada Trainee Workshops

Winning Strategies for Grant Writing (Clinical Sciences) by Dr. An-Wen Chan

Winning Strategies for Grant Writing (Basic Sciences) by Dr. Dieter Reinhardt

Publication strategies - Clinical Sciences by Dr. Jan Dutz

Publication strategies - Basic Sciences by Dr. Andrew Leask

Skin Research Group *of* Canada 2022
Oral Presentation Abstracts

Treatment of Ocular Rosacea: A Systematic Review

Shani Avraham1†, Sophie Khaslavsky2†, Nadia Kashetsky3, **Ilya Mukovozov 4**
†contributed equally
1 Toronto, ON, Canada
2 Vancouver General Hospital, Vancouver, BC, Canada
3 Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada
4 Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

Introduction:
Rosacea is a chronic, relapsing skin disease that manifests primarily around the central face. It is most prevalent in women, middle aged individuals, and those with fair skin. Notably, up to 60-70% of individuals with rosacea have ocular symptoms. Ocular manifestations may occur simultaneously or independent of centrofacial skin changes and include lid margin telangiectasia, blepharitis, scleritis and sclerokeratitis. Treatment methods for ocular rosacea include topical and oral antibiotics, oral vitamin A derivatives, and recently intense pulse light. A direct comparison of treatment methods for ocular rosacea 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.

Results:
Seventy-two articles met the inclusion criteria, representing a total of 1228 patients. Overall, systemic antimicrobials showed the greatest frequency of cases with complete or partial response (91.1%, n=698/766), followed by combination treatments (83.4%, n=146/175), topical antimicrobials (80.0%, n=112/140), topical cyclosporine (79.6%, n=46/57), light and energy-based devices (79.5%, 58/73) and lid hygiene (64.8%, n=67/105).

Conclusions:
Our results suggest that systemic antimicrobials, topical antimicrobials, and topical cyclosporine were the most efficacious single modality treatments with the greatest number of reported cases for ocular rosacea. IPL is a promising new treatment, and our results show that it has good response rate in many patients.

Learning objectives:
1. To describe ocular manifestations of rosacea
2. To review available studies on treatment outcomes of ocular rosacea
3. To compare response rates for different topical, oral, and energy-based treatment modalities for ocular rosacea

Takeaway Message:
Systemic antimicrobials, topical antimicrobials, and topical cyclosporine were the most efficacious single modality treatments with the greatest number of reported cases for ocular rosacea.

Reddit Analysis of Eczema Posts Uncovers Patient Needs

Maxine Joly-Chevrier1, Safin Aly1, Philippe Lefrançois, MD, PhD, FRCPC, DABD2,3,4
1 Faculty of Medicine, Université de Montréal, Montreal, QC, Canada
2 Division of Dermatology, Department of Medicine, McGill University, Montreal, QC, Canada
3 Division of Dermatology, Department of Medicine, Jewish General Hospital, Montreal, QC, Canada
4 Lady Davis Institute for Medical Research, Montreal, QC, Canada

Introduction:
It is estimated that Reddit attracts more than 430 million users monthly. Within Reddit, community groups are separated by topics named "subreddits". The largest eczema community is composed of approximately 57 200 users. Analyzing users and their posts may help physicians and eczema organizations better assess and respond to patient needs.

Methods:
A total of 200 random posts was retrieved from the subreddit "r/eczema". Among the 200 posts, 100 were posted in 2021 and 100 were posted in 2020. For the year 2021, authors of the posts and associated comments were screened and distributed into categories and subcategories for analysis.

Results:
Among the 200 random posts analyzed, 79 (40%) were related to emotional support, 71 (35,5%) to advice seeking (encompassing advice seeking for potential treatment, general advice seeking, non-personal general disease question and skin inquiry with picture), 16 (8%) to treatment update by patient, 11 (5,5%) to treatment recommendation by the patient, 11 (5,5%) to other topics (educational material, treatment promotion, survey and prevention questions) and 12 (6%) to humour. Posts had a median of 99 [interquartile range (IQR): 97, 100] upvotes, which translates to "likes". In 2021, posts had a median of 61 [IQR: 54, 72] comments. Every post had a median of 6 [IQR: 1, 15] comments giving advice on eczema treatment and/or management. Most users who commented (6 579, 99.8%) on these posts did not specifically self-describe as non-physicians. No dermatologists replied to these posts.

Conclusions:
Users of the subreddit "r/eczema" represent an active international eczema patient community regularly seeking emotional and medical support. Given the anonymous identity of users and commenters, the lack of verified medical advice may promote the propagation of false and/or inaccurate information. Dermatologists and medical organizations can benefit from such a large audience to rapidly engage with patients.

Learning objectives:
1. Describe the largest eczema patient community on Reddit.
2. Identify and describe eczema patient needs on Reddit based on their posts.
3. Identify and describe users who commented on these posts to assess their medical expertise.

Takeaway Message:
Eczema patients are actively seeking for emotional and medical support on Reddit. The presence of dermatologists and eczema organizations is limited, near non-existent, on this platform, which may become problematic over time as anonymous users are sharing unverified medical information.

Pneumocystis Pneumonia (PCP) Prophylaxis in Chronic Inflammatory Skin Disease Patients: Systematic Review and Meta-analysis.

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Introduction:
Pneumocystis pneumonia (PCP) is a severe, opportunistic infection caused by Pneumocystis jirovecii. PCP risk increases considerably with immunosuppression. In some specialties, prophylaxis is routine but dermatology lacks prophylactic PCP guidelines. Effective prophylaxis can reduce morbidity; however, unnecessary prophylaxis poses adverse event risk. Therefore, we ask: should PCP prophylaxis be recommended for inflammatory skin disease patients treated with immunosuppressive medications long-term?

Methods:
A systematic search was performed investigating PCP incidence in the general population and iatrogenically immunosuppressed patients. The systematic review included 22 studies and pooled meta-analysis included 8 studies (random-effects model).

Results:
Two studies of the general population determined PCP incidence at 0.01% and 0.005%. Based on four studies, we estimated PCP incidence in autoimmune disease patients between 0.18% and 0.7%. Prednisone increased PCP incidence rate (IR) in a dose-dependent manner: 2.37 per 100 person-years (PY) at ≥30mg/day, 0.5/100 PY at ≥15 to <30 mg/day, and 0.01/100 PY at <15 mg/day. PCP risk factors were methotrexate, cyclophosphamide, and age >65 years. Meta-analysis showed a 75% reduction of PCP in immunosuppressed patients with prophylaxis (RR = 0.25 [95% CI, 0.10-0.65]) and number needed to treat (NNT) of 33.

Conclusions:
PCP risk is significantly increased in autoimmune disease patients. For antibiotic prophylaxis the NNT is 33 and lower than previously reported number needed to harm (NNH ≅ 45-131).

Learning objectives:
1. Estimate PCP risk with long-term immunosuppressant treatment
2. Compare NNT to prevent one PCP case with NNH of prophylaxis.

Takeaway Message:
Dermatological patients treated with immunosuppressants long-term have a significantly increased PCP risk. Antibiotic prophylaxis might be indicated in high-risk patients.

Perspectives and Knowledge of Acne Vulgaris Amongst Pre-Pubescent Youth: Preliminary Results from a New Educational Intervention

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Introduction:
Past research demonstrates that adolescent populations are vulnerable to misinformation about acne which may translate to delayed access to healthcare, mismanagement, and negative sequelae including scarring and depression. While a previous acne education intervention for high school students found improvements in acne quality of life scores, no similar studies have yet investigated the potential benefits for a pre-pubertal population.

Methods:
A virtual presentation on acne pathogenesis, prevention and management, and its psychosocial impacts were provided between Mar - Jun 2022 to 10 grade 5-7 classes. We administered quality improvement surveys prior to presentations to identify knowledge gaps.

Results:
209 responses were collected. Students had an age range of 9-13 and average age of 11.4. 47% (n=99/209) of respondents did not actively seek information about acne and 42% (n=88/209) relied on knowledge passed from unaccredited sources such as family and friends. Approximately 60% (n=125/209) of respondents believed that poor hygiene and dirt buildup could cause acne. 68% (n=142/209) of respondents recognized that acne could be managed, but 50% (n=102/202) disagreed that it could be treated with medications. 52% (n=89/171) of respondents believed that they understood the consequences of unmanaged acne, yet only 34% (67/197) agreed that acne could impact their mental health. 39% (n=79/205) of respondents could identify effective strategies in preventing acne and 37% (n=77/207) were familiar with credible sources of information. 52% (n=109/208) of students expressed comfort in seeking a physician regarding potential acne concerns.

Conclusions:
The body of evidence surrounding acne health literacy in pre-pubescent populations is sparse. Our results demonstrate vulnerability to misinformation and highlight critical knowledge gaps. Knowledge of colloquial self-treatment methods including excoriation or home remedies may explain some of our findings. These results emphasize the importance of early educational intervention to increase acne health literacy and prevent perpetuation of mismanagement and negative downstream sequelae.

Learning objectives:
1. Recognize that pre-pubescent youth are vulnerable to acne misinformation
2. Identify critical knowledge gaps in acne health literacy
3. Recognize the value of early educational intervention

Takeaway Message:
Pre-pubescent youth are vulnerable to misinformation from unaccredited sources and may benefit from the provision of evidence-based, verified educational interventions that improve their health literacy.

Comparison of Clinical Presentations and Treatment Outcomes of Pityrosporum Folliculitis in Immunocompetent versus Immunocompromised Patients

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Introduction:
Pityrosporum folliculitis is a fungal acneiform disease of the hair follicles that often presents with pruritic papules and pustules on the upper body and face. This condition is commonly mistaken for acne vulgaris and can be distinguished from bacterial acne by the presence of fungal spores in the follicular lumen. Patients commonly present with lesions diagnosed as acne vulgaris that do not respond to traditional therapy. PF has been observed in both immunocompetent and immunocompromised individuals, but little work has been done to aggregate and compare data.

Methods:
PubMed, Web of Science, and Embase were searched using the terms "Pityrosporum folliculitis" or "Malassezia folliculitis". Studies were classified as immunocompetent or immunocompromised based on clinical histories. A total of 35 studies were identified, 15 representing immunocompetent patients (n=1238) and 20 representing immunocompromised (n=50).

Results:
Majority of patients were male in both the immunocompetent (64.0%) and immunocompromised cohorts (86.8%) with the average age of presentation of 24.26 years and 38.82 years, respectively. The most common locations of lesions were the chest (70.0% competent vs. 58.8% compromised) and back/shoulders (69.2% competent vs. 61.8%). Pruritus was reported by 71.7% of immunocompetent compared to 22% of immunocompromised. Additionally, 40.5% (competent) and 32.0% (compromised) of patients reported a history of unsuccessful antibiotic treatment. Treatment led to resolution of PF with both oral antifungals (92.0% competent vs. 88.9%) and topicals (81.6% immunocompetent vs. 92.3% immunocompromised).

Conclusions:
The majority of patients in both groups were younger males with lesions most commonly appearing on the chest and back. At least 1/3 of patients in each group were incorrectly treated with antibiotics, suggesting the importance of proper diagnosis. The largest difference between groups reported pruritus being significantly more common in immunocompetent vs. immunocompromised groups. Treatment with both oral and topical antifungals led to resolution in the majority of patients across cohorts.

Learning objectives: Pityrosporum folliculitis:
1. Often appears as a new acneiform eruption following treatment with antibiotics and most commonly affects younger men.
2. Often mimics the appearance of acne vulgaris and most commonly appears as pustules and papules on the chest and back.
3. Can successfully be managed in the majority of immunocompetent and immunocompromised patients with both topical and oral antifungals

Takeaway Message:
Papules and pustules resembling acne vulgaris that are not responding to traditional treatment, are pruritic, or represent a new acneiform eruption following antibiotics should be suspect for Pityrosporum folliculitis. This condition can be properly managed with topical and oral antifungals.

Clinical Course and Treatment Outcomes of IgA Vasculitis in Adults: A Systematic Review

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Introduction:
Immunoglobulin A (IgA) vasculitis, also known as Henoch–Schönlein purpura, is an immune complex vasculitis characterized by IgA deposits. IgA vasculitis is most commonly seen in children, but is also reported in adults. Clinical features include palpable purpura, arthritis, enteritis, and hematuria. Treatment options include corticosteroids, dapsone, colchicine, azathioprine, cyclophosphamide, and mycophenolate mofetil. There is little consensus on the treatment of cutaneous manifestations of IgA vasculitis in the adult population.

Methods:
A systematic review was conducted according to PRISMA guidelines on treatment modalities and outcomes of cutaneous manifestations of IgA vasculitis in the adult population.

Results:
18 articles met the inclusion criteria, representing a total of 1154 adults with IgA vasculitis. Available data showed that mean age of included cases was 51 and 59% (n=605/1033) were male. Overall, 75% (n = 659/881) had complete resolution of their cutaneous manifestations, 17% had partial resolution (n = 146/881) and 9% had no resolution (n = 76/881). Systemic corticosteroids were the most frequently reported treatment modality (47%, n=503/1081). 68% of cases treated with systemic corticosteroids achieved complete response (n=175/256) while 24% (n=63/256) achieved partial response. Immunomodulatory drugs (mycophenolates, azathioprine, cyclophosphamide, intravenous immunoglobulin, sulfasalazine, and unspecified; excluding rituximab) were used in 19% of cases (n=202/1081), with 60% (n=61/101) achieving complete response and 35% (n=35/101) achieving partial response. 16% of cases received no therapy (n=177/1081), with 93% achieving complete remission (n=50/54). Other treatment modalities included topical steroids (n=63), combination corticosteroids and immunomodulatory drugs (n=49), colchicine (n=38), dapsone (n=22), rituximab (n=14), and combination rituximab and immunomodulatory drugs (n=13).

Conclusions:
The most frequently reported treatment modalities in adults with IgA vasculitis were systemic corticosteroids and immunomodulatory drugs, which had comparable treatment response. Increased reporting of treatment outcomes for cutaneous manifestations of IgA vasculitis will clarify disease course and treatment response.

Learning objectives:
1. To describe general course of cutaneous manifestations of adult IgA vasculitis
2. To summarize reported therapies for cutaneous manifestations of adult IgA vasculitis
3. To describe treatment outcomes stratified by type of therapy

Takeaway Message:
There is little reporting of treatment outcomes for cutaneous manifestations of IgA vasculitis in adults. Available data suggests that systemic corticosteroids and immunomodulatory drugs are the mainstay of treatment, though roles for combination therapies, dapsone, and colchicine were also reported.

Interventions for Post-Burn Pruritus: A Cochrane Systematic Review and Meta-Analysis

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Introduction:
Postburn pruritus (itch) is a distressing symptom experienced on healing or healed burn or donor site wounds. Topical, systemic, and physical treatments are available; however, it remains unclear how effective these are.

Methods:
In September 2021, we searched the Cochrane Wounds Specialised Register; CENTRAL; Ovid MEDLINE; Ovid Embase and EBSCO CINAHL Plus. We also searched CT registries and references of relevant publications. There were no restrictions for language, date or setting. We included RCTs that compared antipruritic interventions with other intervention(s), placebo, or no intervention. We used standard Cochrane methodological procedures.

Results:
We included 25 studies evaluating 21 interventions with a total of 1,166 participants. For neuromodulatory agents, while gabapentin (MD -2.40, 95% CI: -4.14 to -0.66), pregabalin (MD -0.8, 95% CI: -1.24 to -0.36), and doxepin cream (MD -2.69, 95% CI: -3.65, -1.72) may be more effective in reducing postburn itch compared to oral antihistamines, we have higher confidence that ondansetron (MD -0.76, 95% CI: -1.50 to -0.02) probably reduces postburn itch compared to oral antihistamines. For topical therapies, while CQ-01 Hydrogel (RR 4.50, 95% CI: 1.43 to 14.13) and enalapril ointment (MD -0.70, 95% CI: -1.04 to -0.36) may reduce postburn itch, Provase moisturizer (MD -1.24, 95% CI: -3.34 to 0.86) and silicone gel cream (MD 0, 95% CI: -2.05 to 2.05) has no appreciable effect. For physical modalities, while massage (SMD -0.75, 95% CI: -1.07 to -0.43), extracorporeal shock wave therapy (SMD -1.2, 95% CI: -1.65 to -0.75), and enhanced education on silicone sheeting (MD -2.60, 95% CI: -4.41 to -0.79) may reduce postburn itch, therapeutic touch probably increases itch (MD 1.20, 95% CI: -0.32 to 2.72).

Conclusions:
There is moderate- to low-certainty evidence on 21 interventions. The efficacy of neuromodulatory agents (e.g., gabapentin, pregabalin, doxepin, ondansetron) suggests that burn pruritus may be partly neuropathic.

Learning objectives:

1. post-burn pruritus presents in two distinct time frames. First is transient wound healing pruritus early in acute wound healing which is ubiquitous but short-lived. The second is burn scar pruritus which is long-lasting and resistant to treatment.
2. Three broad classes of antipruritic interventions include neuromodulatory agents, physical modalities, and topical interventions.
3. The efficacy of neuromodulatory agents such as gabapentin, pregabalin, doxepin, and ondansetron suggests that burn scar pruritus may be partly neuropathic.

Takeaway Message:

1. Neuromodulatory agents show promise in reducing post-burn itch compared to oral antihistamines.
2. Physical modalities showed variance in their effectiveness at reducing itch. While interventions like massage therapy and extracorporeal shock wave therapy may reduce post-burn itch, therapeutic touch may increase post-burn itch.
3. Topical interventions, such as enalapril ointment and Provase moisturizer, may reduce or have little to no impact on post-burn itch.

The Relevance of Skin Biopsies in The Diagnosis of Stevens-Johnson Syndrome And/or Toxic Epidermal Necrolysis

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Introduction:
There are no structured diagnostic guidelines for Stevens-Johnson syndrome (SJS) and/or toxic epidermal necrolysis (TEN), thus it is often thought that skin biopsies are required to confirm the diagnosis of SJS/TEN and to exclude other generalized rashes. The purpose of this study is to determine whether a biopsy is clinically relevant for the diagnosis of SJS/TEN.

Methods:
A retrospective chart review of 463 encounters was conducted at The Ottawa Hospital. Encounters were identified using the SJS/TEN ICD 9/10 code from the hospital database and electronic medical record. Patients were included if there was a primary or differential diagnosis of SJS/TEN clinically or pathologically or both.

Results:
Sixty-five patients were included, 44 of which had pathology diagnoses. The mean age was 55 years, and 46.4% were females. At the time of data collection, 69% were living, 9% passed due to SJS or TEN, and 22% passed due to other causes. The mean total body surface area affected was 53.4%. Most common suspected triggers included antibiotics (61%) or anticonvulsants (25%). 32% of the cases did not have a biopsy taken and were treated based a clinical diagnosis of SJS/TEN. Of the 68 % of cases that did have a biopsy, only 16 % revealed an alternative diagnosis. 14% of the biopsies revealed a non-specific drug reaction that did not show confirmatory evidence of SJS/TEN. The majority (70%) of biopsies confirmed a diagnosis of SJS/TEN or showed features compatible with a diagnosis of SJS/TEN. There was no mortality difference between patients who had a biopsy and those who did not.

Conclusions:
SJS/TEN can be diagnosed and treated based on clinical assessment alone. A biopsy can be considered in cases where the clinical diagnosis is not clear, but should not delay treatment.

Learning objectives:
1. Determine how often a biopsy is done in the process of diagnosing SJS/TEN
2. Determine the frequency of disagreement and agreement between the clinical diagnosis of SJS/TEN and the histological diagnosis of SJS/TEN.
3. Assess the overall relevance and importance of a biopsy to the diagnosis of SJS/TEN

Takeaway Message:
Majority of cases diagnosed with SJS/TEN clinically had a diagnosis of SJS/TEN on pathology. A clinical diagnosis of SJS/TEN can be considered reliable with a high sensitivity and specificity. Skin biopsies may be performed to clarify complicated cases mimicking SJS/TEN.

Internal Medicine Meets External Medicine: Survey of Dermatology Education for Internal Medicine Residents

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Introduction:
Many systemic diseases present with cutaneous findings, yet there is a documented lack of dermatology training in internal medicine (IM) residency. We conducted a needs assessment survey to guide future dermatology education for IM programs.

Methods:
A survey was sent to first, second- and third-year IM residents at the University of British Columbia in 2021. A series of 9 questions were asked, including ratings of their experience and comfort levels in evaluating dermatologic presentations, such as “ulcers” or “bullae”, and narrative opinions regarding dermatology teaching content and format.

Results:
53 of 171 trainees responded to the survey (31% response rate). In terms of residents’ comfort levels, 70% (371/530) of clinical presentations were rated as “uncomfortable” or “very uncomfortable”. On average, residents saw each of the listed dermatologic morphologies 1-3 times annually and were most experienced and comfortable managing a “red leg” and least with “alopecia”. With increasing seniority, residents encountered cutaneous diseases significantly more frequently (p=.002). Despite this, there were no significant differences in comfort levels based on level of training or previous dermatology experience. 94% of residents felt "unconfident" to "not at all confident" with dermatology-focused exam questions. Frequently requested teaching subjects were “common” and “dangerous” conditions, including drug eruptions, SJS/TEN, and morbilliform rashes. Respondents prioritized topics relevant to CTU, and named alopecia, skin cancer, and nail disorders as least useful. Endorsed teaching modalities were consult templates, informal bedside teaching, small group sessions, as well as clinical rotations and lectures. Preferred learning style was by morphology or differential diagnosis, rather than by etiology.

Conclusions:
Through all training levels, the majority of IM residents self-report a general lack of comfort with dermatologic presentations, despite an increasing frequency of encounters through their training. Residents are most interested in learning common and not-to-miss diagnoses, and preferred numerous modalities to do so.

Learning objectives:
1. Outline the typical experience of IM residents encountering dermatologic diseases throughout their training.
2. List the dermatologic conditions that IM residents most frequently encounter.
3. Enumerate the most and least requested teaching topics by IM residents.
4. Make recommendations regarding the format of IM resident teaching initiatives.

Takeaway Message:
Internal medicine residents are generally uncomfortable with dermatologic conditions and request additional teaching on relevant topics.

Barriers to Healthcare Access for Patients with Psoriasis

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Introduction:
Barriers to healthcare access (BtHA) are factors that hinder a patient's access to treatment. Psoriasis is a debilitating chronic inflammatory disease that requires longitudinal treatment and access to care. Previous studies have shown that a substantial number of patients express dissatisfaction with their treatment and healthcare access, but little research has been done to characterize the types of BtHA experienced by psoriasis patients.

Methods:
We conducted a systematic review to examine the BtHA identified in the psoriasis literature. We screened 1253 studies and extracted data from 23. We analyzed and categorized the BtHA expressed as systemic, sociocultural, provider or individual barriers.

Results:
Individual barriers (n=12) were most frequently noted, followed by systemic barriers (n=10), provider (n=7) and sociocultural (n=4). For individual barriers, the themes of non-adherence, lack of patient knowledge, poor perception of treatment efficacy versus side effects and dissatisfaction were found. Common systemic barriers included therapy costs and geography. Provider level barriers consisted of a lack of culturally competent care, long wait times, short appointment durations and unwillingness to make referrals for specialized care. Sociocultural barriers included the reliance on traditional medications, language and limited levels of therapy knowledge or exposure for certain ethnic groups.

Conclusions:
Our findings are consistent with the barriers identified in broader healthcare disparity literature, but certain knowledge gaps were noted. Notably, fewer sociocultural barriers were identified in psoriasis literature compared to general disparity literature. Studies have suggested that psychological factors, prior negative healthcare experience and comorbidities could act as BtHA, but none were found in our review. Future research in this area is important for psoriasis given its psychological and physiological comorbidities. Further investigation into the different BtHA that may be specifically relevant to psoriasis patients and interventions to overcome those barriers is needed.

Learning objectives:
1. Distinguish between different types of barriers to healthcare access (BtHA)
2. Identify the pertinent BtHA expressed in psoriasis literature
3. Describe the interventions and initiatives that may reduce BtHA

Takeaway Message:
1. BtHA are factors that exacerbate differences in healthcare access
2. The most common BtHA to psoriasis patients are related to finance and issues with compliance
3. Further research and work are needed to reduce BtHA

Skin Regeneration Is Enabled in The Absence of Fibroblast Inflammatory Priming

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Introduction:
Mammalian skin wounds typically heal by forming fibrotic scars. Here, we show that adult reindeer (Rangifer tarandus) antler velvet exhibits regenerative wound healing, whereas identical full-thickness injury in back skin forms fibrotic scar.

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. A cross-species molecular comparison of murine, reindeer and human skin was performed to define conserved mediators of skin regeneration and scar-formation. Candidates identified were validated by RNA-Scope and by pharmacologic manipulation of signalling pathways via peri-wound intra-dermal injections.

Results:
Uninjured velvet fibroblasts share 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 elicited a site-specific immune response; back skin fibroblasts amplified myeloid infiltration and maturation during early repair, whereas velvet fibroblasts adopted an immunosuppressive state that restricted leukocyte amassment leading to hastened immune resolution. Consequently, velvet fibroblasts underwent fate reversion to readopt their native regeneration-

competent ground state. Remarkably, transplantation of velvet to scar-forming sites revealed that acquisition of fibroblast inflammatory priming incites a regenerative-to-fibrotic transition akin to scarless fetal to scar-forming adult healing transition seen in humans. Pharmacologic recapitulation of back skin fibroblast immunostimulatory secretome (PLAU) or inhibition of velvet fibroblast regenerative secretome (MDK) dampened velvet regeneration. Conversely, blocking fibroblast-derived cytokines (CSF1/CSF1R and CXCL12/CXCR4 signalling) enhanced regeneration.

Conclusions:
Fibrotic wound healing is driven by fibroblast-potentiated inflammatory signals that amplify effector immune programs at the expense of tissue function. Purposeful decoupling of fibroblast-immune interactions and reinforcement of fibroblast regenerative programs represent important therapeutic avenues for improving skin healing. To this end, Reindeer Atlas (BiernaskieLab.ca/Reindeer_Atlas) provides an accessible conduit for exploring molecular programs underlying skin regeneration versus fibrosis.

Learning objectives:
1. Single-cell mRNA-Sequencing allows dissection of transcriptional dynamics at single-cell resolution to study cell heterogeneity during health, healing, and disease.
2. Single-cell Assay for Transposase-Accessible Chromatin with sequencing (sc-ATAC-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.

Takeaway Message:
1. The adult reindeer represents a powerful mammalian model to directly compare skin regeneration and fibrosis within the same animal.
2. Skin regeneration may be the intrinsic reparative response, but its realization is pre-empted by exuberant inflammation incited by fibroblast inflammatory priming. Purposeful decoupling of fibroblast-immune crosstalk through interception of fibroblast-secreted signals (e.g., CSF1, CXCL12) represents an important avenue for mitigating scar and promoting regeneration.
3. Similar to immunopathologies seen during lung infection (Boyd et al. Nature 2020) or autoimmune skin lesions (Reynolds et al. Science 2021), pathologic skin repair is driven by fibroblast-potentiated inflammatory signals that amplify inflammation at the expense of tissue function.

Mast Cell Degranulation Contributes to Fibrogenesis and Resolution of Dermal Fibrosis

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Introduction:
Mast cells (MC) are resident immune effector cells in many tissues, including skin, and are increased in numbers during fibrosis. MCs interact with resident stromal and immune cells to contribute to the fibrotic microenvironment and are associated with fibrogenesis. However, MC involvement in resolving fibrosis remain unelucidated. We aim to determine MC roles and approaches to exploit MC activities to promote resolution of fibrotic injury.

Methods:
Bleomycin (Blm)-induced skin fibrosis was given to male MC-deficient and wild-type (WT) mouse strains. Mice were allowed to recover for 21 days to assess resolution. Ketotifen was administered to impair MC degranulation. Skin tissues were taken for gene expression and histology assessments. Changes in dermal thickness (ΔDT) and Tgfb1 were used as key indicators of fibrotic change.

Results:
Blm-treated skin showed substantial ΔDT and was reduced in MC-deficient mice ($p<0.05$). MC density increased with Blm treatment, further elevating during resolution. Significant reductions in ΔDT, towards baseline, were seen in WT ($p<0.01$) but not MC-deficient mice during resolution. Ketotifen treatment during Blm reduced ΔDT at the peak of fibrosis, however, continued Ketotifen treatment inhibited fibrosis resolution. Tgfb1 gene expression was reduced in MC-deficient skin compared to WT during fibrosis but remained elevated in MC-deficient skin during resolution. Remodeling-associated enzymes Mmp9, Mmp11, and Mmp13 were modified during fibrosis and resolution.

Conclusions:
MCs have important roles in both fibrotic progression and resolution in this model of skin fibrosis. Mediators released during degranulation may play key roles in fibrosis resolution and tissue remodelling. Selectively modifying MC activities may provide novel approaches to promote fibrosis resolution.

Learning objectives:
1. Role of MCs in fibrosis and resolution
2. Impact of MC degranulation during fibrosis and resolution
3. MC regulation of ECM degradation

Takeaway Message:
MC degranulation promotes fibrogenesis, but promotes better resolution of fibrosis

Baseline Fibroblast States Driving Differences in Scar Formation in Young and Aged Healing Skin

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Introduction:
While adult skin heals by forming a fibrotic scar, a diminished severity of scar production is a widely recognized feature of aged wound healing. The mechanisms underlying the divergent wound healing outcomes remain poorly understood. We hypothesize that this lack of scar production may be due to the dynamic changes in resting fibroblast states within the uninjured skin.

Methods:
To understand whether resting fibroblast states predispose an altered response to injury in aged skin, we performed single-cell RNA sequencing in Hic1CreERT2:RosatdTomato mice (which marks the majority of wound responsive fibroblasts) and compared young (3 months) and aged (18 months) uninjured skin.

Results:
Our analysis revealed differential composition of fibroblasts states in the uninjured young rodent back skin versus the aged uninjured skin. Specifically, there was a striking enrichment of pro-inflammatory Plac8+ fibroblasts in the young skin compared to the aged skin (77% vs 33%). As well, the Plac8+ fibroblasts found in the young skin exhibited preferential enrichment of immunomodulatory cytokines (Ccl2, Cxcl13, Cxcl10, Ptgs2) at baseline. This is further supported by the distinct regulatory architecture where the young uninjured fibroblasts preferentially activate Irf4, Irf7, and Irf9, whereas aged fibroblasts were deficient in these programs. Lastly, young skin exhibited a more differentiated terminal Plac8+ fibroblast state while aged fibroblasts harboured more uncommitted progenitors that did not adopt equivalent terminal states.

Conclusions:
These finding highlight distinct baseline transcriptomic fibroblast states between young and aged skin.

Learning objectives:
Investigate the heterogeneity in gene expression of uninjured fibroblasts, identify differences in gene regulatory programs between age and young skin, and reconstruct the cellular trajectories of the uninjured fibroblasts.

Takeaway Message:
Age dependent changes and fibroblast function changes are important determinants of wound healing. Understanding these dynamics will be essential towards identifying therapeutic targets to mitigate fibrosis and/or promote more effective wound healing across ages.

TGF-β Receptor Internalization Is Impaired in Scleroderma Fibroblasts and Is Associated with Reduced TGF-β Receptor-caveolin-1 Interaction

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Introduction:
Scleroderma (SSc) is a complex connective tissue disease characterized by fibrosis of the skin and internal organs. TGF-β is a pro-fibrotic cytokine that has been strongly implicated in the pathogenesis of SSc. TGF-β receptor internalization via clathrin-coated pits has been shown to promote TGF-β signaling, whereas internalization through caveolae is associated with receptor degradation. As elevated TGF-β receptor levels in SSc fibroblasts is a potential mechanism for constitutive autocrine TGF-β signaling in SSc fibrosis, we determined the TGF-β receptor internalization mechanisms that may enhance signaling in SSc fibroblasts.

Methods:
TGF-β receptor internalization was determined by monitoring the internalization of 125I-TGF-β1, and cell surface TGF-β receptor turnover was determined by affinity crosslink labeling, in SSc and healthy fibroblasts. Interaction of TGF-β receptors with caveolin-1 was assessed by co-immunoprecipitation and by blocking the caveolar pathway

Results:
TGF-β receptor internalization and degradation are impaired in SSc fibroblasts as compared to healthy fibroblasts. In addition, the interaction of TGF-β receptors with caveolin-1, a component of the TGF-β receptor degradation pathway, is markedly diminished in SSc fibroblasts. Dynasore, an inhibitor of receptor internalization, stimulated the interaction between caveolin-1 and TGFβ receptors in healthy fibroblasts but not in SSc fibroblasts, suggesting that TGFβ receptor-caveolin-1 interaction is impaired in these cells.

Conclusions:
TGF-β receptor internalization is impaired in scleroderma fibroblasts and is likely due to decreased TGF-β receptor-caveolin-1 interaction. Together, these perturbations in SSc fibroblasts may lead to excessive TGF-β signaling and fibrosis in SSc.

Learning objectives:
1. TGF-β receptor levels are elevated in SSc
2. Elevated TGF-β receptor levels in SSc is likely due to impaired internalization of receptors via the caveolar pathway

Takeaway Message:
TGF-β is a central mediator of the fibrotic process. Excessive TGF-β signaling and fibrotic responses in SSc fibroblasts are likely due to increased TGF-β receptor levels due to decreased internalization.

Is the YAP Inhibitor Celastrol a Novel Treatment for Scleroderma Fibrosis?

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Introduction:
Scleroderma (systemic sclerosis, SSc) is characterized by progressive fibrosis of the skin and internal organs. The mechanosensitive transcriptional co-activator yes activated protein-1 (YAP1) is activated in SSc fibroblasts. If Celastrol, a YAP inhibitor can alleviate SSc is unknown.

Methods:
We used human dermal fibroblasts isolated from healthy and SSc individuals with early-onset (<18 months) diffuse disease. Cells were treated with or without TGFβ1 (4ng/ml) in the presence or absence of celastrol (500nM) for 6 or 24h. To induce fibrosis, mice were injected bleomycin (0.1U/injection) in the presence or absence of celastrol (1 or 2mg/kg) for 21days. Protein and mRNA expression were examined using ELISA, western blot, RNAseq, and real time PCR analyses. Skin fibrosis was assessed by hematoxylin/eosin and trichrome staining to assess skin thickness, collagen deposition and by indirect immunofluorescence analysis with anti-YAP and α-SMA antibodies to assess localization of YAP1 in myofibroblasts.

Results:
Celastrol impaired TGF β1-induced CCN2, a-SMA, type I collagen mRNA and protein expression in healthy dermal fibroblasts and reversed the pro-fibrotic phenotype of SSc dermal fibroblasts. RNAseq analysis of healthy dermal fibroblasts revealed that 394/406 of TGFβ1-induced mRNAs were celastrol-sensitive. Celastrol blocked bleomycin-induced skin fibrosis, as visualized by reduced skin thickness, collagen deposition, serum TGFβ1 levels, myofibroblast differentiation and YAP nuclear localization (all N=6, $p<0.001$). Celastrol also impaired, in vivo, and in vitro, the induction of PAI-1, TNC, CCN2 mRNAs in response to fibrogenic stimuli.

Conclusions:
Celastrol has anti-fibrotic properties and warrants consideration as a potential treatment for SSc skin fibrosis.

Learning objectives:
1. Celastrol, a YAP inhibitor as a potential treatment option for SSc skin fibrosis.
2. To emphasize the role of YAP pathway in SSc skin fibrosis.

Takeaway Message:
This study provides an insight into the role of YAP pathway in SSc fibrosis and possibility of targeting it using Celastrol as a therapeutic option.

Investigating Angiotensin II Type 2 Receptor Signaling in Cutaneous Wound Healing

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Introduction:
Compound 21 (C21) is a selective angiotensin II type 2 receptor (AT2R) agonist previously shown in vitro and in vivo to reduce cardiac and renal fibrosis by limiting myofibroblast activity and collagen production. We sought to determine the role of AT2R signaling in cutaneous healing.

Methods:
We employed a splinted wound model in mice to recapitulate early phases of wound healing in humans. Mice received two, full-thickness dorsal skin wounds that were splinted with silicone rings. On alternating days, one wound received topical 20uM C21 (n=12) or the AT2R antagonist PD123319 (10uM; n=8) while the other received saline, until sacrifice on day 10. Wounds, including surrounding healthy skin, were harvested for histology and qPCR analyses. Scratch assays were performed on human dermal fibroblasts and keratinocytes to assess C21 and PD123319 activity in vitro.

Results:
C21 treatment did not change the rate of reepithelialisation, while PD123319 treatment accelerated wound closure ($p=0.0347$ vs saline). Collagen density was increased in C21-treated wounds ($p=0.0139$ vs saline) closer to normal unwounded skin but was decreased with PD123319 treatment ($p=0.0440$ vs saline and 0.0001 vs C21). C21 also increased vascular density relative to saline ($p=0.0137$). We observed upregulation of genes associated with regeneration and repair including Col6a1 ($p=0.0073$), NGF ($p=0.0115$), and mast cell markers Ms4a2 ($p=0.0012$) and Tpsb2 ($p=0.009$) with C21 treatment. Similarly, 50uM C21 significantly reduced both fibroblast ($p<0.0001$ vs vehicle) and keratinocyte ($p=0.0038$ vs PD123319) infiltration in vitro.

Conclusions:
In an early wound healing model, AT2R activation was associated with collagen density closer to that observed in unwounded skin with increased angiogenesis. Inhibition of AT2R led to rapid reepithelialisation and reduced collagen deposition consistent with atrophic wounds.

Learning objectives:
1. Understand how AT2R signaling impacts cutaneous wound healing
2. How does C21 alter early wound healing?
3. How does PD123313 impact early wound healing?

Takeaway Message:
AT2R signaling is involved in modulation of early wound healing.

Antibacterial Thermo-Sensitive Silver Hydrogel Nanocomposite Improves Wound Healing

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Introduction:
Among the many factors that may limit effective wound healing in patients with chronic ulcers, bacterial infection and poor cell recruitment are primary causes that contribute to prolonged healing. Thus, a novel strategy that aims to prevent bacterial infection within the wound, while at the same time providing structural scaffolding that promotes endogenous tissue repair, would be of great interest. Here, we developed a thermo-sensitive silver nanoparticle hydrogel composite as an antibacterial nutritional scaffold for the wound that contains all nutrients required for cell growth while preventing bacterial infection with the ability to fill up all the cavities and void areas in wounds regardless of their geometry.

Methods:
Silver nanoparticles (AgNPs) were synthesized by chemical reduction. After characterization, AgNPs–hydrogel composite was developed by reconstitution of Collagen/Glycosaminoglycan (CG) powder in a nanoparticle suspension with different concentrations of AgNPs (200, 400, and 600 ppm). The antibacterial activity of the formulations was examined in vitro and in vivo in subcutaneous implant infected model against Methicillin-resistant Staphylococcus aureus (MRSA). The wound healing efficacy of the hydrogel nanocomposite was also evaluated using a splinted wound model in rats through comparison of clinical wound measurements and histological assessments. The splinted full-thickness wounds were generated on the back of the rats and treated with CG hydrogel, the hydrogel nanocomposite with different concentrations of AgNPs, or no treatment as a control. MTT assay and biochemical analysis of blood at the end of in vivo wound healing study were performed in all groups to evaluate the safety of formulations.

Results:
The synthesized nanoparticles were spherical and stable. While CG hydrogel alone did not show any bacterial reduction in vitro, the inhibition of bacterial growth was significant in all AgNPs hydrogel nanocomposites compared to controls ($p < 0.05$, n=3) and was dose-dependent, with maximum reduction observed in the 600 ppm group (4.56±0.26 LOG CFU/mL, $P<0.001$, n=3). All concentrations of AgNPs hydrogel composites showed significant antibacterial activity against MRSA in vivo compared to hydrogel alone and controls ($P<0.0001$, n= 8). Treatment of splinted wounds with AgNPs hydrogel composite resulted in faster wound closure and accelerated wound re-epithelialization, as well as improved collagen deposition. The formulations did not show any cytotoxicity to human fibroblasts. No statistically significant difference was observed in hematological and biochemical biomarkers among different groups.

Conclusions:
Our results showed the potential antibacterial efficacy of AgNPs hydrogel composite both in vitro and in vivo, without impairing the healing activity of nutritional hydrogel in an animal model.

Learning objectives:
1. To develop AgNPs hydrogel composite as a functional scaffold for wound healing
2. To assess the antibacterial activity of AgNPs hydrogel composite
3. To evaluate safety and efficacy of formulation on wound healing in an animal model

Takeaway Message:
By presenting promising antibacterial and wound healing activity, AgNPs hydrogel nanocomposite offers a safe therapeutic option that can be used as a functional scaffold for an acceleration of wound healing.

Comparison of Split Thickness Skin Graft (STSG) and Self-Assembled Skin Substitute (SASS) Following Burn Trauma Using Three Modalities

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Introduction:
Severely burned patients present great medical challenges as viable skin used for conventional spli thickness skin graft (STSG) gets scarce. Self-assembled skin substitute (SASS), a skin substitute created at the LOEX and used in a previous case series, could become an alternative for such patients. We are conducting a Canada wide trial : SASS 2 (Self-assembled Skin Substitute for the autologous treatment of Severe Burn Wounds in Acute Stage of Burn Trauma) comparing SASS to STSG in patients suffering severe burn wounds in whom standard treatment is impossible.

Methods:
SASS was grafted next to STSG and graft take, as well as long term scar quality (qualitative scale) were evaluated. In a subset of patient's quantitative evaluation of scar was made using the Dermascan® (dermal thickness) the Cutometer (firmness and elasticity), and the Mexameter (melanin and erythema). Measurements of both test sites and other sites were taken at 3, 6, 12, 24 and 36 months. All measures were repeated 3 times.

Results:
The percentage of graft take was not statistically different between SASS and STSG (84% ± 27% for SASS and 96% ± 7% for STSG). No difference has been detected in dermal thickness, skin firmness and elasticity between SASS and STSG. Erythema values were similar between sites and diminished with time in all patients. Melanin levels were significantly lower in SASS than in STSG.

Conclusions:
SASS had similar graft take, thickness and viscoelastic properties when compared to STSG. Its melanin content was inferior, which was expected owning to the poor growth of melanocytes during production of SASS. These results show that SASS could provide a good alternative to STSG

Learning objectives:
1. Recognize the treatment limitations in severely burned patients
2. Describe three skin measurement modalities
3. Define SASS and compare its use to STSG

Takeaway Message:
SASS provides an interesting alternative to STSG in severely burned patients. Further research is needed to assess its long-term evolution.

Ice-Recrystallization Inhibitors from The Gluconamide Family Act as Effective Cryoprotectants for The Long-Term Storage of Dermal Constructs

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Introduction:
New therapies are needed to better address burn victims. Improving treatment prognosis of deep extensive burns lies in fast and effective wound covering. Many burn victims require native skin autografts, a severely limited treatment option in large burn patients. Consequently, autologous engineered skin presents as a suitable alternative. Unfortunately, the production of personalized grafts incurs delays. 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 autologous epithelial cell seeding.

Methods:
Cell suspensions were used to evaluate 6 IRIs in a 1.5%BSA–10%DMSO±IRI solution. Fibroblasts were frozen at -1°C/min to -80°C and transferred to -192°C. TrypanBlue mortality assay was performed immediately post-thaw along with a 96hr cell functionality assay. Fibroblasts were cultured for 35 days using the self-assembly technique to form a dermal sheet. We assessed the ability of single sheets to survive freezing within our cryopreservation mediums. After thawing, tissue-viability was evaluated using metabolic (AlamarBlue) and DNA-staining (SytoxGreen) assays.

Results:
Our BSA based cryopreservation medium showed similar effectiveness to serum in cell suspensions and dermal constructs. DMSO did not show cytotoxicity following our 40min incubation period needed for effective IRI diffusion. Immediate post-thaw mortality was not always concordant with long-term cell functionality. NOGlc and 4-MBA reduced post-thaw cell suspension mortality significantly by 52,0% at 1mM and 37,2% at 5mM, respectively. In dermis, NOGlc, 4-MBA and 2,6-DFB increased viability by 20,4% at 1mM, 27,7% at 5mM and 21,7% at 15mM, respectively. AlamarBlue and SytoxGreen results show good concordance. Epithelial cell seeding on cryopreserved dermis to obtain a complete skin equivalent using IRIs will soon be evaluated to confirm clinical utility.

Conclusions:
IRIs increase cell-viability in suspension, but also in 3D tissue models. However, results obtained in suspension are not always observed in matrix bound cells. BSA showed effectiveness as a cryomedium for dermal tissue, while reducing the risks and costs of serum in clinical translation.

Learning objectives:
Multiple sensitive parameters regulate cryopreservation injury (physical, biochemical, logistical). Results obtained within cell suspensions cannot always 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, not all demonstrate the same cryoprotective effectiveness. Long-term assays are necessary when evaluating post-thaw viability.

Takeaway Message:
Currently, we produce grafts using patient's cells that present similar histological characteristics to native skin. Here, we go a step further by cryopreserving a complete dermal graft which would be suitable for faster transplantation.

Targeting Scar Formation Window for Potential Anti-Scar Drug Delivery Through Smart Solid Lipid Nanoparticles

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Introduction:
Scarring can be a normal step of wound healing; however, untreatable scars can affect people's lives in different aspects (health, social and financial) and raises problems in their daily life. Despite tremendous progress in wound healing, reaching scarless wound healing has not been fulfilled. This project aims to develop a smart nanocarrier to deliver the anti-scar drug in the specific window of wound healing when scar formation begins. The targeted delivery of the drug not only prevents frequent wound dressing changes but also reduces the risk of neo-tissue degradation, as most anti-scar drugs have a destructive nature. We identified a specific biomarker over-expressed during the maturation stage of scar formation (when the activity of MMPs is dawn regulated). This unique biomarker is connective-tissue growth factor (CTGF). CTGF has different domains; one is insulin-like growth factor binding proteins with an affinity to bind to IGF. Therefore, we used CTGF as our targeting moiety to deliver the anti-scar drug by functionalized solid lipids nanoparticles (SLNs) with IGF. To minimize the pre-mature drug release, we coated the SLNs with natural clathrin cage. Upon binding of clathrin-coated IGF-functionalized SLNs to CTGF, the SLNs enter cells via endocytosis and the clathrin cage disassembles, and the drug can be released inside the cytoplasm.

Methods:
SLNs were fabricated based on natural lipids with an ethanol injection technique, and clathrin was extracted from pig's bran with ultracentrifuging and buffer transfer. After coating the SLNs with clathrin, the coated SLNs were functionalized with IGF through EDC-NHS chemistry. FITC was loaded inside SLNs during the fabrication stage to evaluate the internalization of SLNs for healthy fibroblast cells (low CTGF expression) and human breast cancer cells (a model for scar- high CTGF expression). Cells were cultured for 24 hr, and then 200 µL of SLNs, coated SLNs, and IGF-coated SLNs were added to the cells well. The internalization was observed with a fluorescent microscope.

Results:
IGF-functionalized clathrin-coated SLNs had the highest cellular uptake for MCF7 cells, while their uptake was low for fibroblasts.

Conclusions:
The targeted delivery can be a promising alternative for anti-scar drug delivery that can minimize second injuries while delivering the drug on-demand.

Learning objectives:
1. Targeting scar-formation window: anti-scar drugs can comprise the wound healing stage if they are taken in the early or late stages.
2. Non-invasive and targeted delivery of drugs to the skin and On-demand drug delivery to the skin via nanoparticles: NPs help to minimize second injuries due to frequent changes of dressings

Takeaway Message:
Nanoparticles are of great potential for drug delivery during skin wound healing, and by identifying the suitable biomarker as a targeting moiety, we can minimize the side effect of systematic or local drug delivery.

In Silico Profiling of Skin Cellular Infiltrates Reveals Divergent Patterns of Macrophage Dysregulation in Vitiligo and Eczema

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Introduction:
Vitiligo and eczema are two chronic inflammatory skin diseases with distinct clinicopathologic features. It is unclear how the clinical difference is reflected at the gene expression level or in the cellular infiltrates of the lesional skin. The purpose of this study is to compare the gene expression and cellular profiles of these two diseases to identify the shared as well as disease-specific features, and identify novel pathogenic players and therapeutic targets.

Methods:
Whole transcriptome sequencing was performed on skin biopsies of vitiligo patients (N=36), eczema patients (N=15) and healthy volunteers (N=9), which was followed by cellular deconvolution to obtained the in-silico profiles of the cellular infiltrates present in the skin of these two diseases. Flow cytometry and immunohistochemistry were performed to verify the disease-specific cellular changes. Animal models of vitiligo and eczema were employed to evaluate the relevance of these changes to the pathogenesis and therapeutic treatment of vitiligo and eczema.

Results:
The cellular infiltrates of eczema and vitiligo show many important differences, especially in the density and functional polarization of macrophages. Eczema is characterized by market enrichment of M1 macrophages while there were no major changes in M2 macrophages. In vitiligo, M1 macrophages were also increased, albeit to a lower extent than eczema, while M2 macrophages were depleted, which was confirmed by flow cytometry. Mouse models of vitiligo and eczema were highly responsive to treatment with maresin 1, a functional mediator of M2 macrophages, with concomitant suppression of development of vitiligo and eczema.

Conclusions:
While there is a marked enrichment of monocytes and M1-macrophage related cells in both vitiligo and eczema, deficiency of M2 macrophages appears to be disease specific for vitiligo. Modulating macrophages by using maresin 1 boosted skin resident M2 macrophages, and attenuated development of vitiligo as well as eczema.

Learning objectives:
1. Review the clinical and pathological features of vitiligo and eczema
2. Compare M1/M2 polarization patterns of vitiligo and eczema
3. Learn two methods for modulating macrophages in the skin

Takeaway Message:
Macrophage dysregulation contributes to the development of vitiligo and eczema. Therefore, modulating macrophages such as by M2 mediator maresin 1,

Granzyme K-Mediated IL-23 Induction Exacerbates Psoriasis Severity

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Introduction:

Psoriasis affects over one million Canadians and is characterized by increased skin inflammation and epidermal proliferation. The underlying etiology of psoriasis remains unclear; however, activation of the IL-23/IL-17 axis is believed to play an important role in pathogenesis. Unfortunately, the efficacy and safety of current systemic therapies can be challenged by unforeseen off-target side effects. IL-23 inhibition has been identified as an effective treatment intervention. As such, clarifying the mechanisms underlying IL-23 secretion will further the development of psoriasis therapies. Granzyme K (GzmK) is an immune cell-secreted protease that is elevated in human psoriasis and contributes to disease severity in a murine model of psoriasis. However, the mechanism(s) by which GzmK alters skin pathology in psoriasis is unknown. We hypothesized that GzmK contributes to psoriasis disease severity through augmentation of IL-23/IL-17 pathway.

Methods:

The role of GzmK was investigated in a murine model of psoriasis, comparing GzmK knockout (GzmK-KO) to wild-type (WT) mice (n=6/genotype). Murine skin sections were examined for pro-inflammatory markers via histology, PCR, and ELISA. Pro-inflammatory markers identified in mice skin tissues were validated in vitro. In vitro, THP-1-derived macrophages and dendritic cells were treated with or without GzmK for assessment of pro-inflammatory cytokine release.

Results:

GzmK-KO mice exhibited a reduction by 50% ($p<0.01$) in inflammatory cell infiltrate compared to WT mice. To examine associated inflammatory mechanisms, a panel of cytokines were assessed. IL-17 and IL-23, commonly elevated in human psoriasis, were reduced by 46% ($p=0.044$) and 48% ($p<0.001$) in GzmK-KO mice, respectively. Immunostaining for IL-23A staining indicated that the majority of IL-23-positive cells were mononuclear cells within the dermis. In vitro, GzmK-treated macrophages secreted increased levels of IL-23 ($p<0.001$).

Conclusions:

Based on the results observed, topical inhibition of GzmK may represent a novel therapeutic approach for treating psoriasis.

Learning objectives:

1. GzmK is elevated in murine and human psoriasis lesions
2. GzmK depletion attenuates psoriasis severity in a murine model of disease
3. GzmK depletion attenuates inflammation in psoriasis by decreasing levels of pro-inflammatory cell infiltrate and cytokines IL-17 and IL-23 in a murine model of disease
4. GzmK-induces IL-23 release from macrophages and may promote IL-23/IL-17 axis pathogenic mechanisms

Takeaway Message:

GzmK-mediated IL-23 induction exacerbates psoriasis severity. The loss of GzmK could attenuate key inflammatory cascades during psoriasis, rendering GzmK an amenable target for psoriasis drug development research.

Granzyme B: A Novel Therapeutic Target for Radiation Dermatitis

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Introduction:
Radiation dermatitis (RD), characterized in part by epidermal barrier dysfunction, occurs in up to 95% of patients receiving radiation therapy for cancer treatment. As current RD treatments are not always effective, severity of symptoms may prevent subsequent radiation treatments. Granzyme B (GzmB), a serine protease, is secreted by immune and non-immune cells. GzmB is elevated in a number of skin disorders, including atopic dermatitis. E-cadherin and filaggrin are direct GzmB substrates and are key to maintaining epidermal barrier function. GzmB is abundant in human RD skin. We hypothesized that GzmB cleaves epidermal barrier proteins in RD and contributes to increased RD severity.

Methods:
GzmB, E-cadherin, and filaggrin levels were assessed in healthy and RD human skin using immunohistochemistry. GzmB presence in HaCaT culture media, collected 24 and 48 hours post a single 0, 2, 5, 10, 20Gy dose of radiation, was explored using reverse transcriptase PCR, Western blot, and ELISA. An established murine model of RD was utilized, comparing the response of GzmB knockout (GzmB-KO) versus wild type (WT) mice. RD severity was quantified on days 0 to 14.

Results:
Elevated GzmB ($p<0.005$) and reduced E-cadherin ($p<0.02$) and filaggrin ($P<0.0453$) levels were observed in RD human skin compared to healthy human skin. Irradiated HaCaTs did not directly produce GzmB, indicating an alternative GzmB source. Increased CD68 ($p<0.0131$) and mast cell tryptase ($p<0.0306$) positive cells were observed in RD biopsies compared to healthy skin. Co-localization of GzmB with CD68 and mast cell tryptase in human RD tissues suggested that macrophages and mast cells are important cellular sources of GzmB. In a murine model of RD, GzmB-KO mice (N=7) exhibited reduced RD severity compared to WT controls (N=7) at days 4 to12 ($p<0.05$).

Conclusions:
GzmB is abundant in human RD and is associated with reduced E-cadherin and filaggrin. GzmB contributes to RD severity in vivo.

Learning objectives:
1. GzmB is highly elevated in human RD tissue samples when compared to normal human skin samples.
2. E-cadherin and filaggrin, regulators of epidermal barrier function, are direct substrates of GzmB and are reduced in human RD lesions.
3. Loss of GzmB decreases the severity of radiation dermatitis in vivo, providing supporting evidence that GzmB is a target for RD.

Takeaway Message:
Serine protease GzmB is elevated and its substrates E-cadherin and filaggrin, regulators of epidermal barrier function, are reduced in human RD. GzmB is a key contributor to disease severity in vivo and is a novel therapeutic target for RD.

Exposure to Organic Solvents and association with Systemic Sclerosis Disease Severity and Manifestations: A Canadian Scleroderma Research Group Study

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Introduction:
Systemic sclerosis (SSc) is an autoimmune disease with significant morbidity and mortality, thought to be induced by an environmental trigger in a genetically predisposed individual. The aim of this study was to determine effect of exposure to organic solvents 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. Univariate and multivariate logistic regression was performed, stratified by sex, to determine characteristics associated with occupational exposure to organic solvents as compared to unexposed controls. Survival analysis using Kaplan-Meier curve was performed.

Results:
1439 had complete data on organic solvent exposure (86.7% females), of which 20.2% reported exposure. Female to male ratio was reduced in patients with solvent exposure compared to the entire CSRG cohort (2.4:1 vs. 6:1). Univariate logistic regression revealed that exposed patients had significantly lower anti-centromere antibody positivity (OR 0.72; 95% CI 0.54-0.96) and significantly higher risk of renal crisis (OR 2.36; 95% CI 1.34-4.16) and GI disease severity (β 0.95; 95% CI 0.55-1.36). After adjusting for age, sex, ethnicity, and diffuse disease, risk of renal crisis remained significantly higher (OR 2.13; 95% CI 1.15-3.93). Severity of GI disease remained significant after adjusting for age, sex, disease duration, diffuse disease, silica exposure, smoking, and use of immunosuppressives (β 0.89; 95% CI 0.47-1.31). Mortality rate was 54/1000 person-years in the exposed group, compared to 43/1000 person-years in the unexposed. Although there was a trend for increasing mortality, this did not reach statistical significance (HR 1.26; 95% CI 0.95-1.68).

Conclusions:
SSc patients with occupational exposure to organic solvents were more likely to be males, have a higher risk of renal crisis and severe GI disease, as well as higher mortality. In addition to effective workplace protection strategies, taking a detailed occupational history and patient education are critical.

Learning objectives:
1. About 20% of the cohort reported exposure to organic solvents and the ratio of males to females was higher in the exposure group compared to the Canadian Scleroderma Research Group cohort
2. Exposure to organic solvents was associated with a higher GI disease severity and risk of renal crisis
3. Exposure to organic solvents was associated with a trend towards increasing mortality

Takeaway Message:
Screening for occupational exposures in SSc patients may be important as can alter disease phenotype and severity

Supplementation of the Culture Conditions with Eicosapentaenoic Acid Modifies the Th17 and Treg Cell Balance in a Tissue-engineered Psoriatic Skin Model

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Introduction:
Psoriasis is an inflammatory skin disease with an hyperproliferation of keratinocytes. The pathology is also characterized by an excessive T cell infiltration into psoriatic lesions. N-3 polyunsaturated fatty acids (n-3 PUFAs), in particular eicosapentaenoic acid (EPA), are essential metabolites for the organism and their food consumption beneficially impact psoriatic patients. The aim of this study was to evaluate the bioactivity of EPA on T cell polarization in our psoriatic skin model.

Methods:
A monolayer of keratinocytes and polarized T cells was realized using EPA supplemented media or not. Psoriatic skin substitutes were produced according to the self-assembly method. T cells were isolated from blood samples of healthy donors and EPA supplementation was maintained at a concentration of 10 uM throughout cell culture.

Results:
In co-culture of psoriatic keratinocytes and T cells, EPA reduced the polarization of Th17 cells to the benefits of regulatory T cells, noticeable by an increase in the FOX-P3 labeling. In the 3D psoriatic model, the addition of EPA normalized the proliferation and cell differentiation of psoriatic keratinocytes. Moreover, the EPA supplementation decreased the expression of specific markers of psoriasis, including the expression of psoriasin, as well as the degree of phosphorylation of the proteins STAT1 and STAT3. Finally, psoriatic skin substitutes produced with polarized T cells exhibited high quantities of IL-17A, whereas the supplementation of the media with EPA potentiated the production of IL-17A, while increasing the secretion of the regulatory cytokine IL-10.

Conclusions:
Our results showed that in this psoriatic skin model enriched with polarized T cells, EPA mainly exerts its anti-inflammatory actions by decreasing the proportion of Th17 cells infiltrating the psoriatic skin.

Learning objectives:
1. Describe the regulation of n-3 PUFAs on T cell polarization in a psoriatic context
2. Illustrate the influence of EPA on specific psoriatic markers
3. Report the effects of EPA on cytokine production

Takeaway Message:
n-3 PUFAs modifies the T cell profile in a tissue-engineered psoriatic model

Investigating the Effect of Biologic and Systemic Therapies on Mortality and Co-Morbidity Development. A Study of Albertan Psoriasis Patients from 2012-2020

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Introduction:
Psoriasis is a chronic inflammatory condition affecting approximately 3% of adults. Although skin involvement is the dominant clinical feature, psoriasis is associated with numerous extracutaneous comorbidities. It has also been demonstrated that patients with psoriasis have a higher risk of mortality compared to healthy individuals, which has been documented in numerous studies from North America, Europe and Asia.
It has been suggested that cardiovascular comorbidities drive the majority of increased mortality in psoriasis patients, but this has not been unequivocally proven as of yet.
In this study we aim to identify co-morbidities most correlated to psoriasis patient mortality alongside the impact of systemic biologics on all-cause mortality in psoriasis patients.

Methods:
Individuals diagnosed with psoriasis in the province of Alberta (population 4.4 million) were identified using the Alberta Health Services (AHS) data repository of reporting (DRR) and were then sex, age, and observation time matched against control patients in the population. We address the biases of the retrospective study with a population-wide design and careful matching of psoriasis cases to several different control cohorts. Each cohort was compared against its respective control population using survival analyses including Kaplan Meier analyses and cox regression analyses when appropriate.

Results:
Our results confirm previous findings that psoriasis is associated with an increase in all-cause mortality, particularly in otherwise healthy patients. For these and all psoriasis patients overall, those with concurrent liver disease were most associated with increased mortality, along with those with cardiovascular disease. In terms of factors mitigating increased mortality, biologic therapy decreased mortality in multiple groups, both in the overall population and within specific psoriasis subgroups.

Conclusions:
Overall, our results both confirm previous findings and have shown important new findings vital to the future of psoriasis research with respect to associated co-morbidities and the effect of different treatments on overall patient survival.

Learning objectives:
1. Learn about co-morbidities commonly associated with psoriasis
2. Learn about the impact of different treatments on mortality for psoriasis patients.
3. Learn about the effect of biologic therapy on psoriasis-related mortality
4. Hypothesize how current guidelines can be adjusted to better serve psoriasis patients in the future

Takeaway Message:
Psoriasis should be managed as a multi-systemic disease, given significant impacts on co-morbidity prevalence, severity, and all-cause mortality. Specifically, impacts on hepatic, and cardiovascular diseases. An integral part of this management is biologic therapy, given its direct reduction in mortality.

Pharmacological Interventions for Primary Psychodermatologic Disorders Evaluated in Controlled Trials: A Systematic Review

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Introduction:
The management of primary psychodermatologic disorders (PPDs) is challenging. The lack of clinical guidelines for treatment hinders the development of coordinated interventions to improve healthcare delivery. The study objective is to identify, appraise, and summarize the evidence on the effectiveness of pharmacological management of PPDs in controlled trials.

Methods:
The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement was followed. Medline, EMBASE, PsycInfo, and Scopus were searched. Two reviewers independently screened titles and abstracts to identify relevant studies and completed full-text review, quality assessment, and data extraction. The inclusion criteria are any controlled trials that investigated pharmacological interventions for any PPDs.

Results:
21 controlled trials were included on five PPDs including trichotillomania, pathologic skin picking, nail biting, delusional parasitosis, and dermatitis from compulsive hand washing. Seven different classes of medications were investigated: SSRIs (i.e., fluoxetine, sertraline, and citalopram), tricyclic antidepressants (i.e., clomipramine and desipramine), antipsychotics (i.e., olanzapine and pimozide), anticonvulsant (i.e., lamotrigine), N-acetylcysteine (NAC), inositol, and milk thistle.

Conclusions:
Our findings showed RCT-derived evidence supporting the use of antidepressants in trichotillomania (sertraline, clomipramine), pathologic skin picking (fluoxetine), pathologic nail biting and dermatitis from compulsive hand washing (clomipramine or desipramine); antipsychotics in trichotillomania (olanzapine) and delusional parasitosis (pimozide); N-acetyl cysteine in trichotillomania and skin picking.

Learning objectives:
1. List the pharmacological treatment options for various PPDs.
2. Understand the level of evidence for pharmacological interventions for PPDs.

3. Appreciate the challenges of studying the pharmacological interventions for PPDs in controlled trials.

Takeaway Message:

1. Few pharmacological interventions are evaluated through controlled trials in the literature.
2. This study serves as a roadmap for clinicians to develop informed treatment choice with current available evidence and help researchers to explore new interventions.

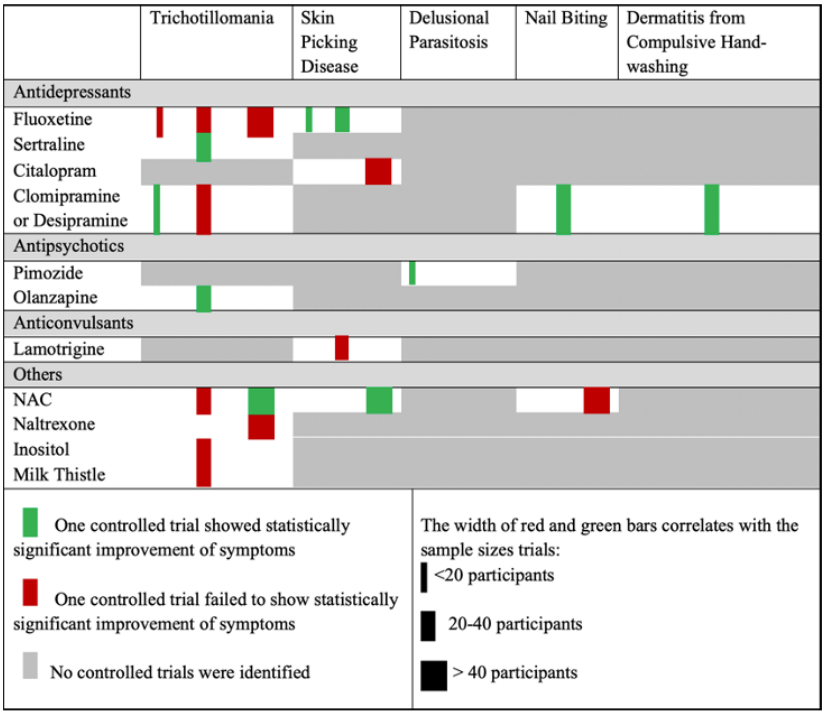

Figure 2. Evidence Mapping of controlled trials on the pharmacological interventions for primary psychodermatologic disorders

Beyond Skin Deep: Case-based Online Modules to Teach Multidisciplinary Care in Dermatology among Clerkship Students

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Introduction:
Canadian medical schools offer limited clinical dermatology training. In addition, there is a lack of educational resources that designed specifically for clerkship students that focus on the multidisciplinary nature of dermatology. After developing case-based educational resources to address the lack of clinical exposure and learning of multidisciplinary care in dermatology, the study aims to evaluate the educational intervention and gather feedback for future module development.

Methods:
Ten online interactive dermatology case-based modules involving 14 other disciplines were created. Medical students (n = 89) from two Canadian schools were surveyed regarding perceptions of the existing dermatology curriculum. Among 89 students, 46 voluntarily completed the modules, and a survey (a five-point Likert scale ratings) including narrative feedback to determine an improvement in dermatology knowledge and understanding of multidisciplinary care.

Results:
Among 89 surveyed students, only 17.1% agreed that their pre-clerkship dermatology education was sufficient and 10.2% felt comfortable managing patients with skin conditions in a clinical setting. Among 46 students, 95.7% of students agreed that the modules fit their learning style (4.17±0.73 on Likert scale) with positive narrative feedback (Figure 1). 91.3% agreed or strongly agreed that the modules enhanced their dermatology knowledge (4.26±0.61). 79.6% of students agreed that the modules helped with understanding the multidisciplinary nature of dermatological cases (3.98±0.81). Student comfort to manage skin conditions increased 7-fold from 10.2% to 78.3% post-module.

Conclusions:
Clerkship students had limited knowledge of dermatologic conditions, the case-based modules were able to successfully address deficits and assist students understand the multidisciplinary nature of dermatology.

Learning objectives:
1. Understand the current status of dermatology education for clerkship students.
2. Understand the ways to enhance dermatology teaching for clerkship students especially when clinical resources are limited.
3. Appreciate the role of interactive online modules to enhance the understand the multidisciplinary care in dermatology for clerkship students.

Takeaway Message:
1. Clerkship students had limited knowledge of dermatologic conditions.
2. The case-based modules were able to successfully address deficits and assist students understand the multidisciplinary nature of dermatology.

Implication of PARP1 In Repair of UV-Damaged DNA to Non-Melanoma Skin Cancers

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Introduction:
Poly (ADP-ribose) polymerase-1 (PARP1) is an abundant nuclear enzyme in higher eukaryotes that is known to be activated rapidly by a variety of DNA damages. The activated PARP1 forms polymers of ADP-ribose (PAR) chains which post-translationally modify proteins in the vicinity of DNA damage and recruit their functions in various cellular responses to DNA damage, ranging from DNA repair to cell death and cancer. Our previous studies showed that PARP1 is activated very rapidly after irradiation with UVB or UVC. Using cellular and mouse models, we have examined the role of PARP1 different cellular responses to DNA damage ranging the nucleotide excision repair pathway to repair UV-damaged DNA and cell death to UV-induced non-melanoma skin cancer.

Methods:
The cellular studies were carried out with human skin fibroblasts or other cells which are proficient or deficient in PARP1 and other DNA repair proteins. The cells were subjected to local or global UV irradiation to examine the responses at site of DNA damage and at global cellular levels. The DNA repair studies were carried out in cellular models and in purified proteins and damaged DNA. Lastly, we used SKH1 hairless mouse model of UVB-induced non-melanoma skin cancer to examine the development of cancer in mice which are impaired for PARP1 by knockout or pharmacological inhibitor approaches.

Results:
We will describe our results clearly showing the expanding roles of PARP1 in the nucleotide excision repair pathway. We will also describe the impact of impaired PARP1 function on development of UV-induced non-melanoma skin cancers.

Conclusions:
There is therapeutic potential for PARP1 targeting in non-melanoma skin cancers.

Learning objectives:
There are many factors involved in the journey of a UV irradiated skin cell to develop cancer, and here we describe different roles of a druggable target PARP1 in this entire journey.

Takeaway Message:
PARP1 is targeted for other cancer therapies and it has a potential for targeted therapy of non-melanoma skin cancer

The gamete specific gene, Gametocyte Specific Factor 1 (GTSF1), contributes to the Th phenotype in Cutaneous T-Cell Lymphomas.

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Introduction:
Cutaneous T-Cell Lymphomas (CTCL) can take up to 6 years to be diagnosed, therefore novel biomarkers are needed. To identify potential biomarkers, several researchers have performed transcriptomic analyses. Gametocyte Specific Factor 1 (GTSF1) is a germline-cell specific gene that has been established as a biomarker of CTCL; despite this, its molecular function remains unknown. Previous research on gametes has established GTSF1 as a retrotransposon control gene.

Methods:
To investigate this, we established shRNA-mediated GTSF1 knockdown CTCL cell lines. We analyzed retrotransposons with qRT-PCR, Western blot and a retrotransposition dual luciferase assay. In addition, we performed transcriptome analysis with RNA-Seq, DESeq2 and pathway enrichment analysis with GO, KEGG, Reactome and WikiPathways. Validation of the RNA-Seq was performed with ELISAs.

Results:
GTSF1 in CTCL is not silencing retrotransposons. Differential gene expression analysis revealed 12496 differentially expressed genes (p adjusted <0.05). Pathway enrichment analysis demonstrated an enrichment of several pathways including response to stimulus, immune response, response to cytokine and inflammatory response. ELISA assay demonstrates a change on the cytokine profile after GTSF1 knockdown.

Conclusions:
Our data suggest GTSF1 as a novel regulator of the Th phenotype on CTCL cells, thereby placing it as a potential treatment target for regulating disease progression.

Learning objectives:
1. Evaluate the ectopic expression of GTSF1 on CTCL.
2. Assess the impact of GTSF1 expression on retrotransposon control in CTCL cell lines.
3. Evaluate a previously unreported role of GTSF1 on Th phenotype.

Takeaway Message:
Ectopic expression of GTSF1 on CTCL patients has been previously reported. In germline-cells, GTSF1 participates on the silencing of retrotransposons. However, in CTCL, it seems to contribute to the Th phenotype thereby potentially regulating the immune response of these patients.

Comparison of the BCC Tumour Microenvironment to other Solid Malignancies

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Introduction:
Most BCC cases are simple to treat and they rarely metastasize because they have a fibromyxoid stroma, a feature characteristic to BCC. However, roughly 1-2% of BCC cases are advanced and they display mesenchymal stem cell-like phenotypes and high amounts of macrophages and Th2 cytokines. These features are believed to contribute to the fatality of advanced BCC tumors.

Methods:
The RNA deconvolution algorithms CIBERSORTx and xCell was performed for genome data extracted from TCGA for over ~11,000 non-BCC tumors. Figures were generated and computational statistic tests were performed to identify non-BCC cancers that display the closest similarities ("relative"). In-depth literature review was performed with the complied results.

Results:
Like BCC, kidney chromophobe relies on TAMs and Th2 cytokines to enhance tumor growth. Secondly, myxofibrosarcoma was studied in depth due to the characteristic fibromyxoid stroma feature that BCCs have. Lastly, for skin cutaneous melanoma, genetic alterations in specific genes involved in gene expression pathways shared with BCC were examined.

Conclusions:
The similarities between BCC and their "relatives" in gene expression pathways, cytokine and mesenchymal stem cell profiles, current and potential treatment approaches were analyzed. The common characteristic between the future orientation of research for all three BCC "relatives" is target therapy with a combination of more accurate identification of makers and more efficient genomic technologies.

Learning objectives:
The purpose of this study it to develop a reliable model to study advanced BCC, since there are currently none that exist. Specifically, through comparison to BCC "relatives", the learning objectives comprise of understanding BCC cancer cells' progression and survival, existing therapies, and potential experimental models and novel treatment approaches.

Takeaway Message:
New targeted therapeutics used in other malignancies with closely related microenvironment changes might provide novel management strategies for BCC.

CD109-IL6Rα Interaction Drives Stemness of Squamous Cell Carcinoma (SCC) Through STAT3/Nrf2 pathway

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Introduction:

Squamous cell carcinoma (SCC), is one of the most prevalent types of malignancy and its incidence is increasing globally. The GPI-anchored membrane protein CD109 is frequently overexpressed in SCC and this overexpression is associated with malignant transformation. The molecular mechanisms by which CD109 may regulate SCC progression are still unknown. The levels of Interleukin-6 (IL-6), a pleiotropic cytokine that regulates cellular proliferation, survival, and invasion, are also elevated in SCC tumors, and the elevated IL-6 expression is associated with increased recurrence and lower survival in SCC patients. As CD109 has been shown to strongly enhance IL-6/Jak/STAT3 signaling in lung adenocarcinoma, we sought to determine whether CD109 regulates IL-6 receptor (IL6Ra) signaling and action in SCC.

Methods:

Two SCC cell lines (A431 and SCC9) and oral SCC patient tissue and patient-derived organoids were used to study CD109 and IL6Rα association dynamics using immunohistochemistry, immunofluorescence, and FACS analysis. CD109 and IL6Rα expression and IL6-induced phosphorylation of STAT3, Nrf2/SOD1/HO1 and stem cell markers (Nanog, Oct4, Bmi, Sox2) were measured by western blot.

Results:

Our results show that CD109 is markedly upregulated in patient-derived tissue, organoids and SCC cell lines. CD109 associates with IL6Rα and potentiates IL6R/STAT3/Nrf2 signaling pathway, and enhances stemness, in SCC cells in culture, SCC tumor tissue, and organoids.

Conclusions:

Our findings show that CD109 potentiates IL6Rα signaling and stemness in SCC cells and reveals a fundamental role for CD109 in IL6R-mediated SCC progression.

Learning objectives:

1. CD109 and IL6R are upregulated in oral and cutaneous Squamous Cell Carcinoma
2. CD109 is associated with the inflammatory receptor IL6R to activate STAT3 and Nrf2/SOD1/HO1, an important cancer promoting signaling cascade
3. CD109 is a promising clinical target for limiting SCC tumor growth and progression

Takeaway Message:

Targeting the CD109/STAT3/Nrf2 axis has the potential to overcome therapy resistance in SCC. Our findings highlight a possible clinical utility for CD109 as a therapeutic target in SCC.

An Updated Systematic Review and Meta-Analysis on Efficacy and Safety of Sonic Hedgehog Inhibitors in Basal Cell Carcinomas

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Introduction:
Basal cell carcinoma (BCC) of the skin is the most common form of skin cancer affecting nearly 4.1 million Americans yearly. In life-threatening locally advanced BCC, sonic hedgehog inhibitors (SSHis) remain as a preeminent treatment option for laBCC and mBCC. In this updated systematic review and meta-analysis, we aimed to better characterize the efficacy and safety of SSHis by including final updates from pivotal clinical trials and new recent studies.

Methods:
A search using electronic databases was performed for articles including clinical trials, prospective case series, and retrospective medical record reviews on human subjects written in English. Overall response rates (ORRs) and complete response rates (CRRs) were the primary outcomes. For safety assessment, the prevalence of adverse effects of the following adverse effects were analysed: muscle spasms, dysgeusia, alopecia, weight loss, fatigue, nausea, myalgias, vomiting, skin squamous cell carcinoma, increased creatine kinase, diarrhea, decreased appetite, and amenorrhea. Analyses were performed in R. Data were pooled using linear models with fixed effects meta-analysis for primary analyses, along with 95% confidence intervals and p values. Intermolecular differences were calculated using Fisher's exact test.

Results:
A total of 22 studies were included for the meta-analysis: 19 studies assessing both efficacy and safety, 2 studies assessing safety only, and 1 study assessing efficacy only. Overall, the pooled ORR for all patients was 64.9% (95% CI 48.2%-81.6%), implicating there is at least a partial response ($z=7.60$, $p<0.0001$) in most patients receiving SSHis. Combined ORR for vismodegib (68.5%) and sonidegib (50.1%). The intermolecular difference was statistically significant for both ORR and CRR ($p<0.0001$). Vismodegib had significantly higher overall and complete response rates, less gastrointestinal disturbance compared to sonidegib. In clinical practice, these findings favor the use of vismodegib over sonidegib.

Conclusions:
This systematic review and meta-analysis showed that SSHis is a promising treatment option for patients with advanced BCC.

Learning objectives:
1. Determine the efficacy of sonic hedgehog inhibitors as treatment for localized and metastatic basal cell carcinoma.
2. Determine the safety of sonic hedgehog inhibitors.
3. Compare the efficacy and safety of vismodegib and sonidegib as treatment options for basal cell carcinoma.

Takeaway Message:
Our meta-analysis leans towards favouring vismodegib over sonidegib in clinical practice due to its higher response for advanced BCC and reduced side effects. It is important to stay updated with the latest discoveries on the efficacy and safety of SSHis.

Preferentially Expressed Antigen in Melanoma (PRAME) Regulates Retinoid Response and Cell Cycle Progression in Basal Cell Carcinoma and Squamous Cell Carcinomas

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Introduction:
Vitamin A derivatives, called retinoids, regulate epithelial homeostasis and are effective chemoprophylactics and chemotherapeutics for some skin and oral cancers. Preferentially Expressed Antigen in Melanoma (PRAME) is a gamete-specific gene that represses retinoid signaling and regulates cell cycle progression. PRAME is re-expressed in subsets of basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) of the skin and tongue. The functions of PRAME in BCC and SCC are unknown.

Methods:
Immortalized keratinocyte, BCC and SCC cell lines were subjected to shRNA-mediated PRAME knockdown or to PRAME overexpression. PRAME knockdown/overexpressing cells and were treated with retinoids. Immunoblotting and RT-qPCR were performed for markers of retinoid response. Cell cycle stage distribution was acquired using propidium iodide flow cytometric analysis and immunoblotting for cell cycle regulatory proteins. Proliferation was measured using label-free live cell imaging and Ki-67 immunocytochemistry.

Results:
PRAME knockdown in A431 cells restored retinoid-induced changes in cytokeratin expression. PRAME knockdown also enabled retinoid-induced increase in the percentage of G0/G1 cells. PRAME overexpression blunted retinoid-induced changes in cytokeratin expression, and abrogated the retinoid-induced S-phase cell cycle arrest in Cal27 cells. PRAME knockdown and overexpression altered expression of p14/ARF, p27/Kip1 and p21/Waf1 proteins, consistent with their cell cycle profiles.

Conclusions:
PRAME may regulate the sensitivity of BCC and SCC cells to retinoids, potentially abrogating retinoid-induced changes in cytokeratin profile and cell cycle arrest. PRAME may regulate cell cycle progression.

Learning objectives:
1. Investigate correlations between PRAME expression in BCC and SCC tumors and clinicopathological features.
2. Determine the impact of PRAME expression on retinoid-induced changes in cytokeratin profile and differentiation.
3. Determine the impact of PRAME expression on the cell cycle progression, proliferation and retinoid-induced proliferation arrest.

Takeaway Message:
PRAME may attenuate response to retinoids used to prevent and treat BCCs and SCCs. PRAME expression in BCC and SCC may bear prognostic and therapeutic relevance that warrant further investigation.

CD109 Promotes Epidermal Growth Factor Receptor (EGFR) Signaling and Tumorigenicity by Blocking EGFR Degradation in Squamous Cell Carcinoma Cells

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Introduction:
CD109 is a GPI-anchored protein, expressed on the surface of many cell types. CD109 levels are upregulated in squamous cell carcinoma (SCC). Previous work from our lab has shown that CD109 is pro-tumorigenic and that deletion of CD109 in A431 cells results in loss of EGFR expression. We hypothesized that CD109 is required for EGFR stability and signaling. Here we determined the mechanisms by which CD109 may regulate EGFR levels, signaling, and tumorigenicity in SCC cells.

Methods:
CD109-mediated regulation of EGFR expression was determined by microarray analysis. Also, the expression profiles of both CD109 and EGFR were derived from TCGA data base by analyzing 515 SCC patients. In addition, CD109-EGFR interaction dynamics was analyzed by co-immunoprecipitation and colocalization studies, using two SCC cell lines, A431, FaDu. Regulation of EGFR levels by CD109 was analyzed by qPCR, degradation studies, and FACS. CD109-mediated EGFR signaling was analyzed by immunoblot and tumorigenicity was determined by a spheroid formation assay.

Results:
We demonstrate that CD109 stabilizes EGFR by associating with EGFR and blocking EGFR degradation via Smurf-mediated inhibition of EGFR-Cbl interaction, in SCC cells. Also, CD109 promotes tumorigenicity by enhancing EGFR signaling via AKT/STAT3/ERK, in these cells.

Conclusions:
CD109 interacts with EGFR and blocks EGFR degradation, leading to enhanced EGFR signaling and tumorigenicity in SCC cells.

Learning objectives:
Increased EGFR signaling is a hallmark of many cancers, especially SCC.
-CD109 is a key regulator of EGFR expression and action.
-The mechanism by which CD109 regulates EGFR action involves CD109 association with EGFR and blockade of EGFR degradation, leading to increased EGFR-mediated signaling and tumor progression.

Takeaway Message:
Targeting CD109-EGFR interaction and thereby blocking EGFR signaling may provide a novel therapy for SCC treatment.

Early Organ Metastasis in Granulomatous Mycosis Fungoides: A Systematic Review

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Introduction:
The granulomatous variant of mycosis fungoides (GMF) is a rare form of MF (<3% of cases) defined by a granulomatous reaction in the vicinity of the malignant lymphoid infiltrate. The impact of granulomatous inflammation on the prognosis of the disease remains controversial as there are both favorable and unfavorable outcomes documented.

Methods:
We reported 4 incident cases of GMF diagnosed in our institutions and performed a systematic review of 116 GMF cases previously described in the literature.

Results:
In contrast to the classic Alibert-Bazin type of mycosis fungoides (MF), cutaneous lesions in GMF tend to involve distal extremities (lower legs, feet, hands) early in the disease course. All our patients with GMF had an aggressive course characterized by a rapid stage progression and organ metastases to the lung, spleen, liver and kidney. In the literature, 30% of GMF patients developed organ metastasis, most frequently to the lung. The median time to stage progression was 25 months.

Conclusions:
GMF is an aggressive form of mycosis fungoides. Therefore, screening for distant metastases should be considered at presentation and repeated during follow-up.

Learning objectives:
1. What is granulomatous mycosis fungoides
2. How is granulomatous mycosis fungoides different from classic mycosis fungoides
3. What is the clinical significance of granuloma formation on the prognosis of the disease

Takeaway Message:
1. GMF has a higher rate of early organ metastasis and shorter survival.
2. Patients with GMF should be offered full staging and close surveillance even in early stages of the disease.

Follow-Up of Patients with Keratinocyte Carcinoma: Systematic Review of Clinical Practice Guidelines

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Introduction:
Patients with keratinocyte carcinoma (KC) are at risk of developing recurrence, metastasis, and additional cutaneous malignancies. However, it is unclear how often patients should be seen for follow-up skin examination. We conducted a systematic review of clinical practice guidelines to summarize recommendations for dermatologic follow-up of patients after a KC diagnosis.

Methods:
We searched PubMed, MEDLINE, and EMBASE databases to identify national or international clinical practice guidelines published between 2010-2021 containing recommendations for follow-up frequency after a diagnosis of localized cutaneous KC in immunocompetent patients. Guideline quality was assessed using the AGREE II tool's 7-point system (1=poor and 7=exceptional) converted to a scaled domain score.

Results:
Fourteen eligible guidelines were included. The recommended overall duration of follow-up after KC ranged from a single visit to lifelong surveillance. Eleven guidelines stratified their recommendations by tumour risk. For high-risk basal cell carcinoma (BCC), one guideline suggested follow-up every 3 months, while four recommended every 6 months. For low-risk BCC and guidelines that did not stratify by risk, follow-up recommendations ranged from every 6-12 months.

For high-risk squamous cell carcinoma (SCC), recommendations included a range of follow-up frequencies, spanning every 3 months (n=5 guidelines), 4 months (n=1), 6 months (n=6), or annually

(n=4). For low-risk SCC, the recommended frequency of follow-up ranged from annually (n=5 guidelines) to every 6 months (n=3) or every 3 months (n=1). One guideline did not use risk stratification and recommended annual screening for all SCC.

Overall quality was fair. The highest scoring AGREE II domain was “scope and purpose”, which assessed the guideline’s overall objectives, (mean domain score=71%, SD±24) and the lowest scoring was “applicability”, which assessed barriers and facilitators to implementation (mean domain score=6%, SD±7).

Conclusions:
There was little consensus among guidelines on the appropriate follow-up schedule for KC patients. Randomized trials are necessary to define an optimal follow-up regimen.

Learning objectives:
1. Understand variations in current follow-up recommendations for KC patients
2. Identify evidence gaps in formulating follow-up recommendations for KC
3. Summarize the strengths and weaknesses of current KC clinical practice guidelines

Takeaway Message:
Our systematic review found that clinical practice guidelines provided diverse recommendations regarding the optimal follow-up frequency and duration for patients diagnosed with BCC or SCC. This is largely because there is little evidence to support these recommendations. Current guidelines are based on recurrence risk assessed through systematic reviews and observational studies. Further work is necessary to identify an optimal follow-up schedule, preferably through randomized trials comparing different follow-up regimens for patients with BCC and SCC.

When Tanning is Trending: A Content Quality Study of Skin Cancer on TikTok

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Introduction:
TikTok is a popular new video-based social media platform, especially amongst young adults. Dermatologists have increasingly used this platform for providing educational content online. This novel study aims to analyze skin cancer content on TikTok.

Methods:
A total of 600 videos were collected from two queries for #skincancer, encompassing Skin Cancer Awareness Month. Two authors categorized videos by content and type. Educational videos were evaluated using PEMAT, a validated tool.

Results:
Among 338 included videos, 21.3% presented medical content with a focus on skin cancer. Only 10% of videos concerned squamous cell carcinoma. 28.1% of videos aimed to raise awareness, mainly by recommending sunscreen and physician skin exams. Clothing and hats were rarely suggested. Photoprotection videos were viewed 7.6 times more than others ($p<0.001$). There were significantly more medical and awareness videos posted during May, Skin Cancer Awareness Month ($p = .02$). While 82.4% of the sample had healthy or neutral messaging, 18.6% of videos using #skincancer were actually pro-tanning, most commonly via tanning beds. There was a trend for flaunting risky behaviors on TikTok, with many users even captioning their tanning videos with "skin cancer." Among the 49 (14.5%) educational videos, average PEMAT scores were 79.6% and 53.1% for understandability and actionability, respectively. The inferior actionability score is due to 41% of videos neglecting to provide a single measure consumers could take towards the prevention or detection of skin cancer. Common issues included not breaking down actions into steps, difficult to read text, and unclear photographs.

Conclusions:
Given the substantial amount of non-educational and even risky content on TikTok, high quality educational videos promoting actionable, protective behaviors against skin cancer are warranted. To specifically combat the extensive tanning bed use and misinformation on TikTok, dermatologists should create more awareness and photoprotection videos, which also receive greater views.

Learning objectives:
1. Enumerate the interventions for skin cancer prevention that are most frequently recommended on TikTok.
2. Describe the impact of the Skin Cancer Awareness Month campaign on the skin cancer content posted on TikTok.
3. Make recommendations regarding video style and content for dermatologists active on TikTok.

Takeaway Message:
The is a significant amount of low-quality and even dangerous skin cancer content on the social media app TikTok.

Understanding Spatiotemporal Principles of Epidermal Stem Cell Differentiation in Live Mice

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Introduction:
Our bodies shed and replace 3 billion skin cells on a daily basis. This remarkable regenerative capacity is due to the activity of epidermal stem cells, which continually generate a supply of new differentiating cells to replace those that are lost. Surprisingly, we still know very little about when epidermal stem cell differentiation starts, how long it takes, and how it occurs in the right places and at the right times to maintain the integrity and barrier functions of the skin.

Methods:
Because epidermal stem cell differentiation is a highly dynamic process, it has been difficult to interrogate with traditional static approaches. Here, we have combined insights from single cell RNA sequencing with 2-photon intravital imaging, allowing us to visualize the early steps of stem cell differentiation in the intact skin of living adult mice.

Results:
Single cell RNA sequencing demonstrated that differentiating stem cells transit through a continuum of transcriptional changes, with upregulation of differentiation genes preceding downregulation of typical stemness genes. By focusing on one of these early markers of differentiation, Keratin 10, we established a fluorescent reporter system that allowed us to watch the stem cell differentiation process, from start to finish, in real time. We found that cells commit to differentiation several days before they migrate out of the stem cell layer. During this time window, they remain intermingled with their undifferentiated neighbors and remain capable of dividing in response to local changes in cell density, a behavior that was previously thought to be limited to bona fide stem cells. Finally, when we blocked the proliferative capacity of differentiating cells, we found that nearby stem cells compensated by accelerating their rates of both division and differentiation to maintain the architecture and function of the epidermis.

Conclusions:
Our results reveal that epidermal stem cell differentiation is a gradual and continuous process that is flexible to the local needs of the tissue, paving the way for future understanding of how the differentiation program adapts in the context of injury and disease.

Learning objectives:
1. Epidermal stem cells 2. Stem cell differentiation 3. Lineage tracing 4. Intravital imaging

Takeaway Message:
Instead of a linear and carefully choreographed process, epidermal stem cell differentiation is a meandering journey that is controlled by inputs from the local environment.

Fibrillin-1 is Required for The Development and Homeostasis of Adipose Tissue

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Introduction:
Fibrillin-1 is present in various tissues like skin, and adipose tissue, where it assembles into bead-on-the-string microfibrils. Mutations in fibrillin-1 lead to connective tissue disorders, including Marfan syndrome, stiff skin syndrome, and others. For Marfan syndrome, the subcutaneous adipose tissue is often severely affected. These patients are frequently lipodystrophic. However, a significant population of these patients is overweight. This points to a differential role of fibrillin-1 during the development and maintenance of subcutaneous tissue.

Methods:
We have developed a novel adipose tissue-specific fibrillin-1 knockout mouse model with deleted fibrillin-1 only in mature adipocytes (Fbn1-AKO). To elucidate the downstream pathways, we used primary mesenchymal stem cells from bone marrow (BM-MSCs) and from adipose tissue (ASCs) harvested from Fbn1-AKO and controls.

Results:
The weight of white adipose tissue from Fbn1-AKO mice was significantly reduced compared to controls in both 16- and 30-weeks old mice. The histological staining of subcutaneous adipose tissue harvested from Fbn1-AKO mice showed larger numbers of smaller adipocytes compared to controls. Isolated BM-MSCs and ASCs resulted in a significant reduction of differentiated adipocytes, which correlated with the in vivo data. The exogenous addition of fibrillin-1 subfragment containing an integrin-binding RGD motif significantly reduced the level of adipogenesis. Contrary, a subfragment with an inactive RGA motif did not affect adipogenesis. These data provide evidence that fibrillin-1 is an important mediator of adipogenesis.

Conclusions:
Fibrillin-1 knockout from mature adipocytes in Fbn1-AKO mice leads to a lipodystrophic phenotype. The data indicate that the RGD containing integrin-binding site plays a role in fibrillin-1 mediated adipogenesis at the mature stage.

Learning objectives:
1. To understand the consequences of a fibrillin-1 deficiency in mature adipose tissue.
2. To determine the potential receptor of fibrillin-1 controlled adipogenesis.

Takeaway Message:
Fibrillin-1 is important for the homeostasis of adipose tissue. RGD binding motif may be involved in regulating this adipocyte differentiation.

Ex Vivo Gene Therapy and Autologous Bilayered Skin Substitutes as A Potential Treatment of Recessive Dystrophic Epidermolysis Bullosa Skin Wounds

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Introduction:
Recessive dystrophic epidermolysis bullosa (RDEB) is a rare genodermatosis (3/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), leading to defective anchoring fibrils at the dermo-epidermal junction (DEJ) and a loss of adhesion between the epidermis and the dermis.

Methods:
RDEB cells were transduced with a gamma-retroviral self-inactivating COL7A1 vector. Transduction efficiency and stem keratinocyte content were assessed through flow cytometry and colony forming efficiency. These cells were used to produce skin substitutes using the self-assembly approach.

Results:
The efficiency of the transduction enhancers polybrene and EF-c was assessed on three RDEB fibroblast populations and showed that EF-c was twice as efficient as polybrene to increase transduction whilst it did not affect fibroblast proliferation and keratinocyte stem cell content whereas polybrene use led to a decrease in both. Using our viral vector and EF-c, Col7 production was restored in up to 55% of fibroblasts and 75% of keratinocytes. In vitro, 60% of keratinocyte expressing keratin 19, an epithelial stem cell marker, were transduced and maintained in the autologous bilayered skin substitutes. Moreover, mechanical peeling tests showed that substitutes produced with transduced fibroblasts or both transduced fibroblasts and transduced keratinocytes had a DEJ adhesion strength comparable to healthy controls. In vivo, grafting on athymic mice for up to 1 year showed that Col7 production and stem cells were maintained overtime.

Conclusions:
We developed an efficient method to restore Col7 production in RDEB cells which led to a long-term restoration of Col7 in skin substitutes. This is a promising approach towards a treatment for RDEB skin lesions.

Learning objectives:
1. Recessive dystrophic epidermolysis bullosa: etiology, clinical observations and standard of care
2. Gene therapy strategy for the treatment of recessive dystrophic epidermolysis bullosa
3. Self-assembly approach for the production of graftable skin substitutes

Takeaway Message:
The progress of gene therapy, particularly in terms of safety, and the advances in tissue engineering now allows researchers to produce genetically modified autologous bilayered self-assembled skin substitutes that could be grafted on RDEB patients for the treatment of wounds.

Fibulin-4 and latent transforming growth factor-β binding protein-4 interact with syndecans to regulate skin elastogenesis

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Introduction:
Elastic fibers provide elasticity as well as a growth factor repository to skin and these fibers are formed by the process of elastogenesis, which involves key matrix proteins such as fibulin-4 (FBLN4) and latent TGF-β binding protein-4 (LTBP4). Cells interact with FBLN4 and LTBP4, but the associated mechanism and cell receptors involved remains to be determined and are the objectives of the present study.

Methods:
Normal skin fibroblasts (NSF) and vascular smooth muscle cells (SMC) were employed as elastogenic cell culture models. Cell interaction to recombinant FBLN4 and LTBP4 was analyzed through cell binding assay. siRNA knockdown (KD) experiments and protein-protein interaction studies were performed to identify the target cell receptors. The effect of FBLN4 and LTBP4 on cell contraction and elastic fiber formation was explored using contractility inhibitor in collagen-gel contraction assays and indirect immunostainings.

Results:
NSFs and SMCs bound strongly to FBLN4 and LTBP4 and the interactions led to increased elastic fiber formation without alterations of the tropoelastin gene expression levels. FBLN4 exclusively interacted as multimers and the multimerization sites were mapped to cbEGF4-5 and the C-terminal domain. Two novel cell interaction epitopes were identified on FBLN4, located in cbEGF2-3 and the C-terminal domain. Additionally, two cell interaction sites on LTBP4 were mapped to the N- and C-terminal halves. Cell interactions with FBLN4 and LTBP4 significantly enhanced focal adhesion (FA) formation and cell contraction, with a significant increase of activated Erk1/2 and RhoA. siRNA KD of syndecan (SDC)-2 or -3 prevented NSF interaction with FBLN4, whereas only SDC-3 KD abolished the interaction with LTBP4. KD of SDC-2 or -3 in NSFs also resulted in compromised elastic fibres. Inhibition with blebbistatin significantly reduced elastic fiber formation.

Conclusions:
The results demonstrate that FBLN4 and LTBP4 cell interactions via (SDC)-2 or -3, promote elastogenesis by enhancing FA formation and cell contractility through Erk1/2 and RhoA activation.

Learning objectives:
1. To analyse cell interactions with elastogenic proteins FBLN4 and LTBP4 and map the interaction sites on these molecules.
2. To identify the cell receptors involved in FBLN4 and LTBP4 cell interactions.
3. 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 FA formation and cell contractility. Inhibition of the identified mechanism leads to compromised elastic fibres. FBLN4 and LTBP4 mediated cell interactions are therefore essential for proper elastogenesis in skin.

Comparison of Two Extraction Methods of Bulge-Derived Keratinocytes of The Hair Follicle: Explant Method and Enzymatic Digestion

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Introduction:

The hair follicle bulge is a niche for stem keratinocytes which can differentiate into epidermis and hair lineage. Even if reconstructed skin substitutes produced by the self-assembly approach have several advantages, skin appendages are lacking. To study the potential of bulge-derived keratinocytes to differentiate into hair follicles within skin substitutes, keratinocytes from the bulge must be extracted. As the commonly used explant culture is slow and offers a low yield, an enzymatic approach is proposed. We hypothesize that trypsin digestion of microdissected bulges would provide a higher yield of stem keratinocytes than the explant technique. The objective of this study was to optimize the isolation procedure of keratinocytes from the bulge to obtain cultures enriched in bulge-derived stem keratinocytes.

Methods:

Biopsies from adult scalps were incubated with thermolysin to separate the dermis from the epidermis. Bulge were separated by microdissection and cultured either by explant or after trypsin digestion. In parallel, simultaneous extraction of epidermal and hair keratinocytes (total extraction) was conducted. These populations were compared.

Results:

After the first passage, bulge-derived keratinocytes extracted by digestion were in higher quantity and showed a shorter doubling time than those of the explant method. Furthermore, a higher number of colonies was obtained, suggesting that the digestion method enriches the culture with stem keratinocytes.

Conclusions:

In conclusion, the dissociation of bulge using trypsin to extract bulge-derived keratinocytes is a faster and easier method compared to the explant technique. Reconstructed skin substitutes will be produced with these cells to evaluate their potential for follicular differentiation.

Learning objectives:

1. Understand the importance of hair follicles in reconstructed skin
2. Compare bulge-derived keratinocyte extracted by different methods
3. Optimize the extraction method of bulge-derived keratinocytes

Takeaway Message:

The enzymatic digestion method yields more bulge-derived keratinocytes than the explant method and enriches the population in hair stem keratinocytes.

Generation of Autologous Mesenchymal Stromal Cells from an Accessible Tissue Source: The Plucked Hair Follicle

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Introduction:
Autologous, personalized stem cell therapies offer the potential to repair and regenerate damaged tissue. However, these therapies come with challenges including acquiring an appropriate cell source, the creation of defects when harvesting cells for the therapy, costs, and extended timelines in creating cell therapies. Recent attention has been given towards finding a tissue source that can mitigate many of these burdens. The human hair follicle acts as a reservoir of multiple cell types, with the potential of being used as starting material in cell therapies. Hair follicles can be collected with a non-invasive (plucking) procedure. The outer root sheath of a hair follicle predominantly contains keratinocytes whereas the dermal papilla contains mesenchymal-like cells.

Methods:
Hair follicles were plucked and cryopreserved from a diverse group of participants. The follicles were outgrown using a feeder-free system. A subpopulation of cells was further cultivated in 15% FBS media. The cells were expanded, characterized and differentiated into adipocytes, osteocytes, chondrocytes and neurons.

Results:
Subpopulation of cells cultivated from cryopreserved plucked hair follicles exhibit key characteristics of mesenchymal stromal cells. They are adherent to plastic and readily expandable. The cells express typical MSC immunophenotype as showcased by both flow cytometry and immunohistochemistry. Alizarin red staining shows abundant calcium deposits in differentiated osteocytes while a collagen-rich extracellular matrix is observed in the differentiated cartilage tissue with high expression of Collagen II. Preliminary Secretome analysis of the cells show high amounts of components which promote scarless wound healing and tissue repair such as fibronectin and VEGF.

Conclusions:
Mesenchymal stromal cells derived from plucked hair follicles have immense therapeutic potential. The ease of collection and transport of plucked hair follicles allows for the scalable production of autologous MSCs across multiple participants. They can be used to create bone, fat, cartilage and neurons allowing for the restoration of functional cell types lost in human disease.

Learning objectives:
Participants will learn about: The anatomy and subpopulations of cells found in the hair follicle and thus its utility as a starting tissue source in regenerative medicine; The Acorn method for collection, transport and cryopreservation and its benefits; The methods of isolation and expansion of mesenchymal stromal cells from the plucked hair follicle and their various therapeutic applications.

Takeaway Message:
Mesenchymal stromal cells derived from plucked hair follicles have immense therapeutic potential. The ease of collection and transport of the follicles allows for the scalable production of autologous MSCs. MSC-derived exosomes also provide a cell free approach in tissue regeneration.

The Superior Angiogenic Potential of Nano-Adipose Tissue Compared with Stem Cell-Derived Small Extracellular Vesicles to Repair 3rd-Degree Burn Injuries

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Introduction:
Proper healing of extensive burn injuries remained to be a major health care challenge. Stem cell therapy and regenerative medicine have offered new possibilities. In the present study, we proposed a distinct therapeutic application of adipose tissue and small extracellular vesicles isolated from menstrual blood-derived mesenchymal stem cells (MenSC-sEVs), as two promising regenerative sources, to enhance the burn injury repair.

Methods:
Nano-fat was prepared from the inguinal fat depot isolated from BALB/c mice. sEVs were isolated from menstrual blood-derived mesenchymal stem cells, and a full-thickness, third-degree, scald burn was created on the back of the mouse using 90oC hot water exposure for 10 seconds. Nano-fat and sEVs transplantation was performed subcutaneously on day 3 post-burn. The healing of burn injury was evaluated for 28 days.

Results:
Nano-fat and sEVs were both capable to enhance wound closure and increase neoangiogenesis. However, Nano-fat was also effective to accelerate the formation of granulation tissue and boost the thickness of the epithelial layer of newly formed skin.

Conclusions:
This study elucidates the effectiveness of Nano-fat and MenSC-sEVs to hasten the healing of third-degree scald burn injury. Nano-fat and MenSC-sEVs may establish a promising therapeutic approach for facilitating the repair of a third-degree full-thickness skin burn injury.

Learning objectives:
1. To find out if the whole adipose tissue as a source of regenerative cytokines can be a remedy for acute skin injury
2. To analyze the proangiogenic potentials of whole adipose tissue
3. To examine the effect of treating burns with whole adipose tissue on the development of new tissue
4. To compare the effectiveness of whole adipose tissue versus stem cell-derived small extracellular vesicles in healing burns

Takeaway Message:
1. The application of whole adipose tissue hasten the wound closure of 3rd degree burns
2. The whole adipose tissue enhances angiogenesis at the site of burn injury
3. Burn wounds treated with the adipose tissue reach the maximum amounts of granulation tissue during the first day's post injury
4. Adipose tissue effectively enhances the healing of burns even at a higher degree of efficiency as compared with stem cell-derived sEVs.

Improving Self-Assembled Skin Substitutes Pigmentation with Melanogenic Physiological Factors

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Introduction:
Severely burned patients in lack of donor sites for the harvesting of autografts can be treated with Self-Assembled Skin Substitutes (SASSs). However, pigmentation is not fully restored after SASS grafting, resulting in local pigmentation defects in treated patients. These pigmentation defects are probably caused by the dilution of melanocytes in epithelial cell cultures that are used to produce the epidermal part of the SASS. It has already been demonstrated in preclinical study that a supplementation of SASS with melanocytes improve pigmentation. However, the technique used is time-consuming and the culture medium used in these in vitro experiments contains carcinogenic factors. Therefore, this option cannot be used in clinic. As an alternative, we hypothesized that the supplementation of the SASS culture medium with melanogenic physiological factors, such as Fibroblast Growth Factor-2 (FGF-2) and/or other factors secreted by keratinocytes could increase melanocyte growth and/or melanogenesis and improve SASS pigmentation.

Methods:
We evaluated the role of FGF-2 in a dose-dependent manner on melanocyte prolifieration and melanogenesis. Then we evaluated the role of FGF-2 on the SASS model with immunofluorescence and histological analyzes. We also evaluated the role of keratinocyte conditioned media on melanocyte proliferation and melanogenesis.

Results:
Our preliminary results suggest that FGF-2 promotes melanocyte proliferation in 2D culture and could improve melanocyte proliferation in the SASS model without stimulating melanogenesis. They also indicate that keratinocyte conditioned media stimulates melanocyte proliferation without stimulating melanogenesis.

Conclusions:
The maintenance of melanocytes in SASS could be possible using FGF-2 or other physiological factors supplementation. Future experiments will aim to confirm these results, to determine whether the combined addition of melanogenic factors can induce melanin production and to characterize the composition of the keratinocyte conditioned media.

Learning objectives:
1. Understand the cause of pigmentation defects in burned patients treated with SASS.
2. Understand the importance of restoring the pigmentation barrier after burn.
3. Learn about new approaches to stimulate melanocyte growth and melanin synthesis.

Takeaway Message:
Physiological factors supplementation such as FGF-2 stimulates melanocyte proliferation and could improve SASS pigmentation.

Skin Research Group *of* Canada 2022
Poster Presentation Abstracts

Skin Research Group *of* Canada 2022
Posters List

Clinical Skin Research

CSR22-01	The Efficacy of Off-Label Use of Omalizumab for Solar Urticaria: A Systematic Review. **Jeffrey Toy,** Faculty of Medicine, University of British Columbia
CSR22-02	Pityriasis Lichenoides Following SARS-CoV-2 Infection/ Vaccination. **Aileen Feschuk,** Memorial University of Newfoundland
CSR22-03	Allogeneic Neonatal Skin Fibroblasts Do Not Trigger Acute Immune Reactions Compared to Allogeneic Adult Skin Fibroblasts. **Brice Magne**, Centre de Recherche en Organogénèse Expérimentale de l'Université Laval/LOEX
CSR22-04	Patch Testing Delivery: A Cross-Sectional Inquiry into The Experiences of Patch Testing Dermatologists. **Aysha Lukmanji,** University of Calgary
CSR22-05	Complications of Body Piercings: A Systematic Review. **Santina Conte,** Faculty of Medicine and Health Sciences, McGill University
CSR22-06	Clinical Features and Treatment of Sebaceous Carcinoma: A Systematic Review. **Thomas Sabljic,** Department of Laboratory Medicine and Pathobiology, University of Toronto
CSR22-07	Cognitive Behavioral Therapy in Primary Dermatologic Disorders: A Scoping Review. **Dong Goo Lee,** Faculty of Medicine, University of British Columbia
CSR22-08	Chilblain-like Lesions (CLL) Coinciding with the SARS-CoV-2 Pandemic: A Systematic Review. **Samantha Starkey,** Faculty of Medicine, University of British Columbia
CSR22-09	Photography and Image Acquisition in Dermatology: A Scoping Review. **Nadia Kashetsky,** Faculty of Medicine, Memorial University of Newfoundland
CSR22-10	Efficacy of N-acetylcysteine (NAC) in Trichotillomania (Hair-Pulling Disorder), Skin-Picking Disorder and Onychophagia (Compulsive Nail-Biting): A Systematic Review. **Nadia Kashetsky,** Faculty of Medicine, Memorial University of Newfoundland
CSR22-11	Infantile Hemangiomas Involving the Ear and Periauricular Area: A Retrospective Study of Patients Referred to a Tertiary Clinic. **Maxine Joly-Chevrier,** Faculty of Medicine, Université de Montréal

Education

EDU22-01 Learning Practical Dermatology Skills Through Animated Vignettes: An Effective Medical School Educational Intervention to Support the Dissemination of National Guidelines.
Harry Chaocheng Liu, University of British Columbia

Wound Healing Fibrosis Regeneration

WHRG22-01 Epidemiology of Severely Burned Patients Requiring Autologous Skin Substitutes.
Ludivine DUBOURGET, LOEX, Centre de recherche du CHU de Québec-Université Laval

WHRG22-02 Compassionate Use of Allogeneic Self-Assembled Skin Substitutes for Recessive Dystrophic Epidermolysis Bullosa Wound Closure.
Martin Barbier, LOEX, CHU de Québec

WHRG22-03 Wound Healing: Exploring Mechanisms Whereby a New Drug Ag373K Augments VEGFA Secretion and Keratinocyte Migration.
Vida Maksimoska, University of Toronto, Institute of Medical Sciences and St Micheals Hospital

Inflammatory Skin Diseases

INFSD22-01 The Endocannabinoid System of Psoriatic Tissue-Engineered Skin Models.
Andrea Tremblay, Université Laval

INFSD22-02 In Vitro Modeling by Tissue Engineering of The Impact of Sensory Innervation in Psoriasis.
Rémy Pépin, Faculty of Medicine, Université Laval

INFSD22-03 Health-Related Quality of Life (HRQL) In A Canadian Atopic Dermatitis (AD) Cohort.
Alexandra Yacovelli, McGill University Health Centre, Faculty of Medicine & Health Sciences, McGill University

Skin Cancer

SC22-01 Skin Colour and Perceptions of Sun Exposure Among Residents of Atlantic Canada: A Preliminary Analysis.
Sauliha Alli, Temerty Faculty of Medicine, University of Toronto

SC22-02 Investigating The Evolution of Sun Protection Habits of The Canadian Population Living in The Atlantic Provinces.
Jonathan Lebeau, Division of Experimental Medicine, Department of Medicine, Faculty of Medicine and Health Sciences, McGill University

SC22-03 Skin Surveillance After a Previous Cutaneous Melanoma Diagnosis: A Scoping Review.
Leah Johnston, University of Calgary

SC22-04 Role of Soluble CD109 In Squamous Cell Carcinoma (SCC) Progression.
Varsha Reddy Durgempudi, McGill University

SC22-05 Transitioning To Pegylated Interferon for The Treatment of Cutaneous T-Cell Lymphoma: Meeting the Challenge of Therapy Discontinuation and A Proposed Algorithm.
Selena Osman, University of Calgary

SC22-06	Evaluating the Impact of BRAF Reflex Mutation Testing on the Management of Melanoma, Lung, and Colorectal Cancers in Canada. **Sera Whitelaw,** Faculty of Medicine and Health Sciences, McGill University
SC22-07	Skin Cancer Risk Factors, Sun Safety Behaviors and Melanoma Concern in Atlantic Canada: A Comprehensive Survey Study. **Francois Lagace,** Division of Dermatology, Faculty of Medicine, McGill University
SC22-08	Translational Landscape of High-Risk Basal Cell Carcinoma. **Misha Fotovati,** Faculty of Medicine, McGill University
SC22-09	The Evolving Trends of Artificial Intelligence Skin Cancer Articles Published in Dermatology Journals. **Maxine Joly-Chevrier,** Faculty of Medicine, Université de Montréal
SC22-10	Comparison of Basal Cell Carcinoma Posts, Comments and Authors Between Reddit and Quora Forums. **Maxine Joly-Chevrier, Faculty of Medicine, Université de Montréal**
SC22-11	Melanoma Survival in Canada: A National Population-Based Study Elucidating Healthcare and Socioeconomic Barriers Affecting Patient Care. **Santina Conte,** Faculty of Medicine and Health Sciences, McGill University
SC22-12	Gene-Environment Analyses in a UK Biobank Cohort of Four Skin Cancers Identify Synergistic Contributions of DNA- And Environment-Based Factors. **Richie Jeremian,** Faculty of Medicine & Health Sciences, McGill University
SC22-13	Evaluating The Expression and Function of Meict Gene, Disrupted Meiotic Cdna1 in Head and Neck Squamous Cell Carcinoma. **Raman Preet Kaur Gill,** McGill University

Basic Sciences

BS22-01	Characterization And Functional Relevance of Microfibrillar-Associated Protein 4 (MFAP4) In Elastic Fiber Formation. **Dieter Reinhardt,** McGill University
BS22-02	Efficient Generation of Induced Pluripotent Stem Cell Derived Mesenchymal Stem Cells from A Non-Invasive, Accessible Tissue Source - The Plucked Hair Follicle. **Amatullah Fatehi,** Acorn Biolabs and University of Toronto

Poster Session: Clinical Skin Research

The Efficacy of Off-label Use of Omalizumab for Solar Urticaria: A Systematic Review

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Introduction:
Solar urticaria is a rare IgE-mediated photodermatosis with limited management options. Omalizumab, an anti-IgE antibody approved for chronic idiopathic urticaria, has been used as an off-label therapy for patients with refractory solar urticaria.

Methods:
We conducted a systematic review to evaluate the efficacy of omalizumab for solar urticaria using Medline, Web of Science and Pubmed databases.

Results:
332 studies were screened and 43 were included for analysis. We identified 100 total solar urticaria patients with a mean age of 40 (SD 16). Non-pediatric omalizumab doses ranged from 150-600 mg every 2-4 weeks and treatment durations ranged from 1-86 months. 74% of patients were reported to have complete clinical response and 10% partial response to omalizumab therapy. 64% of patients had pre- and post-treatment phototesting conducted. Within this group, 97% of patients (n=62) had reduced minimal urticarial dose (MUD) thresholds to visible light, ultraviolet (UV) B, or UV-A before treatment, with improvement seen in 76% of patients (n=56) after therapy. 6% of patients had Dermatology Life Quality Index assessed showing improvement (mean pre and post-treatment: 22 and 3 respectively). 13% of all patients relapse following therapy tapering or discontinuation. Adverse events were reported in 4% of patients.

Conclusions:
Refractory solar urticaria has a limited number of treatment options and omalizumab therapy is well-tolerated with a high response rate. There was large variability between studies for treatment dosing, duration, definition of clinical response, use of objective scales and phototesting. Standardization to include outcome measures and phototesting will enable better assessment of treatment efficacy.

Learning objectives:
1. Recognize that omalizumab is used in the off-label treatment of solar urticaria
2. Identify that omalizumab is relatively safe and efficacious
3. Identify the importance of phototesting and objective scales for patients with solar urticaria

Takeaway Message:
Omalizumab is an effective off-label therapy for refractory urticaria. Incorporation of standardized metrics in further research will improve assessment of treatment efficacy.

Pityriasis Lichenoides Following SARS-CoV-2 Infection/ Vaccination

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Introduction:
Pityriasis lichenoides (PL) is a dermatological condition of unknown etiology with subtypes including pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC). Recently, there have been reports of PL following SARS-CoV-2 infection and vaccination. This review comprehensively summarizes these reports in order to guide diagnosis and management of this condition.

Methods:
PubMed, Embase, and Web of Science were thoroughly searched for relevant articles. Following the PRISMA guidelines, 13 articles, consisting of 14 cases of PL following SARS-CoV-2 infection/ vaccination were included in the review.

Results:
Average age of those affected was 41.4 years, and majority of cases occurred in males (64.3%). Majority of the cases were subtype PLEVA (71.4%) and were diagnosed using biopsy (92.9%). Majority occurred following vaccination (64.3%), most commonly Pfizer-BioNTech (80.0%), with 40.0% following the first vaccine dose, 40.0% following the first vaccine dose with exacerbation after the second, and 20.0% following the second dose. Mean latency period was 13.8 days and the most commonly affected area was the limbs (78.6%). Many different treatment methods and follow-up periods were employed. However, 12/14 patients (85.7%) had either marked improvement or complete resolution of lesions by the time of case report publication. Cases' scores on Naranjo's Adverse Drug Reaction Probability Scale (ADRPS) averaged 6.3 and ranged from 5.0-8.0.

Conclusions:
This review cannot definitively determine causality, but according to Naranjo's Adverse Drug Reaction Probability Scale, the likelihood of causality between SARS-CoV-2 and PL is "probable". The review aims to highlight the importance of taking a SARS-CoV-2 history of a patient presenting with PL, and help guide the recognition, diagnosis, and management of this rare dermatological condition.

Learning objectives:
By the end of this presentation listeners should know:

1. The two most common types of pityriasis lichenoides
2. The clinical characteristics of pityriasis lichenoides
3. Naranjo's Adverse Drug Reaction Scale suggests SARS-CoV-2 infection/ vaccination is a "probable" cause of pityriasis lichenoides
4. To take a SARS-CoV-2 infection/vaccination history in pityriasis lichenoides
5. Possible treatment options for pityriasis lichenoides

Takeaway Message:
Naranjo's Adverse Drug Reaction Probability Scale suggests SARS-CoV-2 is a "probable" cause of pityriasis lichenoides. Therefore, this article highlights the importance of clinicians taking a thorough SARS-CoV-2 infection/ vaccination history for new or exacerbated pityriasis lichenoides.

Allogeneic Neonatal Skin Fibroblasts Do Not Trigger Acute Immune Reactions Compared to Allogeneic Adult Skin Fibroblasts

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Introduction:
Upon severe injuries, skin grafts can be necessary to keep victims alive. However, autografts are not always available and allogeneic skin grafts only offer a temporary solution, since allogeneic keratinocytes are rejected within two to three weeks. An alternative is the production of skin substitutes from patient's own cells. This method has been successfully used by our group to treat major burn patients across Canada. However, skin substitute production is time consuming, and these patients are likely to die from infections before even receiving their first grafts. In order to reduce production times, we are envisioning a semi-allogeneic approach, in which the dermis would be made from allogeneic skin fibroblasts and the epidermis from autologous keratinocytes. The aim of the present study is to investigate the effects of allogeneic skin fibroblasts on host immune responses.

Methods:
Fibroblasts and peripheral blood mononuclear cells (PBMCs) were isolated from healthy human donors. Allogeneic fibroblasts were co-cultured with mononuclear cell derived-dendritic cells (mo-DCs) and T cells, both derived from donors' PBMCs. Phagocytic activity of mo-DCs and proliferation of T cells were assessed by immunofluorescence and flow cytometry. Allogeneic dermal substitutes were subcutaneously implanted into immunocompetent balb/c mice. Cytokine and immunoglobulin expression were assayed by ELISA.

Results:
The phagocytic activity of mo-DCs and the proliferation of T cells were reduced in the presence of allogeneic neonatal skin fibroblasts compared to adult skin fibroblasts. This effect was mediated by the soluble factors secreted by allogeneic neonatal skin fibroblasts. Long-term follow-up study in mice showed that allogeneic dermal matrices produced trigger humoral responses after implantation.

Conclusions:
These data indicate that allogeneic neonatal skin fibroblasts do not induce acute immune responses, but can trigger mild humoral responses after long-term implantation. More studies are necessary to determine whether these neonatal allogeneic cells could be used clinically.

Learning objectives:
1. Learn about immune responses to allotransplantation;
2. Familiarise with in vitro and in vivo models to study immune responses;
3. Gather information about neonatal skin fibroblasts.

Takeaway Message:
Neonatal skin fibroblasts are less immunogenic than adult skin fibroblasts.

Patch Testing Delivery: A Cross-Sectional Inquiry into The Experiences of Patch Testing Dermatologists

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Introduction:
Allergic contact dermatitis (ACD) is a prevalent condition of which up to 20% of the global population suffers. Patch testing is the gold standard procedure to diagnose and identify a causative agent of ACD. Despite its utility, the patch testing process is lengthy and costly. The purpose of this study is to investigate the dermatologist experience of patch testing including wait times and identifying barriers to providing patch testing services.

Methods:
A 15-item electronic survey was developed by the project team and sent via email to staff physician members of the American Contact Dermatitis Society (ACDS).

Results:
A total of 39 ACDS members responded to the survey. All respondents practiced in the USA. On average, patch testing was performed on 5 patients per week. The mean wait time for general vs. urgent referrals were 2 months and <1 month respectively. The greatest barriers to providing patch testing were: interest (25%), overhead and remuneration (21.6%), and experience (20.47%). Respondents identified higher remuneration (42.86%), decreased overhead costs (25.40%) and more training for patch testing (14.29%) as areas where patch testing provision could be improved. Respondents also identified lower costs (36.11%), reduced wait times (36.11%), and rural patch testing sites (13.89%) as areas where patch testing could be improved for patients.

Conclusions:
Overall, our study describes that cost is a major barrier to the provision and receipt of patch testing services in the United States.

Learning objectives:
1. Cost is a major barrier to providing patch testing services.
2. Patch testing is a time and resource-consuming process for dermatologists.
3. Future research aimed at lowering costs may improve the delivery and efficiency of patch testing services.

Takeaway Message:
Efforts to reduce the cost and wait times for patch testing would benefit dermatologists and patients.

Complications of Body Piercings: A Systematic Review

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Introduction:
The practice of body piercing has been present in many cultures around the world for centuries, whether for religious or spiritual reasons or as a form of self-expression. In recent years, body piercings have become increasingly popular in both sexes, with the most common sites being the ears, mouth, nose, eyebrows, nipples, navel and genitals. Common problems following piercing include infections, keloid formation, allergic contact dermatitis, site deformation and tooth fractures. However, despite the widespread utilization of piercings, a comprehensive literature review of their complications is lacking.

Methods:
A literature search was conducted utilizing Embase, MEDLINE and PubMed databases in accordance with PRISMA guidelines.

Results:
In total, 338 articles summarizing 29,341 complications of both cutaneous and non-cutaneous piercings were identified. Complications were reported in patients with a mean age of 28.3 years, and 77% of individuals included in our review were female. Overall, the most common reported complications were inflammatory responses (n=6493), infections (1861), keloids (n=812), edema/swelling (n=591), increased incidence of hepatitis (n=5067) and site sensitivity (n=11,110). Piercing location was reported in 11,908 patients, with the ears (n=7675), tongue (n=1695), navel (n=496) and nose (n=403) being the most common sites. Finally, the most common treatment modalities were surgical excision (n=467), antibiotics (n=590), piercing removal (n=237) and steroid injections (n=126).

Conclusions:
With piercings becoming increasingly popular, it is of utmost importance that clinicians recognise associated complications and are aware of available and commonly employed treatment modalities.

Learning objectives:
1. Clinicians should be aware of the variety of complications associated with both cutaneous and non-cutaneous piercings, given their increasing popularity.
2. Inflammatory responses, infections, keloids and site sensitivity are among the most commonly reported complications associated with piercings.
3. The most common treatment modalities include surgical excision, antibiotics, piercing removal and steroid injections.

Takeaway Message:
Inflammatory responses, infections, keloids and site sensitivity are among the most commonly reported complications associated with ear piercings, and are most commonly treated with surgical excision, antibiotics, steroid injections and through piercing removal.

Clinical Features and Treatment of Sebaceous Carcinoma: A Systematic Review

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Introduction:
Sebaceous carcinoma is a rare, but potentially aggressive malignancy, capable of regional and distant metastasis. Often misdiagnosed as benign entities, up to 75% of all sebaceous carcinomas present as periocular tumours arising from sebaceous glands. Extraocular sebaceous carcinomas commonly arise on the head and neck, have an indeterminate origin, and behave differently than periocular sebaceous carcinomas. Patients diagnosed with sebaceous carcinoma should undergo screening for Muir-Torre syndrome (MTS), a hereditary cancer syndrome associated with sebaceous neoplasms, and other internal malignancies.

Methods:
A literature search was conducted utilizing Embase, MEDLINE and PubMed databases in accordance with PRISMA guidelines.

Results:
A total of 688 articles identifying 9985 cases of sebaceous carcinoma were identified. Overall, 71% (n=7097) were periocular sebaceous carcinoma, while 29% (n=2888) were of extraocular origin. The most common extraocular sites were the face (15%, n=1477), neck (5%, n=491), and trunk (3%, n=267). Overall, 66.4% of cases were reported in males. There was a significant difference ($p<0.001$) in the mean age of patients with sebaceous carcinoma and MTS (55.8 years), compared to those without MTS (63.2 years). Surgical excision (wide local excision, Mohs micrographic surgery, and orbital exenteration) is the most common treatment modality for sebaceous carcinoma, however many studies report the use of radiotherapy, chemotherapy, and cryotherapy.

Conclusions:
Sebaceous carcinoma is a potentially aggressive neoplasm, often presenting with clinical features associated with benign entities. It is important for clinicians to recognize the diverse presentations of sebaceous carcinoma to ensure these cases are diagnosed and treated early.

Learning objectives:
1. To summarize the distinction between periocular and extraocular sebaceous carcinoma
2. To review features of sebaceous carcinoma in individuals with MTS compared to individuals without MTS
3. To provide an overview of the most common sites of sebaceous carcinoma, including extraocular sites
4. To summarize reported treatments for sebaceous carcinoma

Takeaway Message:
Sebaceous carcinoma is an uncommon neoplasm with a potentially aggressive clinical course, occurring at an earlier age in individuals with MTS than without. Surgical excision is the mainstay of treatment, although roles for chemotherapy, radiotherapy, and cryotherapy have been reported.

Poster Session: Clinical Skin Research

Cognitive Behavioral Therapy in Primary Dermatologic Disorders: A Scoping Review

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Introduction:

Cognitive behavioral therapy (CBT) utilizes cognitive restructuring to correct maladaptive thoughts and behaviors. CBT interventions have demonstrated effectiveness in primary psychiatric disorders, including conditions with cutaneous manifestations such as trichotillomania. However, there is a paucity of studies comprehensively evaluating patient outcomes of CBT in primary dermatologic disorders. This study aims to fill this knowledge gap and consider the future directions for CBT use in dermatology.

Methods:

A scoping literature review was performed to summarize outcomes of CBT in all primary dermatological disorders. Medline, Embase and PsycINFO databases were searched to identify studies of dermatological conditions that incorporate CBT in disease management.

Results:

The search identified a total of 1,357 studies. Fourteen studies were included following full text review, including 6 randomized clinical trials, 3 pilot studies, and 1 clinical trial. Multiple forms of CBT were identified, including internet-based CBT, and all CBT modalities demonstrated improved objective and subjective outcomes. Atopic dermatitis (AD) (n=5), psoriasis (n=4), vitiligo (n=3), rosacea (n=1) and alopecia areata (AA) (n=1) were the dermatological conditions explored in these studies. For patients with AD, CBT led to improved severity of skin lesions, overall disease severity (ODS), quality of life (QoL), and reduced corticosteroids use and perception of disease stigma. In psoriasis, improvement in ODS, general health, QoL, self-perceived body image and decrease in pruritus, stress, and depression were found. Rosacea patients demonstrated reduced stress and social anxiety. For patients with vitiligo, self-perceived body image, self-esteem, QoL, and social anxiety were all improved. In AA, findings showed decreased hair loss, distress regarding condition, depression, improved QoL, and satisfaction.

Conclusions:

Improved biopsychosocial outcomes after CBT were demonstrated in primary dermatologic disorders such as AD, psoriasis, rosacea, vitiligo, and AA. However, the results were mixed and additional studies with larger sample sizes are needed to quantify the impact of CBT and the potential utility of internet- and app-based CBT.

Learning objectives:

1. To review the role of CBT in the management of skin disorders
2. To comprehensively summarize the available literature on use of CBT in dermatology
3. To evaluate the applicability and accessibility of CBT in an online format

Takeaway Message:

Skin disorders have significant psychiatric comorbidities and CBT has demonstrated biopsychosocial benefits in patients with primary dermatologic disorders. Further research is needed to evaluate the benefits and limitations of CBT as the current literature is sparse.

Chilblain-like Lesions (CLL) Coinciding with the SARS-CoV-2 Pandemic: A Systematic Review

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Introduction:
Chilblain-like lesions (CLL) coinciding with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been described in the literature. Previous systematic reviews suggest CLL are associated with younger age, an equal sex ratio, negative testing for SARS-CoV-2, and mild to no extracutaneous symptoms. This study aims to clarify the prevalence, clinical characteristics, resolution outcomes, and prognostic value of CLL associated with SARS-CoV-2.

Methods:
A systematic review was conducted according to PRISMA guidelines on human cases of CLL coinciding with the COVID-19 pandemic.

Results:
One hundred and twenty-eight studies, published between March 2020 and January 2022, met inclusion criteria and were summarized in this review, representing 4,982 cases of CLL. The majority of studies, 92% (n=110/119), reported cases from the first wave of the pandemic (Spring and Summer 2020). CLL were mostly reported on the feet (90%, n=2195/2429). There was a slight female predominance in reported cases (55%, n=2471/4472). Mean age was 25 years, ranging from 0 to 95 years. Most cases were not associated with extracutaneous symptoms (63%, n=1649/2636). Overall, 19% (n=347/1838) of patients tested positive for SARS-CoV-2 using PCR, serology, or tissue biopsy. In the majority, clinical course was benign with 80% (n=979/1224) of cases resolving without recurrence, and 47% (n=204/432) resolving without receiving treatment. CLL were unresolved in 7% of cases (n=91/1224) with follow up ranging from 9 to 495 days with mean 64 days. CLL recurred in 13% (n=154/1224) of cases. Mean time to recurrence was 71 days, range 5 to 196 days.

Conclusions:
This review provides a comprehensive summary of CLL associated with SARS-CoV-2. CLL occurred at a mean age of 25 years with slight female predominance. The majority had negative COVID-19 testing, no extracutaneous symptoms, and resolved without recurrence.

Learning objectives:
1. To describe the demographic features of chilblain-like lesions (CLL) associated with COVID-19
2. To review clinical characteristics of CLL associated with COVID-19, including extracutaneous symptoms and lesion topography
3. To review resolution, recurrence, and treatment outcomes of CLL associated with COVID-19

Takeaway Message:
Chilblain-like lesions (CLL) associated with COVID-19 occur at a mean age of 25 years and most cases have negative COVID-19 testing, no extracutaneous symptoms, and a benign clinical course.

Poster Session: Clinical Skin Research

Photography and Image Acquisition in Dermatology: A Scoping Review

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Introduction:
Clinical photography is essential in dermatology and has been evolving rapidly. However, a comprehensive literature review of photography in dermatology is lacking. This scoping review aims to summarize the literature regarding photography practices in dermatology, techniques for high-quality photography, photography of skin of color, patient preferences, and medical-legal considerations.

Methods:
A literature search was conducted utilizing Embase, MEDLINE, PubMed, and Evidence Based Medicine databases in accordance with the PRISMA extension for Scoping Reviews.

Results:
Clinical photography is commonly used in biopsy site marking, assessment and diagnosis, disease monitoring, evaluation of treatment response, medical education, research, seeking advice from colleagues, and teledermatology. Camera type, resolution, lens choice, camera settings, environment and set-up, standardization, and types of clinical photography are all important factors in acquisition of high-quality photography. Although, dermatologic photography remains devoid of skin of color representation, several photographic considerations for darker skin are available. Majority of patients support medical photography, with preference for clinical photographs taken by their own physicians, and clinic/hospital-owned cameras over personal devices. Pertinent medical-legal issues include concerns around privacy, personal device use, and documentation of consent.

Conclusions:
Photography in dermatology is continuously evolving with broader applications. Photography techniques can optimize high quality images. Majority of patients support clinical photography, however, concerns remain regarding privacy and consent. Most studies report on photography of lighter skin types, and future studies evaluating clinical photography for all skin types are recommended.

Learning objectives:
1. To comprehensively summarizes literature regarding photography in dermatology
2. To review common uses of photography in dermatology
3. To summarize evidence supporting high quality clinical photography
4. To review patient and physician preferences for clinical photographs
5. To evaluate optimization of clinical photography for all skin colors

Takeaway Message:
High quality images of skin of all colors, for a variety of applications in dermatology, can be optimized by using specific equipment, environmental elements, and standardized protocols.

Efficacy of N-acetylcysteine (NAC) in Trichotillomania (Hair-Pulling Disorder), Skin-Picking Disorder and Onychophagia (Compulsive Nail-Biting): A Systematic Review

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Introduction:
Due to limited efficacy of current treatments for trichotillomania (hair-pulling disorder, TTM), skin-picking disorder (SPD) and onychophagia (compulsive nail-biting), novel treatments, including N-acetylcysteine (NAC), are being evaluated. This systematic review summarizes treatment outcomes of NAC in patients with TTM, SPD and onychophagia.

Methods:
This review was registered on PROSPERO. Embase, MEDLINE, PubMed, and EBM databases were searched in accordance with PRISMA guidelines using a combination of relevant search terms. Title, abstract, and full text screening were done in duplicate. Studies were included if they met predetermined our PICOS framework. Results are presented in descriptive form.

Results:
Nineteen articles, representing 126 patients (mean age: 26.2 years; range: 3.5 to 65 years; adult: 63%; pediatric: 37%; sex: 81% female) were included in the pooled analysis. Majority of patients responded to NAC with a 58% (n=31/53), 58% (n=23/40) and 100% (n=19/19) response rate in patients with TTM, SPD and onychophagia, respectively, with a mean response time of 2.1 months, 2.9 months and 1.4 months. Adverse events of NAC were reported in 20% (n=12/60), 21% (n=9/43) and 8% (n=2/26) of patients with TTM, SPD, and onychophagia, respectively.

Conclusions:
Despite small sample sizes and heterogeneity between included studies, our findings suggest that NAC is an effective treatment for patients with TTM, SPD and onychophagia with majority of patients achieving marked or complete response (65%, n=73/112). NAC is safe and minor adverse events occurred in a minority of patients (18%, n=23/126).

Learning objectives:
1. Discuss N-acetylcysteine (NAC) as a novel treatment for excoriation (skin-picking) disorder (SPD), trichotillomania (hair-pulling disorder, TTM), and onychophagia (compulsive nail-biting).
2. Discuss safety of NAC for SPD, TTM and onychophagia.
3. Discuss efficacy of NAC for SPD, TTM and onychophagia.

Takeaway Message:
NAC is a safe and effective treatment for patients with SPD, TTM and onychophagia with adverse events occurring in a minority of patients (18%, n=23/126), and majority of patients achieving marked or complete response (65%, n=73/112).

Poster Session: Clinical Skin Research

Infantile Hemangiomas Involving the Ear and Periauricular Area: A Retrospective Study of Patients Referred to a Tertiary Clinic

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Introduction:
Infantile hemangioma (IH) is the most common vascular tumor which affects 4-12% of infants during the first year of life. Despite considered a benign tumor, this vascular anomaly represents a burden for patients and their families. The literature is currently limited on IH involving the ear. The present study aims at documenting the clinical characteristics of these hemangiomas.

Methods:
This study was done within the context of the multicenter international Hemangioma Investigator Group. A retrospective chart review (January 1st, 2022 – May 31st, 2021) of IH patients treated at the Sainte-Justine University Hospital Center was conducted. Clinical photographs were retrieved and analyzed to assess eligibility. Demographic data, clinical characteristics of the IH, treatment interventions and associated complications were collected.

Results:
In our center, 67 cases met the inclusion criteria, of which 46 were girls (69%) and 21 (31%) were boys. The majority was born at term (n=44, 65.7%). Most infants were Caucasian (n=60, 89.6%). Median age of IH onset was at 0 [0, 2] weeks. Median size of the estimated hemangioma was 1- ≤5 cm. Most IH subtypes were segmental (n=49, 73.1%), while the rest were localized (n=18, 26.9%). 30 (44.8%) were mixed, 28 (41.8%) were superficial and 9 (13.4%) were deep. 53 (79.1%) infants were treated actively (topical, local, or systemic treatment), while 14 (20.9%) remained under observation. Main complications were disfigurement (57, 85.1%), cartilage deformity (15, 22.4%) and ulceration (13, 19.4%).

Conclusions: IH involving the ear are more present in girls and were found to be predominantly segmental and mixed or superficial.

Learning objectives:
1. To analyze the clinical characteristics and course of infantile hemangiomas involving the ear.
2. To describe the complications and deformities associated with these hemangiomas.
3. To describe management practices (active intervention vs observation) for these infantile hemangiomas.

Takeaway Message: IH involving the ear may present with more complications than other body sites and should be managed attentively.

Poster Session: Education

Learning Practical Dermatology Skills Through Animated Vignettes: An Effective Medical School Educational Intervention to Support the Dissemination of National Guidelines

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Introduction:
Choosing Wisely is a global initiative to improve outcomes in patient care by reducing unnecessary tests and treatments. The Canadian Dermatology Association developed five recommendations for Choosing Wisely Canada (CWC) to guide diagnosis and management of common dermatology conditions. Traditional models of dermatology education (i.e., didactic teaching, clinical rotations) are increasingly being complemented by novel educational tools, such as problem-based learning. We assessed the impact and reception of animated case-based videos of CWC recommendations for a medical student audience.

Methods:
Five 10-minute animated educational videos with a case-based approach were created for a pan-Canadian audience. Medical students reviewed the videos and were surveyed (using a five-point Likert scale) on video format and content and impact on their dermatology knowledge and resource stewardship.

Results:
53 students from 8 Canadian medical schools received an average of 6 hours of educational information. For 47%, the dermatologic content had not been encountered previously. Post-intervention, 94% of participants agreed or strongly agreed that the video format fit their learning style (Likert scale 4.3±0.6). 98% of participants better understood the rationale behind the recommendations (4.4±0.6) and 96% reported the videos enhanced their dermatology knowledge (4.6±0.6). The videos stimulated an interest in resource stewardship among 70% of participants. The major barriers of following the recommendations in clinical practice included: opinions from supervisors, unfamiliarity with recommendations, and impacting relationship with supervisors.

Conclusions:
Case-based animated educational videos are an effective means to develop practical dermatology knowledge and convey guidelines in an engaging way at the medical student level.

Learning objectives:
1. Understand the effective ways to teach medical trainees Choosing Wisely Canada (CWC) recommendations in dermatology;
2. Assess the impact and reception of animated case-based videos of CWC recommendations in dermatology for a medical student audience;
3. Appreciate the barriers for medical trainees to apply CWC dermatology recommendations in clinical practice.

Takeaway Message:
Case-based animated educational videos are an effective means to develop practical dermatology knowledge and convey guidelines in an engaging way at the medical student level.

Epidemiology of Severely Burned Patients Requiring Autologous Skin Substitutes

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Introduction:
Since 1986, the Experimental Organogenesis Lab (LOEX) has been producing autologous skin substitutes as an experimental treatment option for severe burn patients. Two types of substitutes are produced: Cultured Autologous Epidermis (CAE) and more recently, autologous Self-Assembled Skin Substitutes (SASS). The goal of this study was to create a data base from all the culture data and the medical records available since the beginning of the LOEX's activity to analyze the demographic characteristics of the burn patients for whom a culture was requested.

Methods:
538 clinical and cell culture datasets of 300 Canadian patients were grouped in Excel. First, we focused on sex, age, mortality, biopsy location chosen for cell extraction, etiology of the burn, and the percentage of the body surface burned.

Results:
Most patients are male (71%). The average age is 41 years (sd = 19.79 years); female patients are slightly older than male with an average of 44 years (sd = 20.49 years) compared to 40 years (sd = 19.36) for men. Mortality was similar between men and women (34.12% vs 31.40%). Most burns were due to a house fire, followed by burns related to cooking. Work accident was only reported for men and was the second most described etiology, after domestic accidents. The pubis was the most collected body site for the biopsy.

Conclusions:
Even if burns can occur to everybody, a typical profile for whom the LOEX is asked to produce skin substitutes can be identified from our data. It is a man around forty, burned by a house fire on 70% of his surface area and the biopsy would be collected at the pubis.

Learning objectives:
1. Describe the two types of autologous skin substitutes produced by the LOEX for the treatment of burned patients
2. Identify the general characteristics of the Canadian burned patients requiring autologous skin substitutes
3. Compare these statistics with worldwide statistics from the WHO

Takeaway Message:
Do not play with the fire… especially if you are a man around 40!

Compassionate Use of Allogeneic Self-Assembled Skin Substitutes for Recessive Dystrophic Epidermolysis Bullosa Wound Closure

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Introduction:
A patient with a severe form of RDEB due to mutation in the collagen VII (C7) gene presenting open wounds covering 30% of his body was treated with skin substitutes (TES) in an n-of-1 compassionate clinical trial. The hypothesis was that the addition of normal cells within TES could produce enough C7 to restore normal skin adhesion.

Methods:
Combinations of autologous RDEB keratinocytes (RDEB-K) and fibroblasts (RDEB-F) and healthy allogeneic keratinocytes (N-K) and fibroblasts (N-F) were used to produce autologous (RDEB-F/RDEB-K), mixed (N-F/RDEB-K) or chimeric (N-F/RDEB-K/N-K) TES using the self-assembly approach. C7 production was analyzed by immunofluorescence and dermo-epidermal junction (DEJ) strength was quantified through mechanical peeling tests. Mixed and chimeric TES were applied on chronic wounds situated on the back of the patient.

Results:
In vitro, the deposition of C7 at the DEJ and the adhesion strength of the DEJ of mixed TES were higher compared with autologous TES. The chimeric TES, containing both allogeneic and autologous keratinocytes, allowed for an intermediate increase in C7 in vitro. After two weeks of grafting, a loss of the epidermis was observed in chimeric TES. Keratinocytes are known to be highly immunogenic. Interestingly, the epidermis rapidly reepithelialized thereafter. At the site grafted with mixed TES, the epidermis persisted for the first 6 weeks, with 2% of wounded surface per grafted area. However, wounds started to reappear after 8 weeks (13%) and 6 months (47%) but decreased after 1 year (12%).

Conclusions:
The use of mixed TES allowed for the closure of chronic wounds but did not persist long term in an n-of-1 compassionate clinical trial, indicating that it is not a permanent treatment for RDEB.

Learning objectives:
1. Physiopathology of recessive dystrophic epidermolysis bullosa
2. The potential of allogeneic cells for the treatment of epidermolysis bullosa
3. Self-assembly approach to produce graft able skin substitutes

Takeaway Message:
The use of chimeric skin substitutes can close chronic wounds of RDEB patients.

Wound Healing: Exploring Mechanisms Whereby a New Drug Ag373K Augments VEGFA Secretion and Keratinocyte Migration

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Introduction:
Keratinocytes are key for repair of skin wounds, failure of which leads to chronic wounds. This common condition significantly reduces patients' quality of life and results in high mortality. Infection with antibiotic-resistant pathogens often contributes to failed healing. Thus, there is an urgent need for new anti-microbial therapeutics that also promote healing. Ag373K is a promising new antimicrobial drug. However, its impact on skin cells remains unknown.

Methods:
In this study we used HaCat keratinocytes. Effects of Ag373K on cell viability were studied using an MTT assay. Cell migration was observed using a gap closing assay. Secreted mediators were identified using a cytokine screen. Gene and protein expression changes were detected using qPCR and Western blotting.

Results:
5-10 μM Ag373K had potent antimicrobial effects that did not affect cell viability. It significantly increased cell movement and the development of lamellipodia at the migrating front. Addition of Ag373K to migrating HaCat cells elevated soluble VEGF-A and EGF levels, that are known to promote migration and healing. Ag373K treatment also augmented VEGF-A mRNA in migrating cells. Moreover, both Ag373K and VEGF treatment increased mRNA and protein levels of the small GTPases RhoA and Rac1.

Conclusions:
Ag373K is a promising antimicrobial agent that can promote keratinocyte migration, key for re-epithelization. We found that this might be due to increased VEGF-A released from keratinocytes, that in turn augments RhoA and Rac1 expression. Since these small GTPases are central for dynamic cytoskeletal remodeling during cell migration, this effect may be central for augmented migration.

Learning objectives:
1. Characterization of the effect of Ag373K on human skin cells to validate its use in a clinical setting
2. Exploring the effectiveness of Ag373K on keratinocyte migration
3. Uncovering molecular mechanism whereby Ag373K and VEGF-A accelerate cell migration

Takeaway Message:
Beneficial effects of a potent anti-microbial agent, Ag373K, may be attributed to the release of VEGF-A that augment keratinocyte migration. Our studies will help validate a new drug for chronic wound treatment and promote understanding of the underlying molecular mechanisms of wound healing.

The Endocannabinoid System of Psoriatic Tissue-Engineered Skin Models

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Introduction:
Psoriasis is an inflammatory skin disease marked by red patches covered with white scales. Moreover, studies have shown that this disease includes a disturbed lipid metabolism. In fact, n-3 polyunsaturated fatty acid (n-3 PUFAs) dietary supplements are now known to attenuate the symptoms of psoriatic patients, as seen in many clinical studies. The aim of the present study was to evaluate the implication of the endocannabinoid system in the treatment of psoriatic skin with n-3 PUFAs, using tissue-engineered reconstructed skin.

Methods:
To achieve this, cells from healthy and psoriatic donors were used to produce healthy (HS) or psoriatic (PS) skin substitutes according to the self-assembly method. Then psoriatic skin substitutes were either treated with 10 µM of α-linolenic acid (PSALA+), N-eicosapentaenoyl-ethanolamine (PSEPEA+), EPEA combined with a known inhibitor of CB1, rimonabant (PSEPEA+R) or were left untreated (PS-). Liquid chromatography analyses were conducted on HS-, PS- and PSALA+ substitutes.

Results:
The results showed a significant increase (p-value<0.05) of EPEA levels in PSALA+ compared with PS- (10.7-fold), implying that the treatment of PS with ALA could be effective due to its conversion to EPEA. Subsequently, the thickness of the living epidermis was analyzed for the remaining conditions and results showed that the thickness of PSEPEA+ epidermis was significantly reduced compared with PS- or PSEPEA+R. Moreover, the number of cells marked by Ki67 was also diminished in PSEPEA+ compared with PS- and PSEPEA+R, indicating that EPEA decreased the hyperproliferation of psoriatic keratinocytes.

Conclusions:
In conclusion, our results suggest that the beneficial effects of n-3 PUFAs in psoriasis could, in part, be mediated by the endocannabinoid system, mainly EPEA.

Learning objectives:
This study provides a better understanding of the mechanisms of action by which n-3 PUFAs mediate their beneficial effects, highlights the importance of the endocannabinoid system and lipid metabolism in the skin and contributes to fundamental knowledge concerning tissue-engineering applications.

Takeaway Message:
Overall, the endocannabinoid system is highly implicated in the n-3 PUFAs treatment of psoriatic tissue-engineered reconstructed skin.

In Vitro Modeling by Tissue Engineering of The Impact of Sensory Innervation in Psoriasis

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Introduction:
Psoriasis is a chronic inflammatory skin disease characterized by the formation of scaly lesions following the epidermis' hyperproliferation and the infiltration of inflammatory cells in the dermis. The cause and mechanisms governing the localization and remodeling of psoriatic lesions remain unknown. Currently, the therapies offered to the patients aim to reduce inflammation, but at the cost of significant side effects. In order to solve this issue, we exploit the identified link between emotional and/or mechanical stress and worsening of the extent and intensity of lesions. Moreover, an interruption of nerve impulses upstream of a psoriatic lesion induces a complete remission of the latter. We hypothesize that the role of nervous stress in the psoriatic context can be studied in vitro by modeling an innervated and immunocompetent psoriatic skin.

Methods:
Tissue engineered, innervated and immunocompetent 3D psoriatic skins are manufactured on a sponge composed of collagen/chitozan. The skins produced are subjected to the appropriate stimulations and are then analyzed by microscopy, ELISA or flow cytometry.

Results:
With this model, we highlight the effect of the induction of the release of substance P and CGRP on the aggravation of the psoriatic phenotype as well as the modulating role of substance P and CGRP on dendritic cells.

Conclusions:
This study will demonstrate for the first time the decisive effect of the sensory innervation in the formation of psoriatic lesions. This study will make possible the development of a whole new field of expertise for treating psoriasis by targeting the innervation of the skin via topical application, which will have fewer side effects than the current therapies.

Learning objectives:
Our objective is to recreate in vitro the psoriatic environment and nervous disorder. From cells of psoriatic participants and by adding a sensory innervation as well as an immune component (dendritic cells), we hope to determine the cause of the nervous disorder and to develop a novel treatment to block it.

Takeaway Message:
Sensory neurons have a decisive effect in psoriasis via CGRP, as shown in this work, involving in vitro modeling tissue engineering. The learning of the modulation of sensory neurons or their neuropeptides could allow us to deeper our comprehension of psoriasis and work toward therapies with few sides effect, or, perhaps toward a cure of the disease.

Poster Session: Inflammatory Skin Diseases

Health-Related Quality of Life (HRQL) In A Canadian Atopic Dermatitis (AD) Cohort

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Introduction:
Adult patients (N=193) ages 16 to 78 were diagnosed with AD as per Hanifin and Rajka criteria and consented to the Dermatitis BioBank cohort.

Methods:
We collected data on demographics, comorbidities, and HRQL at baseline.

Results:
White (48.2%) women (56.0%) predominated, with 18.7% reporting adult-onset AD. 30.1% missed work or school in the last year because of AD; for 16.6% at least three times. Comorbid asthma (40.9%), allergic rhinitis (56.5%), food intolerance (37.8%), and anxiety/depression (51.8%) were common.

Spearman's correlations were calculated to explore HRQL as assessed by history of remission with clear skin in the past year (33.2%) and self-reported depression or anxiety secondary to AD (36.3%). Patients with anxiety or depression less often reported remission ($\rho = -0.160$, $p = 0.035$) and more often reported missing work or school in the last year ($\rho = 0.422$, $p<0.001$).

Conclusions:
This uniquely large and diverse cohort provides an opportunity to explore determinants of disease outcome in tertiary care AD patients.

Learning objectives:
1. Describe demographics of tertiary care AD patients.
2. Describe common comorbidities in AD patients that influence HRQL.
3. Understand factors affecting HRQL in AD.

Takeaway Message:
Mental health comorbidities, common in this cohort, are related to poor HRQL in AD and merit in-depth exploration.

Skin Colour and Perceptions of Sun Exposure Among Residents of Atlantic Canada: A Preliminary Analysis

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Introduction:
Recent studies have shown that the Atlantic provinces of Canada have one of the highest rates of melanoma in the country. While sun exposure is an important modifiable risk factor for the prevention of skin cancer, sun protective habits have not yet been extensively studied in this population. Given the variation in ancestry and skin tones among these provinces, we sought to understand how skin colour might affect perceived risk of skin cancer, and in turn, sun exposure habits.

Methods:
In the context of a consensual qualitative research study, we conducted 22 focus groups in Atlantic Canada, in which a total of 98 adults recruited from both the mailing list of the AtlanticPATH study and word-of-mouth participated. Discussions revolving around sun exposure habits were recorded, transcribed verbatim, and thematically analysed. A preliminary analysis on five focus groups was conducted.

Results:
Participants referred to two main types of skin colour that they related to their sun exposure habits. The first one was the perception that having lighter skin, eyes, and hair increased skin cancer risk and required, consequently, major sun exposure protective efforts. Instead, having darker features and a baseline tan reduced cancer-related risks, rendering protective habits regarding skin cancer upon sun exposure less necessary.

Conclusions:
Taken together, our findings suggest that perception of skin colour is an important factor people in Atlantic Canada use to assess skin cancer risk and decide on sun protection. This evidence can be used to develop public health campaigns aiming to increase sun exposure awareness.

Learning objectives:
1. Understand perceptions of skin cancer risk among communities in Atlantic Canada.
2. Appreciate how skin colour affects attitudes toward sun protection.
3. Identify targets for a public health campaign on sun exposure in Canada.

Takeaway Message:
In Atlantic Canada, where a high skin cancer incidence has been noted, skin colour affects the perceived risk of skin cancer, and in turn sun protective behaviours. This evidence can be used to develop targeted public health campaigns.

Investigating The Evolution of Sun Protection Habits of The Canadian Population Living in The Atlantic Provinces

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Introduction:
Worldwide, an augmentation in UV rays that increasing risk to sun exposure has been observed. Effective programs to raise awareness of UV radiation exposure have been developed in various countries around the globe. However, and despite the incidence rate of melanoma growing, there is no such program in Canada. Given the variation in the incidence rates of melanoma in the Atlantic provinces of Canada, we aimed to explore participants' perspectives regarding the evolution of sun protection habits. Has there been an evolution in sun exposure habits?

Methods:
A consensual qualitative research study in which focus groups were conducted was performed. Discussions were audio recorded and transcribed verbatim. A reflective-evolving coding schema was developed and discussed bi-weekly by all team members.

Results:
In total, 22 focus groups were conducted. Participants referred to "evolution of sun protection habits" as being the result of: (a) awareness in the younger generation, (b) shift from using tanning substances to UV preventing ones; and (c) increased caution with age.

Conclusions:
This study shows that a shift on how participants perceived and approached sun exposure over time took place. While this evidence indicates a shift from the zeitgeist of careless to active tanning, much work is still needed to understand Canadians' sun protection habits and reasons underlying them.

Learning objectives:
The overarching purpose of this project is to develop a public health campaign to increase awareness of the dangerous effects of the sun through behavior change. To do that we hoped to gain an insight into the sun protection skin cancer habits implemented by Canadian living in the Atlantic provinces of Canada.

Takeaway Message:
Though there seems to be marked change in social behavior surrounding tanning and sun exposure since older generations, there remains much to be done in developing tailored messaging for public health campaigns to lower skin cancer rates in Canada.

Poster Session: Skin Cancer

Skin Surveillance After a Previous Cutaneous Melanoma Diagnosis: A Scoping Review

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Introduction:
The incidence of cutaneous melanoma in Canada has increased in recent decades. Individuals with a primary cutaneous melanoma are at risk for developing recurrence and subsequent primary melanomas (SPMs). There is significant heterogeneity in recommendations from national clinical practice guidelines on follow-up surveillance of melanoma patients. The purpose of this scoping review is to provide an overview of evidence-based recommendations on follow-up surveillance of melanoma patients.

Methods:
A literature search was conducted utilizing MEDLINE and PubMed databases in accordance with the PRISMA extension for Scoping Reviews checklist. Original and review articles reporting on melanoma follow-up surveillance, recurrence and/or SPMs were included. Articles were excluded if they had a small sample size (<40 patients) or focused on uveal or mucosal melanomas, staging or re-staging of symptomatic recurrent disease, or monitoring of response to treatment.

Results:
The scoping review included 142 studies. The median Oxford Centre for Evidence-Based Medicine Level of Evidence was 2b. Patient education on sun safety and self-skin exams had the strongest support from the literature. More frequent surveillance in the first 2-3 years following diagnosis may be beneficial due to the peak in recurrence rates and incidence of SPMs during this period. Routine surveillance imaging is not recommended in stage 0-IIA but may be considered in stage IIB-IV melanoma, though there is a risk of false-positive test results and a lack of data to support a survival benefit.

Conclusions:
Further study in randomized control trials is needed to determine the optimal frequency of clinical follow-up and surveillance imaging and to characterize the potential benefits and risks of surveillance in asymptomatic patients.

Learning objectives:
1. Recognize the potential need for more intensive surveillance in advanced stages of melanoma and in individuals at increased risk for SPMs.
2. Identify the current challenges in developing melanoma follow-up surveillance guidelines, including limitations of the current literature.
3. Understand how follow-up surveillance protocols can be applied within the context of Canada's healthcare system, including rural and remote communities.

Takeaway Message:
Many current clinical practice guidelines on melanoma follow-up surveillance are based on consensus statements and there is significant variability in recommendations. Randomized controlled trials are needed to determine the optimal frequency of clinical follow-up and surveillance imaging in melanoma patients.

Role of Soluble CD109 in Squamous Cell Carcinoma (SCC) Progression

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Introduction:
Squamous cell carcinoma (SCC) is the second most common form of skin cancer and its incidence is on the rise. CD109 is a GPI-anchored protein that our lab has identified as a TGF-β co-receptor and antagonist of TGF-β signaling. CD109 is upregulated in SCC, and the premalignant lesions overexpressing CD109 show a greater risk of metastatic progression. Research from our lab has shown that CD109 may exhibit potent pro-tumorigenic effects in vivo by enhancing EGF signaling and responses. However, we have previously shown that CD109 can be endogenously released from the cell surface and that the soluble CD109 (sCD109) may oppose the action of membrane CD109 (mCD109) in vitro. The goal of my study is to determine the role of released sCD109 in SCC progression.

Methods:
The effect of sCD109 on EGF signaling was determined by treating SCC cells with recombinant sCD109 protein and measuring EGF-induced responses such as phosphorylation of EGFR, STAT3, AKT, and ERK1/2, and expression of cancer stem cell markers such as Nanog, OCT4 and SOX2.

Results:
sCD109 inhibited EGF-induced EGF receptor phosphorylation and STAT3 activation and decreased the expression of cancer stem cell markers, Nanog, OCT4 and SOX2, while mCD109 enhanced these parameters.

Conclusions:
sCD109 exhibits opposing effects when compared to mCD109 as detected by inhibition of EGF receptor phosphorylation, STAT3 activation, and stem cell marker expression.

Learning objectives:
1. mCD109 is highly upregulated in cancer, especially SCC.
2. sCD109 inhibits the EGFR activation and its downstream signaling pathway STAT3.
3. sCD109 blocks the synthesis of EGF-induced stem cell markers.

Takeaway Message:
Increasing evidence shows that the soluble forms of oncoproteins and tumor suppressor proteins have substantial effects on cancer progression. mCD109 is pro-tumorigenic but sCD109 exhibits potential anti-tumorigenic property. Understanding the role of sCD109 would augment the development of therapy for the treatment of this second most common form of skin cancer.

Poster Session: Skin Cancer

Transitioning To Pegylated Interferon for The Treatment of Cutaneous T-Cell Lymphoma: Meeting the Challenge of Therapy Discontinuation and A Proposed Algorithm

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Introduction:
Cutaneous T-cell lymphoma (CTCL) is an uncommon group of non-Hodgkin lymphoma, with the most recognized subtypes being mycosis fungoides (MF) and Sézary syndrome (SS). Interferon is an established treatment for MF/SS and is integrated into management guidelines internationally. In 2019, manufacturers abruptly discontinued production of interferon-α2b and interferon-α2a. Alternative systemic therapies in MF/SS remain unfunded or unavailable in Canada, and although the use of pegylated-interferon is a logical substitute, there are no established guidelines and limited published experience. We present a single-centre experience on pegylated-interferon-α2b in place of interferon-α2b for MF/SS, a suggested management protocol, and review of the literature.

Methods:
All patients identified in The Calgary Cutaneous Lymphoma Program database with Stage IIB – IVB MF/SS treated with interferon-α2b were switched to pegylated-interferon (90 μg). Response was monitored using the accepted national standards, including mSWAT and SkinDex29.

Results:
A total of 8 patients (6=MF, 2=SS) with a median age of 68 (range: 50-86) were switched from interferon-α2b to pegylated-interferon. Median duration of disease was 69 months (range: 8 – 275 months). Five out of eight patients with MF remain on pegylated interferon, with sustained response at 12-month follow-up. No patients required dose escalation. The 3 patients with progressive disease requiring discontinuation had SS (n = 2) or MF with large cell transformation (n = 1). One patient developed grade-2 anemia and a second patient experienced grade-2 depression, warranting a dose reduction. All other patients had normal laboratory investigations and no side effects. The presented literature review suggests that pegylated-interferon is as effective as its standard counterpart.

Conclusions:
MF/SS have limited treatment options, and the impact of abrupt product discontinuation is substantial. We propose a dosing and management algorithm for transition from interferon to pegylated-interferon. Pegylated-interferon is an alternative that should be considered as a new standard in MF.

Learning objectives:
1. Describe the most recognized subtypes of Cutaneous T-cell lymphoma and the available systemic and topical treatment regimens.
2. Describe the timeline of interferon discovery, production, and subsequent discontinuation.
3. Review the literature describing the use of pegylated-interferon for cutaneous T-cell lymphoma.
4. Describe a management algorithm for Stage IIB – IVB MF/SS using pegylated-interferon for patients initially on interferon treatment.

Takeaway Message:
Rare diseases like MF/SS are at risk of abrupt product discontinuation requiring a change in treatment planning. We demonstrate a management algorithm and review of the limited literature showing that pegylated-interferon is as good or better than its standard counterpart.

Evaluating the Impact of BRAF Reflex Mutation Testing on the Management of Melanoma, Lung, and Colorectal Cancers in Canada

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Introduction:
Recent advances in our understanding of molecular pathways have fostered the development of novel treatments and are rapidly improving outcomes in cancers that have previously had poor prognoses. Although BRAF mutation status is the only validated predictor for response to therapy in melanoma, such testing is not reliably available. Reflex molecular testing – the process of organizing profiling of the specimen at the time of diagnosis – is an emerging concept in medical oncology. For metastatic melanoma, ordering BRAF testing by preceding members of the treating team will allow medical oncologists to initiate therapy promptly, which may impact disease outcomes.

Methods:
An institutional pathology database was searched to identify all patients who underwent molecular testing. A list of patients with an available BRAF mutation test result was generated, and electronic medical records were searched to identify these patients. Records were retrospectively reviewed in a sequential manner to identify patients with melanoma, lung and colorectal cancer who had underwent molecular testing and had an available BRAF mutation result. Desired variables were obtained from the patient records and a descriptive analysis was performed.

Results:
BRAF mutation testing was most frequently ordered by surgical oncologists (38.9%) and medical oncologists (36.1%). More than half (58.3%) of the molecular testing algorithms employed were immunohistochemistry, and only 44.4% of patients had an available test result at the time of first medical oncology appointment. The median days from first medical oncology appointment to available BRAF mutation test result was 17 (IQR, 0-41) days. The median days from when the BRAF mutation test result became available, and initiation of treatment was 53 (IQR, 24-565) days.

Conclusions:
Our findings raise concerns about the availability and timeliness of BRAF mutation testing. The findings of this study will assist in the optimization of reflex BRAF mutation testing in melanoma, lung, and colorectal cancers in Canada.

Learning objectives:
1. Understand which type of molecular testing algorithms were employed and which medical specialist ordered the testing
2. Examine when the BRAF mutation test result became available in relation to the first medical oncology appointment
3. Evaluate the impact of reflex mutation testing on time to treatment initiation

Takeaway Message:
The findings of this study will assist in the optimization of reflex BRAF mutation testing in melanoma, lung, and colorectal cancers. The outcomes of this study will form the foundation to establish reflex mutation testing recommendations in Canada.

Poster Session: Skin Cancer

Skin Cancer Risk Factors, Sun Safety Behaviours and Melanoma Concern in Atlantic Canada: A Comprehensive Survey Study

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Introduction:
The incidence of cutaneous melanoma (CM) is increasing at an alarming rate in Canada and significant regional differences have been identified in the Atlantic provinces. The overall goal of this article is to compare ultraviolet exposure, sun protective behaviours, level of worry and baseline CM knowledge in high and low incidence provinces, as well as between various demographic groups.

Methods:
A cross-sectional survey study was conducted in the Canadian Atlantic provinces between July 2020 and March 2022. Participants were invited to complete an electronic modified validated patient questionnaire consisting of 42 multiple-choice and short-answer questions. The survey assessed CM risk factors, sun protection behaviours and baseline CM knowledge. All participants aged 16 years and older with a complete survey were included. Survey responses were summarized using frequency counts, percentages, and means. Two-sided Z-tests for equality of proportions were used to compare survey results between geographic and demographic groups.

Results:
A total of 7,861 participants were included. Provinces with a high incidence of CM (Prince Edward Island and Nova Scotia) had significantly more sunburns (OR 1.7), total sun exposure (OR 2.0), recreational sun exposure (OR 1.9), and tans (OR 1.6) than individuals in the low incidence province (Newfoundland and Labrador). However, individuals in high-incidence provinces used fewer tanning beds (OR 0.8), checked their skin more frequently for new moles (OR 1.3) and practiced more sun protection overall. Additional comparisons are presented based on education, income, sexual minorities, and gender.

Conclusions:
This study will allow us to gain valuable and actionable insight into specific factors which will improve targeted efforts and help develop key messages that resonate with impacted populations, thereby increasing their efficacy and potentially influencing changes in policies.

Learning objectives:
1. Compare ultraviolet exposure between geographic and demographic groups in Atlantic Canada
2. Compare sun protective behaviours between geographic and demographic groups in Atlantic Canada
3. Compare level of worry for cutaneous melanoma between geographic and demographic groups in Atlantic Canada
4. Compare baseline melanoma knowledge between geographic and demographic groups in Atlantic Canada

Takeaway Message:
High-incidence provinces have more overall sun exposure. However, interestingly, they use fewer tanning beds, perform more self-skin checks, and practice more sun protection overall. The findings of this study will act as a steppingstone to guide future public health efforts.

Translational Landscape of High-Risk Basal Cell Carcinoma

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Introduction:
Basal Cell Carcinoma (BCC) is a non-melanoma skin cancer affecting up to 60,000 Canadians each year. BCC comprises of low-risk (nodular/superficial) and high-risk (infiltrative/morpheaform/metatypical) histopathological subtypes. High-risk BCC is difficult to eradicate, often recurs, and can become locally destructive and metastatic. Despite their high disease burden, BCC advancement is poorly understood. This project aimed to determine gene expression changes and their implication across biological processes and pathways distinguishing high-risk and low-risk BCC.

Methods:
Genomic data comprising 44 samples (38 low-risk, 6 high-risk) was processed in R to generate a list of differentially expressed genes (Q-value <0.05) in four comparisons: Low-risk vs High-risk, Metatypical, and Morpheaform BCC, as well as Morpheaform vs Metatypical BCC. Pathway and Gene Ontology analyses were completed on enriched genes using ToppFun, EnrichR and GSEA.

Results:
Compared to low-risk, high-risk BCC showed enrichment of SUZ12 (Q-value: 1.87E-03) and EZH2 (Q-value: 2.93E-02) of the polycomb repressor complex, alongside genes encoding the ECM (Q-value: 9.40E-05). Morpheaform showed upregulation of collagen-related pathways, alongside cancer pathways including PI3K/Akt/mTOR (Q-value: 5.28E-04), IL6-JAK-STAT3 (Q-value: 6.37E-04) and BETA-Catenin Signaling (Q-value: 3.80E-02). Compared to both metatypical and low-risk, up-regulation of Cancer Testis Antigens MAGE genes were found in morpheaform BCC (Q-values 1.01E-06 and 1.50E-03 respectively).

Conclusions:
This study supports previously studied processes in BCC progression including over-expression of EZH2 and known cancer pathways such as PI3K/Akt/mTOR and IL6-JAK-STAT3. Further, it offers a novel role of Cancer Testis Antigens as therapeutic targets for high-risk BCC. Once externally validated, these biomarkers can screen for predisposition to aggressive BCC.

Learning objectives:
1. Identify biological processes and pathways implicated in high-risk BCC.
2. Explain their role in avenues of cancer advancement including cell proliferation, invasion, and metastasis.
3. Propose different biomarkers to profile high-risk BCC.

Takeaway Message:
Differentially expressed pathways in high-risk BCC can generate prognostic profiles to manage treatment for patients according to the nature of their BCC.

Poster Session: Skin Cancer

The Evolving Trends of Artificial Intelligence Skin Cancer Articles Published in Dermatology Journals

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Introduction:
The applications of artificial intelligence (AI) in dermatology range from screening to diagnostics. These promising AI uses have been documented in the dermatologic oncology literature. This study is the first to examine the evolving trends of AI skin cancer literatuure.

Methods:
AI articles focusing on melanoma, non-melanoma skin cancers (NMSC) and both were extracted from the Web of Science using the keywords AI, machine learning (ML) and deep learning (DL). Articles were assessed based on title, abstract and full-text review. The AI characteristics retrieved included the type of machine learning (ML), use of deep learning, type of algorithms tasks, algorithm performance, type of datasets and databases used. The general characteristics retrieved included the type of skin cancer, imaging modalities, publication year, article type, research area and number of citations.

Results:
171 articles were analyzed: 25 focusing on NMSCs (45% of which were on basal cell carcinoma and 45% on squamous cell carcinoma), 78 on melanoma studies and 68 on both. All articles were published between 2000 and 2022, with 29% of them published in 2021. The leading journals were Journal of Investigative Dermatology (11%), Journal of the American Academy of Dermatology (7%), Journal of the European Academy of Dermatology (6%) and British Journal of Dermatology (6%). 106 (62%) studies were original articles and 28 (16%) were reviews. The most used imaging modalities were standard dermoscopy (45%) and clinical images (24%). Among 88 studies which specified their type of ML, 86 used supervised learning (98%). Among 83 studies which specified the presence of deep learning in their algorithms, 61 (73%) used it. 85 studies specified their databases: 61(72%) were private and 11 (13%) were public.

Conclusions:
Most AI studies in skin cancer focused on the development and assessment of algorithms in the realm of computer vision and image classification.

Learning objectives:
1. To analyze the characteristics of AI articles on skin cancer published in dermatology journals.
2. To compare the differences in characteristics of AI articles on non-melanoma and melanoma studies.
3. To identify challenges and solutions regarding the implementation of AI in the field of skin cancer.

Takeaway Message:
While AI remains at its debuts in dermatology, AI in skin cancer is a growing research field. Most studies focused on melanoma, followed by basal cell carcinoma and squamous cell carcinoma.

Comparison of Basal Cell Carcinoma Posts, Comments and Authors Between Reddit and Quora Forums

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Introduction:
The rise of social media is transforming how patients seek out medical information. Social media may play a central role in better responding to patient needs and in raising basal cell carcinoma awareness. Analyzing patients' use of social media forums can help better understand and potentially adapt to current needs by patient-driven priority setting.

Methods:
All basal cell carcinoma posts, comments and authors were extracted from Reddit and Quora online forums using the keyword "Basal cell carcinoma". All posts were screened and assessed by full-text review to validate basal cell carcinoma relevance. Posts, comments, and authors were compared between Reddit and Quora using a one-way ANOVA test.

Results:
217 Reddit posts were published between 2012 and 2022. 212 Quora posts were published between 2011 and 2022. 237 comments from Quora were collected and analyzed. Posts had a median of 293 views (IQR: [153-559]) and 0 (IQR: [0-1]) comments. 1578 comments from Reddit were collected and analyzed. The number of views per post was unavailable on Reddit. Posts had a median of 2 comments (IQR: [1-3]). No BCC community threads, or groups were found on Reddit, unlike on Quora. Reddit posts are more geared towards educational material content ($p<0.0001$) and skin inquiries with pictures ($p<0.0001$), while Quora posts focus more on non-personal general disease questions ($p<0.0001$) and advice-seeking for potential treatment ($p<0.0001$). Authors of comments differed as most users on Reddit did not specifically self-describe as non-physicians unlike on Quora ($p<0.0001$). The medical community was significantly more represented on Quora than on Reddit ($p<0.001$).

Conclusions:
To date, this is the first study to compare Reddit and Quora forums in patients' basal cell carcinoma posts. The present analysis helps target online screening and educational needs.

Learning objectives:
1. Understand the differences in basal cell carcinoma patients' needs between Quora and Reddit.
2. Understand the differences in basal cell carcinoma comments and medical qualifications of commenters between Quora and Reddit.
3. Identify strategies to improve online patient support and disease awareness.

Takeaway Message:
Reddit and Quora respond to different patient needs. Dermatologists and medical organizations can benefit from these forums to rapidly share accurate information and engage with skin cancer patient communities.

Poster Session: Skin Cancer

Melanoma Survival in Canada: A National Population-Based Study Elucidating Healthcare and Socioeconomic Barriers Affecting Patient Care

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Introduction:
Cutaneous melanoma (CM) causes more deaths than any other skin cancer. On average, an individual who dies of melanoma loses 20.4 years of life, and we hypothesize that mortality may be impacted by a variety of factors, whether personal, socioeconomic or healthcare-related. The mortality-to-incidence ratio (MIR) can be used to approximate case-based survival and compare it between subgroups of the population.

Methods:
We extracted incidence and mortality data for Canadian CM patients from 3 independent, population-based registries. Age-standardized incidence and mortality rates per 100,000 person-years were calculated for each province, and crude rates were calculated for each census division. Linear regression models and Wilcoxon Rank-sum tests were used to establish differences and determine factors relevant to MIR across the country.

Results:
Between 1992 and 2016, 106,015 CM cases and 20,570 CM-related deaths were recorded in Canada. The overall MIR in Canada was 19.4. The provinces with the highest MIR were Saskatchewan (18.71), Ontario (18.52) and Manitoba (18.33). The yearly MIR in Canada between increased linearly in a statistically significant fashion. Census divisions with crude MIRs higher than the national MIR were clustered in Northwestern/Southern Ontario, central Newfoundland and Labrador, Southeastern Manitoba and the central-inferior portion of British Columbia. Significant factors with a negative impact on MIR include median household income, individuals with a tertiary education and density of dermatologists and family physicians per 100,000 people.

Conclusions:
By better understanding the socioeconomic and geographical factors that impact melanoma survival in Canada, this study allows us to better comprehend its disease burden and to make specific public health recommendations.

Learning objectives:
1. The MIR of CM in Canada has increased over time, indicating poorer outcomes for those diagnosed with this cancer.
2. Manitoba, Ontario and Saskatchewan had the highest MIRs.
3. Factors associated with a poorer MIR include higher median household income, individuals with tertiary education and density of dermatologists and family physicians.

Takeaway Message:
The MIR of CM in Canada provides us with valuable knowledge and can guide public health campaigns aimed at reducing CM incidence and mortality rates in the future.

Gene-Environment Analyses in A UK Biobank Cohort of Four Skin Cancers Identify Synergistic Contributions of DNA- and Environment-Based Factors

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Introduction:
Skin cancers arise from the poorly-understood interplay between genetic and environmental risk factors. Despite the well-established relationship between sun exposure and skin cancer pathogenesis and progression, the interactions between specific genetic variants and sun exposure-linked behaviours in genetically-predisposed individuals remain largely unknown.

Methods:
To quantify the synergistic involvement of genetic and environmental factors in predisposing to disease, we leveraged a UK Biobank cohort of four skin cancers (basal cell carcinoma [BCC, n=17,221]; cutaneous squamous cell carcinoma [cSCC, n=2,331]; in-situ melanoma [Mis, n=1,158]; invasive melanoma [Minv, n=3,798]) and matched healthy controls (n=448,164). We surveyed 8,798 single nucleotide polymorphisms (SNPs) from 190 genes functioning in/associated with DNA repair, as well as 11 demographic and environmental variables (age, sex, self-reported skin and hair colour, time spent outdoors in both summer and winter, use of sun protection, ease of tanning, self-reported aging appearance, annual frequency of sunlamp use, and frequency of lifetime sunburn events). Both disease-environment and SNP-disease analyses were performed using logistic regression (multinomial and binomial, respectively), while SNP-environment analysis was performed using both model-based and robust joint interaction tests.

Results:
We observed numerous significant ($p<0.05$) overlapping but distinct trends corresponding to demographic and environmental factors for each cancer group, notably associations between cSCC and brown skin (OR≈0.00), and paradoxically between all skin cancer groups and frequent ("always") sun protection (OR=2.25~3.92). Further, we identified 11 alleles that were significantly associated (FDR $q<0.05$) with BCC, of which three were also significantly associated with Minv. We also identified 101 alleles across four disease groups that have a significant interaction (Bonferroni $p<3.29 \times 10^{-5}$) with at least one participant variable.

Conclusions:
This work has identified novel environmental risk factors and their interactions with DNA repair genes in predisposing to skin cancers, and cumulatively informs genetic screening programs and public awareness campaigns of diligent use of sun protection.

Learning objectives:
1. DNA repair gene alleles are strongly implicated in the pathogenesis of skin cancers
2. Demographic and environmental factors are associated with risk of skin cancers in a distinct but overlapping manner
3. Consideration of demographic and environmental factors adds relevant context to genetic findings

Takeaway Message:
Quantifying the precise risk of skin cancers requires consideration of both genetic and environmental factors, which cumulatively provide insights into the pathophysiology and progression of these diseases.

Poster Session: Skin Cancer

Evaluating the Expression and Function of meiCT gene, Disrupted Meiotic cDNA1 in Head and Neck Squamous Cell Carcinoma.

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Introduction:

DNA meiotic recombinase 1/ Disrupted meiotic cDNA 1 (DMC1) is known to be a meiosis specific protein that is required for the process of meiotic recombination. Albeit meiosis specific, it has been found to be ectopically expressed in glioblastoma, cervical, breast cancer and other cancer cell lines as well as CTCL biopsy samples and Sézary patient lymphocytes. Analysis of RNA-seq data from TCGA revealed increased expression of DMC1 is observed in testicular germ cell tumour (TGCT), ovarian serous cystadenocarcinoma (OV), cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), head and neck squamous cell carcinoma (HNSCC), esophageal carcinoma (ESCA) and lung squamous cell carcinoma (LUSC). Nonetheless, the role of DMC1 in tumorigenesis remains unknown Our studies aim to evaluate the role of DMC1 in cell cycle progression, cell proliferation and cell survival.

Methods:

We used Cal27 (Head and Neck Squamous cell carcinoma) cell line to evaluate the expression of DMC1 using western blotting and RT-qPCR. With the use of shRNA mediated knockdown of DMC1, we evaluated the effects of DMC1 on cell proliferation, cell cycle progression and cell survival. Cell proliferation was evaluated by using Vi cell counter. Cell cycle analysis was carried out using flow cytometry. Clonogenic assay was performed to evaluate cell survival.

Results:

First, knockdown of DMC1 in Cal27 was confirmed by western blotting and RT-qPCR. Our experiments demonstrate that knockdown of DMC1 results in reduced cell proliferation ($p<0.05$), cell survival ($p<0.05$) and more cells in G0/G1 phase compared to control scramble cells.

Conclusions:

Our study shows that DMC1 knockdown is responsible for attenuating proliferation, cell survival and cell division in HNSCCs.

Learning objectives:

1. expression of DMC1 in HNSCC cell lines.
2. role of DMC1 in cell proliferation and cell survival.
3. role of DMC1 in cell cycle.

Takeaway Message:

DMC1 expression in HNSCC contributes to increased cell proliferation, cell survival and cell division, and thus may be involved in carcinogenesis. The function of DMC1 must be explored further to determine if its expression can be used as novel diagnostic and prognostic marker in HNSCCs.

Characterization And Functional Relevance of Microfibrillar-Associated Protein 4 (MFAP4) In Elastic Fiber Formation

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Introduction:
Skin requires various extracellular proteins to synthesize functional elastic fibers. Microfibrillar-associated protein 4 (MFAP4) is a glycoprotein involved in elastogenesis by binding to tropoelastin, fibrillins, type I collagen, lysyl oxidase, desmosine and insoluble elastin. MFAP4's structural conformation and specific interaction with other elastogenic proteins are not sufficiently explored.

Methods:
Structural properties of MFAP4 were analyzed by dynamic light scattering (DLS), atomic force microscopy (AFM), negative stain transmission electron microscopy (TEM), and cryo-TEM. MFAP4 binding to elastogenic proteins including LTBP4, fibrillin-1, short fibulins and fibronectin was assessed by surface plasmon resonance (SPR) spectroscopy.

Results:
AFM and negative staining TEM showed MFAP4 as rounded particles with approximately 15 nm diameter. DLS revealed that these particles represent octamers, very stable structurally as reduction to smaller units was not possible by high salt nor by chaotropic reagents. Single-particle analysis by cryo-TEM confirmed that MFAP4 forms an octameric assembly with D4 symmetry, each subunit (monomer) approximately positioned at a cube vertices. Intra-molecular disulfide bonds were resolved between four of the five cysteine residues within each monomer. A fifth cysteine residue in MFAP4 remained unresolved by our 3.2 Å map, suggesting that it forms a more flexible structure. This is the candidate residue mediating inter-molecular disulfide bond forming dimers. SPR confirmed binding to the N terminal fibrillin-1 fragment rFBN1-N (KD=5.7 nM). Surprisingly, MFAP4 also binds via a second binding site to a central region (rF1M) of fibrillin-1 with high affinity (KD=6.4 nM). MFAP4 binds relatively strongly to LTBP4L and S isoforms (KD=22-27nM), and moderately to fibulin-4 (KD=121 nM) and fibulin-5 (KD=357 nM). MFAP4 does not bind to fibulin-3 and fibronectin.

Conclusions:
We report new structural and functional properties of MFAP4 required to understand mechanistic aspects in elastogenesis and pathogenesis. The intra-molecular, but not inter-molecular disulfide bonds are stable structural components of the octameric MFAP4.

Learning objectives:
1. To characterize the structure of the MFAP4 - a glycoprotein involved in elastogenesis, but with unknown yet functional properties.
2. To determine the interactome of MFAP4 with elastogenic proteins.
3. To study the importance of a stable MFAP4 oligomeric structure (octamer) in the context of elastic fiber formation.

Takeaway Message:
Microfibrillar-associated protein 4 (MFAP4) is a protein highly relevant to skin as it participates in the process of elastic fiber formation. MFAP4 forms a very stable octameric assembly and interacts with crucial elastogenic proteins fibrillin-1, LTBP4-L and -S, fibulin-4 and fibulin-5.

Efficient Generation of Induced Pluripotent Stem Cell Derived Mesenchymal Stem Cells from A Non-Invasive, Accessible Tissue Source - The Plucked Hair Follicle

Fatehi A, Fayyad M, Farahat M, Taylor D, Rogers I

Introduction:
The development of induced pluripotent stem cell (iPSC) technology has introduced innovative ways in the field of regenerative medicine, where patient's own cells can be used as starting material for disease-modeling, drug testing and cell replacement therapies. These patient-specific, stem cell-based therapies are advantageous because they decrease the risk of adverse reactions due to immune rejection. However autologous therapies are still far away from being a commercially viable option due to the cost and complexity of scaling out manufacturing for each patient. Extraction of somatic cells found in umbilical cords, embryos, bone marrow and amniotic fluids, pose ethical uncertainties and are highly invasive to the patient, requiring extended recovery time. On the other hand, keratinocytes, located in the hair follicle, can be reprogrammed. The hair follicle is a multi-germ layer, versatile cell source containing both mesenchymal and epithelial components. It can also be obtained non-invasively, at any age and can be transported via regular mail channels, making it the ideal starting material for an autologous biobank. Currently mesenchymal stem cells (MSCs) are used to create skin grafts for wound healing. However, inter donor variability, limitations in availability and expansion senescence make it difficult to treat large burn wounds. Deriving MSCs from hair follicle iPSCs allows us to circumvent the limitations while facilitating large scale production.

Methods:
Keratinocytes are expanded from cryopreserved plucked hair follicles from various participants. The keratinocytes are reprogrammed using an Episomal vector system. The resultant iPSCs are expanded, characterized and differentiated towards mesenchymal stem cells using the Tran (small molecule) protocol. The iMSCs are validated and used in a pig wound healing model.

Results:
Primary keratinocytes, containing basal keratinocyte markers (K14 and K5) are expanded directly from the hair follicle till passage 4. Keratinocytes are easily reprogrammed using a feeder-free, non-integrative system. Any one regardless of age or sex has a chance of creating an iPS cell line. Younger individuals [18-40] may have higher reprogramming efficiencies. Reprogrammed cells express pluripotency markers at high amounts and pass residual vector testing. Hair Follicle derived iPSCs can be differentiated into mesenchymal stem cells using the Tran protocol.

Conclusions:
From a single hair follicle, we can derive scalable amounts of mesenchymal stem cells regardless of the age and sex of the donor. These iMSCs are capable of wound healing properties and can be used to treat deep wounds previously thought to be limited by the starting tissue material.

Learning objectives:
Participants will learn about: The subpopulations of cells found in the hair follicle and thus its utility as a starting tissue source in regenerative medicine; The Acorn method for collection, transport and cryopreservation; The method and benefits of reprogramming keratinocytes and the effect of sex and age on reprogramming; The ability to derive MSCs from iPSCs and their clinical application.

Takeaway Message:
Patient-matched, high quality iMSCs can be obtained from a diverse group of participants using cryopreserved, plucked hair follicles for wound healing and skin regeneration applications

Skin Research Group *of* Canada

SRGC

Nov 24-26 | 9th Annual Conference

Toronto 2022

Program at a Glance

Thursday, NOV 24	Friday, NOV 25	Saturday, NOV 26
Registration & Poster Set up 7:30 - 8:00am	Registration 8:00 - 8:30am	Registration 8:00 - 8:30am
Plenary Session 1: Clinical Skin Research 8:00 - 10:00am	Plenary Session III: Inflammatory Skin Diseases 8:30- 10:00am	Plenary Session V: Basic Sciences 8:30 – 10:00am
Come See My Poster (Moderated Poster Walks) Visit Our Sponsor Booths 10:00 - 12:00pm (Coffee and refreshments will be provided)	Come See My Poster 10:00 - 12:00pm (Coffee and refreshments will be provided)	Poster Take down 10:00 - 10:30am (Coffee Break) SRGC Keynote Lecture **"Studying Skin Cancers in Patients, Cell Lines and Mouse Models"** Ivan V. Litvinov, MD, PhD, FRCPC McGill University Health Centre President, SRGC 10:30 - 11:30am
SkIN Canada Workshop 12:00 - 2:00pm	SkIN Canada Workshop 12:00 - 2:00pm	SkIN Canada Workshop 12:00 - 2:00pm
SRGC Keynote Lecture Frontiers in Clinical Research **"Dupuytren's Disease – A riddle inside a mystery, wrapped in…skin?"** David O'Gorman, MSc PhD Western University 2:00 - 3:00pm	SRGC State-of-the-art Lecture **"Physiopathology of Human Skin Pigmentation: Biogenesis of Pigment Granules and Functions of Extracellular Vesicles"** Maria Da Graca Raposo, PhD CNRS | Institut Curie 2:00 - 3:00pm	**Closing and Awards Ceremony** **2:00 - 2:30pm**
Plenary Session II: Wound Healing and Regeneration 3:00 - 5:00pm	SRGC Plenary Session 1V: Skin Cancer 3:00 - 5:00pm	
SRGC Keynote Lecture Frontiers in Translational Research **"Anatomical Diversity of Skin in Development, Health & Disease"** Tanya Shaw, PhD King's College London 5:00 - 6:00pm	**FREE NIGHT**	
Welcome Reception (Space Limited) 6:00pm		

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