RE: Application to the GRAPPA Pilot Grant

Dear Review Committee,

I am submitting this application titled: *Sex differences in serum proteomic biomarkers in psoriatic arthritis.* This study will be conducted as part of my MSc studies at the University of Toronto under the supervision of Dr. Lihi Eder.

This project aims to identify sex-specific biological pathways in psoriatic arthritis (PsA) by integrating serum proteomic data in male and female patients with active PsA vs. healthy controls. This exciting project has the potential to unravel sex-specific serum protein biomarkers in PsA, which will address gaps in the knowledge surrounding the role of sex and gender. The results of this study will help develop sex-specific approaches to monitoring and managing PsA and ultimately advancing personalized medicine.

The mentor of the proposal is Dr. Lihi Eder, MD, PhD, Rheumatologist, Women's College Hospital, University of Toronto.

The mentee of the proposal is Steven Dang, BSc (MLS), MSc candidate, Institute of Medical Science, University of Toronto.

We thank you for taking the time to read our proposal and for your consideration.

Sincerely,

Steven Dang, BSc (MLS), MLT
MSc candidate
Institute of Medical Science
University of Toronto

Sex differences in serum proteomic biomarkers in psoriatic arthritis

Scientific Abstract

While the prevalence of psoriatic arthritis (PsA) is similar in males and females, the differences in the disease course, clinical presentation and response to therapy show sex dimorphisms. It remains unclear whether different biological mechanisms in immune pathogenesis are driving these differences between males and females with PsA. By unveiling the underlying mechanisms of sex dimorphisms, we move beyond simply reporting these differences between males and females with PsA and toward understanding how these differences arise and the means to address them. **The study aim** is to identify sex-specific serum proteins and biological pathways that influence PsA presentation. **We hypothesize** that sex dimorphisms exist in the immune and inflammatory profiles in PsA and that the profiles are correlated to the clinical features present in male and female patients. We will analyze serum samples from 100 males and females with active PsA (matched by age and psoriasis severity) and 50 age and sex-matched non-psoriatic controls from our biobank. A proteomic discovery analysis will be performed on a custom 1,500 protein multiplex SomaScan® assay. We will identify sex-specific protein biomarkers for PsA using machine learning methods and protein pathway analysis. The study's results will spearhead investigations of sex differences by correlating proteins to clinical and imaging features of PsA.

Lay Abstract

Male and female patients living with PsA experience the disease differently. Males develop more severe psoriasis and joint damage, whereas females suffer more pain and disability. The causes of these differences remain unknown. The proposed study aims to identify proteins and biological pathways that explain these sex variations in PsA. Blood samples from 100 patients (50 males, 50 females) with PsA will be identified from the University of Toronto PsA database and biobank. We will assess the levels of 1,500 proteins in the blood that represent biological pathways that are relevant to PsA. We will use complex analytical methods to identify differences in protein levels and biological pathways between male and female patients with PsA. This knowledge will inform the development of sex-specific approaches to monitor and manage PsA.

Background

The lack of sex-specific knowledge in psoriatic arthritis (PsA) limits the ability of clinicians to treat and diagnose patients effectively. While PsA is equally distributed among males and females, they experience differences in the disease course, clinical presentation and response to therapy. Females report higher disease activity scores, more significant loss of function and worse health-related quality of life[1–5]. They are 1.3 to 2.6 times more likely to discontinue biologic treatment due to reduced efficacy and adverse effects than males. In contrast, males experience worse skin psoriasis, increased radiographic progression and more severe axial disease of the spine and sacroiliac joints[1]. Male patients are 2 to 3 times more likely to achieve lower disease activity states than females[6–10]. Biological (sex-related) mechanisms could explain some of these differences between male and female patients with PsA.

The role of sex hormones, sex-chromosome-linked genes and genetic polymorphisms could affect the immune system[11,12]. Estrogen's bi-phasic nature in females induces a Th1 polarization in the luteal phase (low estrogen levels) and a Th2 polarization in the follicular phase (high estrogen levels). Suppressed estrogen levels enhance TNFα, IL-1β and IL-6 levels, all of which

factor in inflammatory conditions such as ankylosing spondylitis (AS) and PsA[12,13]. AS is an example of a sex dimorphism in the Th17 profile[14]. A Th17 signature is elevated in male patients, while a Th1 signature is similar for males and females[14]. While AS and PsA share some similar clinical and immunological features, there is an unmet need to identify the underlying mechanisms driving sex dimorphism in PsA. To date, much of the translational research in PsA focuses on understanding the pathophysiology, identifying diagnostic and prognostic biomarkers and studying novel treatment targets. However, little attention has been given to understanding the molecular and biological mechanisms driving the differences between males and females. Until we understand the phenomenon behind the differences, the ability to provide the best treatment for patients is hindered.

Study Objective and Hypothesis

The study's overall objective is to improve our understanding of how sex, as a biological variable, plays a role in PsA presentation and course. **The specific aim of the study** is to identify sex-specific serum proteins and biological pathways that influence PsA. **We hypothesize** that sex dimorphisms exist in the immune and inflammatory pathways in PsA and that the profiles are correlated to the clinical features present in male and female patients. Data regarding sex dimorphisms of immune and imaging data in AS support our hypothesis[14].

Significance for Psoriatic Disease

Our understanding of PsA will improve by unveiling sex-specific immune and inflammatory pathways that may explain the clinical differences in PsA presentation and course. Utilizing sex is one aspect of achieving precision medicine, but it is often neglected and can result in lost opportunities to inform care and could even result in safety issues. <u>This study will aim to establish sex-specific serum proteins that can be used to facilitate the development of sex-specific approaches to monitoring and managing PsA.</u>

Methods

Study Design: This cross-sectional study utilizes previously collected clinical information and serum samples from the University of Toronto PsA cohort. 50 male and 50 female patients with active PsA matched by age and psoriasis severity will be identified from the cohort database. 50 individuals with no prior diagnosis of psoriasis or PsA (1:1 male and female) matched by age and sex will be included as controls.

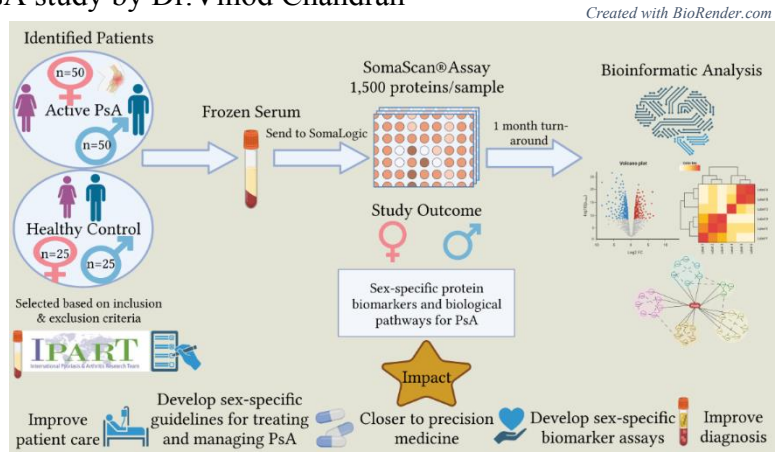
Inclusion Criteria: 1) Meet classification criteria for PsA (CASPAR); 2) Active PsA: about to initiate systemic therapy for peripheral musculoskeletal manifestations of PsA; 3) Have serum sample <u>prior</u> to initiating therapy in the biobank.

Exclusion Criteria: 1) Active cancer or end-stage major organ disease; 2) Are taking systemic corticosteroids.

Proteomic Analysis: Identified serum samples will be shipped to the SomaLogic core facility (Denver, US) for proteomic analysis. SomaLogic employs a unique slow off-rate modified aptamer (SOMAmer) that leverages single-stranded DNA to form 3-dimensional structures similar to antibodies. The SOMAmers are utilized in the multiplex SomaScan® assay to detect and measure relative protein levels. The assay offers high sensitivity, specificity and the ability

to measure 7,000 proteins simultaneously. We will measure 1,500 serum proteins using a custom multiplex discovery protein panel.

As preliminary work, we selected 1,500 proteins from the list of 7,000 in the SomaScan panel. Using the information on relevant PsA biomarkers from our group (proteins, genes, microRNA), previously identified targeted protein biomarkers in PsA and knowledge of potential sex dimorphisms of the immune, pain and metabolic pathways in other musculoskeletal conditions. An initial list of 80 mRNA biomarkers combined with targets of the top 80 microRNAs was identified as important from an ongoing PsA study by Dr.Vinod Chandran (unpublished) using mirDIP[15]. Proteins from the TNF and IL-17 pathways (using pathDIP) and relevant physical protein interactions (using IID) expanded the list[16,17]. 1,554 proteins were reduced to 1,481 by removing genes that met the following conditions: 1) not among top mRNA biomarkers or targeted by top microRNA biomarkers; 2) are not in any Reactome pathways; 3) present in only 1 pathway/source. The remaining 19 proteins were selected based on existing literature on biomarker research in PsA[18]. Overall, the selected panel includes a broad range of proteins related to multiple immune, inflammatory, and metabolic pathways. The proteins included a wide range of cytokines, chemokines, growth factors, hormones, bone and extracellular matrix markers, neutrophil end-products and more.



Bioinformatic Analysis: We plan to use machine learning classifiers in the mlr package in R to build predictive models from the proteomic data to predict sex-specific disease status. Two hundred predictive variables from the best-performing models will be analyzed to find correlated groups of variables and enriched pathways. Spearmen correlations will be calculated between pairs of variables. Weighted graphs from the selected variables, with edge weights corresponding to Spearmen correlation coefficients will be created using the igraph package in R. Communities will be selected using community-finding algorithms, and pathway enrichment analysis will be conducted using pathDIP version 4 using all 22 pathway database sources[16]. The study outcome will be a list of differentially expressed proteins and biological pathways for males and females with PsA.

Feasibility and Timeline: The applicant will perform the proposed work as part of his Master's thesis at the University of Toronto (UofT). Dr. Lihi Eder, Associate Professor of Medicine (UofT) and clinician-scientist who studies sex/gender in PsA, is his primary supervisor for his degree and will oversee the project. The applicant has written the study protocol, will identify study patients from the biobank and will facilitate the proteomic analysis of the SomaScan results. He will be involved in analyzing the proteomic data under the supervision of Dr. Igor Jurisica (Professor of bioinformatics, UofT). Dr.Vinod Chandran, Associate Professor of Medicine (UofT), an expert in translational research in PsA, is also involved in this project.

Budget

	Budget	Covered by Local Funds	Request from GRAPPA
SomaScan® Assay	$38,535	$13,535	$25,000
Master's Student (1 year)	$16,200	$16,200	$0
Bioinformatic Analysis	$5,500	$5,500	$0
Total	$60,235	$35,235	$25,000

Budget Justification

We request $25,000 from the GRAPPA Pilot Research Grant to partially cover the cost of conducting the SomaScan® assay. The cost of conducting the proteomic analysis is $257 per sample (Dec 2022 pricing). A total of 150 samples (100 patients with PsA and 50 controls) will be analyzed by SomaLogic. Local funds from the PsA program at the Women's College Hospital (Lihi Eder, PI) will cover the remaining costs of the study ($35,600).

References

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3. Queiro R, Tejón P, Coto P, et al. Clinical Differences between Men and Women with Psoriatic Arthritis: Relevance of the Analysis of Genes and Polymorphisms in the Major Histocompatibility Complex Region and of the Age at Onset of Psoriasis. *Clin Dev Immunol*. 2013;2013:1-7. doi:10.1155/2013/482691

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5. Theander E, Husmark T, Alenius GM, et al. Early psoriatic arthritis: short symptom duration, male gender and preserved physical functioning at presentation predict favourable outcome at 5-year follow-up. Results from the Swedish Early Psoriatic Arthritis Register (SwePsA). *Ann Rheum Dis*. 2014;73(2):407-413. doi:10.1136/annrheumdis-2012-201972

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15. Hauschild AC, Pastrello C, Ekaputeri GKA, et al. MirDIP 5.2: tissue context annotation and novel microRNA curation. *Nucleic Acids Res*. 2023;51(D1):D217-D225. doi:10.1093/nar/gkac1070

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Steven V. Dang
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(780) 807-7532

EDUCATION

University of Toronto, Institute of Medical Science, Toronto, ON
- Master of Science in Medical Science — Fall 2022 - Present

University of Alberta, Division of Medical Laboratory Science, Edmonton, AB
- Bachelor of Science in Medical Laboratory Science with Distinction — Fall 2014 - Spring 2019

RESEARCH EXPERIENCE

University of Toronto, Institute of Medical Science, Women's College Hospital — Fall 2022 - Present
Master's student with Dr. Lihi Eder & Dr. Vinod Chandran
- Thesis: Sex Dimorphisms of Immune Profiles in Psoriatic Arthritis

University of Alberta, Department of Laboratory Medicine & Pathology — Fall 2019 - Summer 2020
Undergraduate student with Dr. Joshua Raizman & Dr. Albert Tsui
- Developed laboratory reporting guidelines for patient results with hydroxocobalamin interference
- Assessed the interference across chemistry, urinalysis, hematology, coagulation and blood gas instruments in a clinical laboratory
- Research was highlighted by the University of Alberta and Alberta Health Services

Charité Universitätsmedizin Berlin, Department of Otolaryngology — Summer 2018
Research assistant with Dr. Agnieszka Szczepek
- Examined the impact of different concentrations of TNF-alpha and Cisplatin on the inferior and superior colliculi of newborn Wistar rats
- Assisted in setting up neuronal cell cultures followed by performing immunostaining on the cells
- Organized and translated lab procedures from German into English for international students

University of Alberta, Department of Chemistry — Summer 2015 - Fall 2016
Research assistant with Dr. Ratmir Derda
- Investigated the consensus sequence of O-GlcNAc transferase enzyme using phage display technology
- Assisted graduate students with their experiments
- Responsible for keeping stock of supplies such as agar, pipette tips and clean lab equipment

EMPLOYMENT

Dynalife Dx, Base Lab, Edmonton, AB
Medical Laboratory Technologist I, Microbiology — Summer 2019 – Present

Alberta Precision Labs, Misericordia Community Hospital, Edmonton, AB
Medical Laboratory Technologist I, Core Lab (Chemistry, Hematology) — Summer 2019 - Fall 2022

A Medical Laboratory Technologist (MLT) is a certified healthcare professional that uses complex instrumentation to analyze tissue samples, blood and other bodily fluids as part of the diagnostic procedure. They provide results to physicians, allowing them to make an accurate diagnosis and appropriate treatment.

SKILLS, TECHNIQUES and INSTRUMENTS

• DNA/RNA Extraction • PCR and quantitative PCR • Creating and interpreting gel electrophoresis • Phage Display Technology • Phage Amplification • Fluorescent Microscopy • Mammalian Cell Culture • Immunostaining • Beckman Coulter DxC600, DxH800, Access II	• Stago STA Compact Max • Siemens Clinitek Atlas • Siemens Clinitek Advantus • Roche Cobas c503, 801, ISE • ACL TOP 350 • Sysmex XN3100 • Vitek Mass Spectrometry • BD Kiestra • Sunquest & EPIC LIS • R Programming

LEADERSHIP EXPERIENCE

University of Toronto Fall 2022 - Current
Deputy of Sporting Events, Institute of Medical Science Students' Association
- Organize and facilitate sporting events with the Director of Sporting events for students attending the Institute of Medical Science graduate program

University of Alberta Fall 2019 - Spring 2020
President, Medical Laboratory Students' Association
- Led a group of 20 students to facilitate a welcoming environment for students in the program
- Oversee every position to ensure events, bake sales, graduation ceremony run smoothly
- Created the first student website (mlsassociation.wordpress.org)
- Initiated the annual Health sciences Workshop for high school and university students to spread awareness of several less-known healthcare fields

University of Alberta, Division of Medical Laboratory Science Fall 2019 - Spring 2020
Teaching Assistant, Clinical Hematology, Hemostasis and Transfusion Medicine
- Assisted the instructor in facilitating labs twice a week with three other teaching assistants
- Responsible for critiquing and assisting first-year medical lab students' in lab practices and theory
- Enforced proper clinical laboratory etiquette, procedures, safety and professionalism
- Provided daily feedback to reinforce proper behavior and to help students move in the right direction

PUBLICATIONS

Dang S, Tsui A, Herndon R, Babiak C, Szkotak A, Füzéry A, Raizman J. Hydroxocobalamin interference in routine laboratory tests: Development of a protocol for identifying samples and reporting results from patients treated with CyanokitTM. Clinical Biochemistry. 10.1016/j.clinbiochem.2021.01.001

CONFERENCE PRESENTATIONS

Dang S, Tsui A, Raizman J. Wine Coloured Samples? Development of laboratory guidelines for hydroxocobalamin interference in patients pulled from house fires. Poster session presented at Discovery, Research, Innovation and Education (DRIvE) (April 2019), Labcon (May 2019), Canadian Society of Clinical Chemists Conference (e-poster) (June 2019)

INVITED TALKS

Dang S, Tsui A, Raizman J. Wine Coloured Samples? Development of laboratory guidelines for hydroxocobalamin interference in patients pulled from house fires. Alberta Society of Clinical Chemists Symposium (September 2019)

PROFESSIONAL ASSOCIATIONS

College of Medical Laboratory Technologists of Alberta
Canadian Society of Medical Laboratory Science

AWARDS

Medical Laboratory Science Teaching Assistant Award	2019
Discovery, Research, Innovation and Education (DRIvE) Best Poster Presentation	2019
University of Alberta Medical Staff Proficiency Award	2018
The College of Medical Laboratory Technologists of Alberta Award	2017
Jason Lang Scholarship	2015-2017
University of Alberta Academic Excellence Scholarship	2014
Alexander Rutherford Scholarship	2014

LANGUAGES

German (B1, Intermediate - TelC Certification) 2018

PROFESSIONAL DEVELOPMENT

Introduction to Computer Science and Programming with Python
Massachusetts Institute of Technology (MIT), edX.com, 2020

- 9-week online course covering the fundamentals of computer science and basics of python programming (data types, functions, bisection search, approximation method, structured types, exceptions, assertions, classes, debugging, inheritance, searching and sorting algorithms, big O, introduction to pylab)
- Certificate earned on 26Mar2020

Statistics with R Specialization
Duke University, Coursera.com, 2020

- An online five-course specialization covering probability and data, inferential statistics, linear regression and modelling, Bayesian statistics and a capstone project.
- Certificate earned on 29Nov2020

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Women's College Research Institute
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Toronto, Ontario, Canada, M5S 1B2
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February 27, 2023

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

RE: Steven Dang (MSc candidate) - Nomination for Pilot Research Grant

Dear Review Committee:

It is a pleasure for me to provide a letter of endorsement for Steven Dang in support of his nomination for the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis Pilot Research Grant for the academic year 2023-2024.

Steven graduated from the University of Alberta in 2019 with a Bachelor of Science in Medical Laboratory Science (Distinction). During his time as an undergraduate, Steven completed several short research projects in medical laboratories in both Canada and Germany, where he gained valuable experience in research methodology and laboratory technical skills. Additionally, following his graduation and prior to starting his master's degree, Steven worked for 3-years as a Medical Laboratory Technologist, further enhancing his skills and knowledge. This experience allowed him to develop a keen understanding of the complexities involved in conducting scientific research, especially that of biomarker studies, which is highly relevant to his thesis.

I have had the privilege of working with Steven as his supervisor for his master's degree in the Institute of Medical Science at the University of Toronto since September 2022. Steven is working on a thesis-based master's degree in the field of translational research in rheumatology with a focus on sex dimorphisms in psoriatic arthritis (PsA). Although Steven only started working with me on this project a few months ago, he has demonstrated a deep understanding of the latest research in the field and has shown a remarkable ability to apply this knowledge to his own work.

Steven's proposed thesis project aims to identify sex specific biomarkers in patients with PsA, with the goal of improving diagnostic abilities, monitoring and treatment outcomes in this patient population. This project requires understanding in several clinical and research fields, and methods including clinical rheumatology, immunology, biomarker studies and bioinformatics. He will use advanced proteomic technology to identify and quantitate unique blood proteins which will be used, when correlated with clinical features, to explain the mechanisms causing differences in the disease course, clinical presentation, and response to therapy between males and females with PsA.

Steven's proposed project will utilize the extensive longitudinal data available from patients who were previously recruited to the well-established International Psoriasis and Arthritis Research

WOMEN'S COLLEGE HOSPITAL
Health care for women | REVOLUTIONIZED

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Team program. This includes clinical, laboratory and imaging data as well as biological samples stored in our biobank collected prospectively for over 39 years.

The University of Toronto Psoriatic Disease program is therefore the ideal setting for this research project, and I will ensure that Steven has full support of the Psoriatic Disease Research Program team including database programmers, research assistants and biostatistical experts from the University of Waterloo who work closely with our program. This research will form the basis of Steven's thesis and I'm sure will result in many important findings.

In addition to being a formal thesis supervisor, I will mentor Steven by having regular meetings to monitor his progress.

I enthusiastically support the nomination of this promising young researcher.

Sincerely,

Lihi Eder

Lihi Eder MD PhD
Associate Professor of Medicine
Canada Research Chair in Inflammatory Rheumatic Diseases (Tier 2)
Research Director, Division of Rheumatology
University of Toronto
Scientist, Women's College Research Institute, Rm 6326

BIOGRAPHICAL SKETCH

NAME: Eder, Lihi, MD PhD

POSITION TITLE: **Associate Professor of Medicine, University of Toronto**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completio n Date MM/YYYY	FIELD OF STUDY
Ben Gurion University, Beer Sheva, Israel	MD	02/2002	Medicine
Technion – Israel Institute of Technology, Haifa, Israel	Internal Medicine specialist	07/2007	Internal Medicine
University of Toronto, Toronto, Canada	Rheumatology specialist	08/2011	Rheumatology
University of Toronto, Institute of Medical Science, Toronto, Canada	PhD	08/2011	Clinical and Genetic Epidemiology
University of Toronto, Toronto, Canada	Post-Doctoral Fellow	12/2015	Rheumatology

Dr. Eder is Clinician-Scientist and Director of the Psoriatic Arthritis (PsA) Program, Division of Rheumatology, Women's College Hospital and Associate Professor of Medicine, University of Toronto. Dr. Eder has a broad background in rheumatology with specific training and expertise in clinical epidemiology and translational research in the field of PsA. Additionally, Dr. Eder has a particular interest in the application of musculoskeletal ultrasound as a research tool in PsA for understanding the underlying mechanisms of the disease.

More recently her research program focuses on studying the role of sex and gender as determinants of disease outcomes in patients with psoriatic disease. Dr. Eder has been awarded a Canada Research Chair in Inflammatory Rheumatic Diseases (2021-2026) for studying barriers of equitable care in rheumatology.

Dr. Eder serves in leadership roles in several organizations in the fields of psoriatic disease and rheumatology. She is President of the Canadian Rheumatology Ultrasound Society (CRUS), elected member of the GRAPPA (Group for Research and Assessment in Psoriasis and Psoriatic Arthritis) steering committee and co-chairs the ultrasound working group in GRAPPA. She currently leads the SAGE-PsA study, a GRAPPA-supported study (40 sites across the world), that will assess how sex and gender influence response to advanced therapies in PsA.

This leadership experience and expertise in ultrasound and clinical and translational research are critical for the success of this project. As PI on a number of national and international grants (CIHR, The Arthritis Society, NPF, GRAPPA), Dr. Eder laid the groundwork for the proposed research by developing expertise in sex/gender based analysis and musculoskeletal ultrasound and by establishing strong collaborations with expert investigators in biomarker research and bio-informatics that are relevant to this project.

Her research efforts have resulted in 154 peer-reviewed publications in medical journals (86 as senior or principle author, H-index 45; Google Scholar Jan 2023). As a recognized emerging expert in rheumatology she received several distinction awards including the Canadian Rheumatology Association Emerging Investigator Award (2023), The Arthritis Society New Investigator Award (2016) and the Ontario Ministry of Research and Innovation Early Researcher Award (2018).

B. Positions and Honors

Positions and Employment

2007-2008	Attending Physician Internal Medicine	Carmel Medical Centre, Haifa, Israel
2008-2011	Clinical Fellow-Rheumatology	University of Toronto
2009-2011	PhD Student	Institute of Medical Science University of Toronto
2011-2012	Attending Physician Rheumatology & Internal Medicine	Carmel Medical Centre, Haifa, Israel
2012-2015	Post-Doctoral Research Fellow Rheumatology	University of Toronto
2016-	Director Psoriatic Arthritis Program	Women's College Hospital, Toronto
2016-2021	Assistant Professor of Medicine	University of Toronto
2016-	Clinician Scientist	Women's College Research Institute
2017-2021	Associate Member	Institute of Medical Science University of Toronto
2021-	Full Member	Institute of Medical Science University of Toronto
2021-	Associate Professor of Medicine	University of Toronto
2021-	Research Director	Division of Rheumatology, University of Toronto

Other Experience and Professional Memberships

2008-currrent	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) – Elected Steering Committee member (since 2020) Ultrasound Committee – co-Chair (since 2018) Enthesitis Working Group - Chair, Treatment Recommendations (2021) Co-Chair Trainee symposium (since 2021)
2015-current	Canadian Rheumatology Ultrasound Society – President (since 2023) Executive Board Member and Research Director (since 2016) Co-Director, Basic Ultrasound Course for Rheumatologists (2019, 2022)
2018-current	Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN) – Steering committee (since 2021)
2023-current	European League Against Rheumatism (EULAR) – Treatment recommendations for PsA task force (Invited member)
2022-current	National Psoriasis Foundation – Scientific Advisory Committee (Invited member)
2017, 2018	USSONAR – Ultrasound School of North American Rheumatologists Lecturer and Instructor in Basic Ultrasound Courses
2013-current	Canadian Rheumatology Association – Member Research committee – Member (since 2019)
2009-current	American College of Rheumatology – Member

Honors and Awards

2023 Emerging Investigator Award, Canadian Rheumatology Association ($2,500)
2022 Institute of Medical Science Faculty Recognition Award for Strong Citizenship
2021 Canada Research Chair (Tier 2) in Inflammatory Rheumatic Diseases ($120,000)
2018 Ontario Ministry of Research and Innovation Early Researcher Award ($140,000)
2016 New Investigator Salary Award – The Arthritis Society ($180,000)
2017 Future Leaders in Rheumatology Training (FLIRT), Canadian Rheumatology Association
2017 Jean Davey Honorary Award, Women's College Hospital
2014 Canadian Institute of Health Research (CIHR) Fellowship Award ($110,000)
2014 The Heart and Stroke Foundation-Research Fellowship Award ($80,000, declined)
2014 Post-Graduate Research Award, University of Toronto ($10,000)
2014 American College of Rheumatology Travel Award - OMERACT
2013 Post-Graduate Research Award, University of Toronto ($10,000)
2009 Post-Doctoral Fellowship Award - The Canadian Arthritis Network ($80,000)
2009 University of Toronto Open Fellowship Award ($7,500)
2007 Fellowship Award - The Israeli Medical Association/American Physician Fellowship

C. Contribution to Science

Sex and Gender in Psoriatic Disease: Dr. Eder studied sex disparities in PsA. She was one of the first to report significant differences in PsA outcomes between men and women. More recently she described sex differences in response to advanced therapies among patients with PsA participating in RCTs. These results demonstrated sex dysmorphism in treatment response across modes of action suggesting that underlying mechanisms driving PsA activity may be different between males and females. Dr. Eder also described sex disparities in utilization of healthcare resources prior to the diagnosis of PsA at the population level in Ontario, which may explain the delays in diagnosis of the disease among women. Dr. Eder leads the SAGE-PsA study in GRAPPA, an international study that involves 40 sites across the world that will assess how sex and gender related mechanisms affect response to advanced therapies in PsA.

1. Eder L, Thavaneswaran A, Chandran V, Gladman DD. Gender differences in disease expression, radiographic damage and disability among patients with psoriatic arthritis. Ann Rheum Dis. 2013; 72: 578-82
2. Eder L, Hans-Peter T, Odhav S, Galindez Agirregikoa E, Korkosz M, Schwartzman S, Trevelin Sprabery A, Gellettt AM, Young S, Bertram CC, Ogdie A. Responses to Ixekizumab in Male and Female Patients with Psoriatic Arthritis: Results from Two Randomized, Phase 3 Clinical Trials. Rheumatol Ther. 2022; 9: 919-933
3. Tarannum S, Widdifield J, Wu CF, Johnson SR, Rochon P, Eder L. Understanding sex-related differences in healthcare utilization among patients with inflammatory arthritis: a population- based study. Ann Rheum Dis. 2022 Online ahead of print
4. Tarannum S, Leung YY, Johnson SR, Widdifield J, Strand V, Rochon P, Eder L. Sex- and Gender-related differences in psoriatic arthritis. Nat Rev Rheumatol. 2022; 18: 513-26

Musculoskeletal ultrasound in psoriatic arthritis: Dr. Eder is a recognized expert in the field of musculoskeletal ultrasound. By using ultrasound to identify imaging endo-phenotypes of PsA she studies genetic and other molecular biomarkers that may drive the various clinical manifestations of PsA. She described a link between genetic markers and sonographic enthesitis and showed that gene expression drives imaging phenotypes in PsA. As co-chair of the ultrasound committee in GRAPPA she is involved in the development of sonographic outcome measures for PsA. She currently leads the development of a novel diagnostic sonographic enthesitis score that will help differentiate PsA from other rheumatic conditions (DUET study).

1. Eder L, Li Q, Rahmati S, Rahman P, Jurisica I, Chandran V. Defining imaging sub-phenotyps of psoriatic arthritis: integrative analysis of imaging data and gene expression in a PsA patient cohort. Rheumatology (Oxford) 2022; 28: 4952-61.
2. Polachek A, Cook R, Chandran V, Abji F, Gladman D, Eder L. The Association Between HLA genetic Susceptibility Markers and Sonographic Enthesitis in Psoriatic Arthritis. Arthritis Rheumatol. 2018; 70: 756-62.
3. Eder L, Kaeley GS, Aydin SZ. Development and Validation of a Sonographic Enthesitis Instrument in Psoriatic Arthritis: The GRAPPA Diagnostic Ultrasound Enthesitis Tool (DUET) Project. J Rheumatol Suppl. 2020; 96: 50-52.
4. Polachek A, Cook R, Chandran V, Gladman DD, Eder L. The association between sonographic enthesitis and radiographic damage in psoriatic arthritis. Arthritis Res Ther. 2017; 19: 189

The transition from Psoriasis to PsA: Dr. Eder studies pre-clinical phases of PsA, in particular the transition from psoriasis to PsA. Her research identified risk factors for the development of PsA among patients with psoriasis. Additionally, she was the first to describe a prodromal, pre-diagnosis phase of PsA, which highlighted some of the difficulties in early diagnosis of the disease. These findings contributed to the understanding of the etiology of PsA. As site PI in IPART (International Psoriasis and Arthritis Research Team), she developed a novel prediction score to estimate the risk of development of PsA (PRESTO tool) at the level of an individual patient.

1. Eder L, Haddad A, Rosen CF, Lee KA, Chandran V, Cook R, Gladman DD. The Incidence and Risk Factors for Psoriatic Arthritis in Patients with Psoriasis: A Prospective Cohort Study. Arthritis Rheumatol 2016; 68: 915-23.
2. Eder L, Polachek A, Rosen CF, Chandran V, Cook R, Gladman DD. The Development of Psoriatic Arthritis in Patients with Psoriasis is Preceded by a Period of Nonspecific M
3. Eder L, Widefield J, Rosen CF, Cook R, Lee KA, Alhusayen R, Paterson MJ, Cheng SY, Jabbari S, Campbell W, Bernatsky S, Gladman DD, Tu K. Trends in the prevalence and incidence of psoriasis and psoriatic arthritis in Ontario, Canada: A Population based study. Arthritis Care Res (Hoboken) 2019; 71: 1084-91

A complete list of publications can be found at:

https://pubmed.ncbi.nlm.nih.gov/?term=lihi%20eder

D. Research Support

Current and Prior Research Support (Selected grants)

1. **Title:** Sex- And Gender-based analysis of Effectiveness of advanced therapies in Psoriatic Arthritis (SAGE-PsA) (**Role:** Principal Investigator)
   Funding Source: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (Jan 2023- Jan 2025)
   Total Funding: 700,000 (USD)
2. **Title:** Methods for assessing real-world causal effects with electronic health records: biologic therapies in autoimmune diseases (**Role:** Co-Investigator; **PI:** Richard Cook)
   Funding Source: Canadian Institute of Health Research (CIHR) (Oct 2022- Sep 2027)
   Total Funding: 61,113 (Canadian Dollars)
3. **Title:** Sex Dysmorphism in Immune Profiles in Psoriatic Arthritis (**Role:** Principal Investigator)
   Founding Source: Spondyloarthritis Research Consortium of Canada. Research Pilot Project Grant (Jul 2022- Jun 2023)
   Total Funding: 25,000 (Canadian Dollars)

4. **Title:** Derivation of a Psoriatic Arthritis Risk Estimation Tool (PRESTO): A Step Towards Prevention (**Role:** Principal Investigator)
   Founding Source: Physicians' Services Incorporated (PSI) Foundation (Oct 2020- Sep 2023)
   Total Funding: 219,000 (Canadian Dollars)

5. **Title:** Dietary Interventions in psoriatic arthritis (DIPsA): A Randomized, controlled, pilot trial. (**Role:** Principal Investigator)
   Founding Source: Canadian Institute of Health Research (CIHR). (Apr 2020- Mar 2023)
   Total Funding: 351,900 (Canadian Dollars)

6. **Title:** Deep cellular immune profiling in psoriatic arthritis: A step towards individualized therapy (**Role:** Principal Investigator)
   Funding Source: National Psoriasis Foundation (USA) (Aug 2020- Jul 2021)
   Total Funding: 75,000 (USD)

7. **Title:** Development and Validation of Sonographic Enthesitis Instrument in PsA - The GRAPPA Diagnostic Ultrasound Enthesitis Tool (DUET). (**Role:** Principal Investigator)
   Funding Source: Group for Research and Assessment of Psoriasis and Psoriatic (GRAPPA). (Jan 2020- Dec 2023)
   Total Funding: 1,000,000 (USD)

8. **Title:** Derivation and Validation of a Disease-Specific Cardiovascular Risk Prediction Score for Psoriatic Disease Using Patient Registry and Population-Based Study (**Role:** Principal Investigator)
   Funding Source: Canadian Institute of Health Research (CIHR) (2019-2020)
   Total Funding: 100,000 (Canadian Dollars)

9. **Title:** Defining imaging subphenotypes in PsA and their correlation with molecular signature – A step towards precision medicine (**Role:** Principal Investigator)
   Funding Source: National Psoriasis Foundation (2018-2019)
   Total Funding: 75,000 (USD)

10. **Title:** Investigation of the Interplay between Inflammation, Metabolic Abnormalities and Cardiovascular Risk and Development of Cardiovascular Risk Score in Psoriatic Disease (**Role:** Principal Investigator)
    Funding Source: The Arthritis Society (2017/5-2020/4)
    Total Funding: 309,266 (Canadian Dollars)
11. **Title:** Could systemic anti-psoriatic therapy modify psoriatic arthritis risk in patients with moderate-severe psoriasis? – A population-based cohort study (**Role:** Principal Investigator) **Funding Source:** GRAPPA (2017/8-2019/7)
    Total Funding: 25,000 (American Dollars)

12. **Title:** Raising Awareness of the Under-Recognized Burden of Psoriatic Diseases (**Role:** Principal Investigator)
    Funding Source: The Canadian Rheumatology Association (2017/7-2019/6)
    Total Funding: 119,024 (Canadian Dollars)

13. **Title:** Metabolomics Profiling for Identification of Potential Biomarkers for Atherosclerosis Progression in Psoriatic Disease (**Role:** Principal Investigator)
    Funding Sources: National Psoriasis Foundation (2016/7 - 2017/6)
    Total Funding: 73,860 (USD)