October 2020

To our Stakeholders,

As we are all aware, COVID-19 has presented significant challenges not only in Canada but globally, and over the past months, the focus has been to prevent the spread of this virus, keep people safe and healthy, and contain the virus so that we can build a more resilient Canada.

At the University Health Network (UHN) which is the lead site of the SPARCC Research Program in Toronto, research operations have been halted since mid-March 2020, as well in all other core and collaborating sites of SPARCC across Canada. All coordinating efforts are in place at UHN to ensure that our processes are aligned and in compliance with municipal and provincial directives. The UHN Research Restart Committee have developed and made recommendations for the eventual restart of research activities that include, among others: adherence to government and institutional directives, safety of staff and readiness of the institution (e.g., capacity and PPE), prioritization of staff to resume activities with equity considerations, and staff screening and monitoring. We have recently transitioned to a gradual restart phase adapting to the new virtual format. Most recently, a decision has been reached at UHN to remain in a modified Phase 2 for the foreseeable future. This means that for now, we will continue with the two-shift model and 50% on-site density for research laboratories. This approach has allowed for a safe and productive work environment which is also aligned with those at other research hospitals.

Therefore, while recruitment across the SPARCC network is gradually evolving, sample dispatch to our biobank facility at UHN from core and collaborating sites remains suspended. These sites continue to keep their samples in their respective sites until further notice. As we now experience a second wave of COVID-19, we are hopeful that a vaccine will soon be available, and this pandemic will come to an end at the not-so-distant future. By then, our research operations will be fully operational at UHN as well as in all of SPARCC's core and collaborating sites; if not realistic towards the end of 2020, at least in early next year.

In light of the above reality, our productivity in SPARCC has somehow been affected. We are therefore providing you an interim progress report as outlined below, with the resources available to us at this time. Please bear with us during these unprecedented times amid COVID-19.

Thank you for your understanding and cooperation. Stay safe!!!!

Sincerely,

The SPARCC Executive Committee

DATABASE UPDATE

The following table illustrates the distribution of patients entered into the SPARCC database since its inception in 2006 through mid-March 2020.

The database is the platform for phenotype ascertainment and includes all SpA patients recruited from core sites as well as collaborating sites: ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), undifferentiated spondyloarthritis (uSpA), and non-radiographic axial spondyloarthritis (nr-axSpA).

SPARCC Dataset

Site	AS	PsA	nr-ax	ReA	USpA	Total
TWH	1250	1590	266	33	104	3243
St. John's	287	542	0	0	0	829
Edmonton	836	0	0	0	0	836
Montreal	74	97	7	2	14	194
Winnipeg	39	0	0	0	0	39
Saskatoon	16	16	1	4	4	41
London	164	181	6	0	0	351
Newmarket	55	10	9	2	0	76
Vancouver	140	0	11	0	0	151
Hamilton	6	0	0	0	0	6
Calgary	21	2	0	0	1	24
McGill	52	13	2	0	0	67
WIRRA	24	28	1	0	1	54
Ottawa	4	17	0	0	0	21
WCH	0	232	0	0	0	232
Total	2968	2728	303	41	124	6164

SUMMARY OF KEY IMPACTS ACHIEVED

Overview of SPARCC Genetic Studies

(A report by Dr. Proton Rahman, SPARCC Executive Committee and Co-Principal Investigator, Memorial University of Newfoundland)

Advances in Genetics of AS and PsA

To provide better elucidation of the heritability of psoriatic disease subsets, we used two mixed-effect modelling methodologies to assess the additive contribution of common single nucleotide polymorphisms from genome-wide association studies to estimate the heritability of cutaneous psoriasis, psoriasis vulgaris and psoriatic arthritis. We found that cutaneous psoriasis and psoriatic arthritis both exhibit considerable heritability, with a greater contribution coming from cutaneous psoriasis.

We provided a general overview and current challenges regarding the genetics of psoriatic disease. With the use of integrative medicine, multiple candidate loci identified to date in psoriatic disease was annotated, summarized and visualized. Recent studies reporting differences in genetic architecture between psoriatic arthritis and cutaneous only psoriasis were highlighted.

Recently completed a phamacogenetic study that interrogated 40 PsA patients initiating either tumour necrosis factor inhibitors (TNFi) or interleukin-17A inhibitors (17Ai) for active PsA. Using transcriptomic data at initiation of therapy, we identified over 100 differentially expressed genes (DEGs) that differentiated IL-17Ai response from non-response and TNFi response from non-response. Integration of cell-type-specific DEGs with protein-protein interactions (PPIs) and further comprehensive pathway enrichment analysis revealed several pathways.

Publications:

1. *Rahmati S, Tsoi L, O'Rielly D, Chandran V, Rahman P. Complexities in Genetics of Psoriatic Arthritis. Current Rheumatology Reports. 2020. 22(4): 1-8.*

2. *Li Q, Chandran V, Tsoi L, O'Rielly D, Nair RP, Gladman D, Elder JT, Rahman P. Quantifying Differences in Heritability among Psoriatic Arthritis (PsA), Cutaneous Psoriasis (PsC) and Psoriasis vulgaris (PsV). Scientific Reports. 2020 Mar 18;10(1):1-6.*

3. *Chandran V, Rahman P. Predicting therapeutic response through biomarker analysis in psoriatic arthritis, an example of precision medicine. Expert Review of Precision Medicine and Drug Development. (2020). 5(1): 35-42.*

Overview of SPARCC AS (Ankylosing Spondylitis) Related Studies

(A report by Dr. Robert Inman, SPARCC Executive Committee and Co-Principal Investigator, UHN- Toronto Western Hospital)

Advances in Immunophenotyping T cells in AS

Current evidence suggests that immune events in the gut may impact joint inflammation in ankylosing spondylitis (AS) but the expression of gut-related trafficking molecules in the inflammed joint is poorly characterised. We aimed to (1) assess differential expression patterns of trafficking molecules between patients and controls, (2) generate joint-specific cellular signatures and (3) obtain transcriptomic profiles of noteworthy cell subpopulations. In a recent study we examined male subjects under 40 years of age fulfilling the mNY criteria for AS. The following cells were surface stained using a 36-marker mass cytometry antibody panel: (1) peripheral

blood mononuclear cells from AS patients, and healthy controls; (2) synovial fluid mononuclear cells from AS and rheumatoid arthritis (RA) patients. Additionally, RNA-seq was performed on CD8+ T cell subpopulations from the synovial fluid (SF). We discovered that mature CD8+ T cells were enriched in AS SF, with a distinct pattern of integrin expression (β7, CD103, CD29 and CD49a). RNA-seq analysis of SF-derived CD103+CD49a+CD8+ T cells revealed elevated TNFAIP3, GZMB, PRF1 and IL-10. Thus, we have identified a novel integrin-expressing mature CD8+ T cell population (CD49a+CD103+β7+CD29+) that appears to be more prevalent in AS SF than RA SF. These cells seem to possess dual cytotoxic and regulatory profiles, which may play a role in AS pathogenesis.

Publications:

1. *Kelly OB, Li N, Smith M, Chan J, Inman RD, Silverberg MS. The prevalence and clinical association of subclinical sacroiliitis in inflammatory bowel disease. Inflamm Bowel Dis 25: 1066-1071, 2019.*

2. *Gracey E, Dumas E, Yerushalmi M, Qaiyum Z, Inman RD, Elewaut D. The ties that bind: skin, gut and spondyloarthritis. Curr Opin Rheumatol. 31: 62-69, 2019.*

3. *Passalent L, Hawke C, Lawson D, Omar A, Alnaqbi K, Wallis D, Steinhart H, Silverberg M, Wolman S, Derzko-Dzulynsky L, Haroon N, Inman RD. Advancing early identification of axial spondyloarthritis: An interobserver comparison of extended role practitioners and rheumatologists. J Rheumatol. 2019 May 1.(Epub ahead of print)*

4. *Mease P, Walsh JA, Baraliakos X, Inman R, de Vlam K, Wei JC, Hunter T, Gallo G, Sandoval D, Zhao F, Dong Y, Bolce R, Marzo-Ortega H. Translating improvements with ixekizumab in clinical trial outcomes into clinical practice: ASAS40, Pain, Fatigue, and Sleep in Ankylosing Spondylitis. Rheumatol Ther. 6: 435-450, 2019.*

5. *Feld J, Ye JY, Chandran V, Inman RD, Haroon N, Cook R, Gladman DD. Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis? Rheumatology (Oxford). 59: 1340-1346, 2020.*

6. *Qaiyum Z, Gracey E, Yao Y, Inman RD. Integrin and transcriptomic profiles identify a distinctive synovial CD8+ T cell subpopulation in spondyloarthritis. Ann Rheum Dis.78: 1566-1575, 2019.*

7. *Sari I, Lee S, Tomlinson G, Johnson SR, Inman RD, Haroon N. Factors predictive of radiographic progression in ankylosing spondylitis. Arth Care Res Nov 1, 2019 (Epub ahead of print)*

8. *Gracey E, Yao Y, Qaiyum Z, Lim M, Tang M, Inman RD. Altered cytotoxicity profile of CD8+ T cells in ankylosing spondylitis. Arthritis Rheumatol. 72: 428-434, 2020*

9. *Qaiyum Z, Gracey E, Yao Y, Inman RD. Paradox of circulating TRM. Ann Rheum Dis 2019 Dec 18 (Epub ahead of print)*

10. *Gracey E, Hromadová D, Lim M, Qaiyum Z, Zeng M, Yao Y, Srinath A, Baglaenko Y, Yeremenko N, Westlin W, Masse C, Müller M, Strobl B, Miao W, Inman RD. TYK2 inhibition reduces type 3 immunity and modifies disease progression in murine spondyloarthritis. J Clin Invest. 130: 1863-1878, 2020.*

11. *Lin A, Inman RD, Streutker CJ, Zhang Z, Pritzker KPH, Tsui HW, Tsui FWL. Lipocalin 2 links inflammation and ankylosis in the clinical overlap of inflammatory bowel disease (IBD) and ankylosing spondylitis (AS). Arthritis Res Ther 22:51-58, 2020.*

12. *Lawson DO, Eraso M, Mbuagbaw L, Joanes M, Aves T, Leenus A, Omar A, Inman RD. Tumour necrosis factor inhibitor dose reduction for axial spondyloarthritis: A systematic review and meta-analysis of randomized controlled trials. Arthritis Care Res 2020 Mar 12.*

(A report by Dr. Nigil Haroon, SPARCC Co-Investigator, Co-Director –Spondylitis Program, UHN - Toronto Western Hospital)

COVID-19 and Rheumatology: Challenges and Opportunities

A very unusual year indeed. The outpatient visits were restricted and this has affected our recruitment for ongoing studies. Given the significant impact of COVID19 on our lives, we decided to systematically study the effects of this pandemic on AS patients. We struck up a collaboration with UCSF and sent out a survey to identify the factors affecting disease activity during this period. The results now published in ACR Open Rheum suggests that anxiety and stress were the most important factor that positively correlated with disease activity as assessed by BASDAI. Follow up questionnaires in this population will help us understand the changes in medications and other factors related to care that were altered by the COVID19 pandemic.

Mental Health and AS

Mental health (MH) is an important aspect of chronic diseases and assessing this in AS patients is an important aspect of clinical care. We studied mental health service use in AS ad RA patients using an Ontario-wide administrative database. The risk of MH hospitalizations was significantly increased in AS (HR 1.36, 95% CI 1.12-1.63) and RA patients (HR 1.34, 95% CI 1.22-1.47). In a separate study in the same cohort of patients, AS patients were identified to have a 59% higher risk of deliberate self-harm compared to controls while this was not significant in RA patients.

Publications:

1. *Liew JW, Castillo M, Zaccagnino E, Katz P, Haroon N, Gensler LS. Patient- reported Disease Activity in an Axial Spondyloarthritis Cohort during the COVID-19 Pandemic. ACR Open Rheumatol. 2020 Sep;2(9):533-539. doi: 10.1002/acr2.11174. Epub 2020 Sep 6. PMID: 32893508; PMCID: PMC7504475.*

2. *Ajrawat P, Touma Z, Sari I, Taheri C, Diaz Martinez JP, Haroon N. Effect of TNF-inhibitor therapy on spinal structural progression in ankylosing spondylitis patients: A systematic review and meta-analysis. Int J Rheum Dis. 2020 Jun;23(6):728-743. doi: 10.1111/1756-185X.13829. Epub 2020 May 17. PMID: 32419337.*

3. *Nakamura A, Talukdar A, Nakamura S, Pathan E, Haroon N. Bone formation in axial spondyloarthritis: Is disease modification possible? Best Pract Res Clin Rheumatol. 2019 Dec;33(6):101491. doi: 10.1016/j.berh.2020.101491. Epub 2020 Apr 15. PMID: 32305314.*

4. *Kuriya B, Vigod S, Luo J, Widdifield J, Haroon N. The risk of deliberate self-harm following a diagnosis of rheumatoid arthritis or ankylosing spondylitis: A population-based cohort study. PLoS One. 2020 Feb 21;15(2):e0229273. doi: 10.1371/journal.pone.0229273. PMID: 32084192; PMCID: PMC7034875.*

5. *Kuriya B, Tia V, Luo J, Widdifield J, Vigod S, Haroon N. Acute mental health service use is increased in rheumatoid arthritis and ankylosing spondylitis: a population-based cohort study. Ther Adv Musculoskelet Dis. 2020 Jun 7;12:1759720X20921710. doi: 10.1177/1759720X20921710. PMID: 32550868; PMCID: PMC7278302.*

Overview of PsA (Psoriatic Arthritis) Studies

(A report by Dr. Dafna D. Gladman, SPARCC Executive Committee and Co-Principal Investigator, U H N - Toronto Western Hospital)

Comparison between Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA)

A question that has often arisen regarding Spondyloarthritis (SpA) is whether radiographic axial SpA (AS) is different from axial PsA which affects 25-70% of patients with PsA. We aimed to address this question through the Toronto component of SPARCC (1). Since patients in the PsA clinic and AS clinic in Toronto have been followed according to the same protocol we were able to carry out such comparison. One thousand three hundred and three patients with PsA were included, of whom 477 had axial PsA, 61% had axial disease at presentation and the rest developed axial disease during follow-up. Patients with axPsA were followed for 6.7 year and those with peripheral PsA (pPsA) were followed for 12.7 years. We included 766 patients with AS of whom 675 did not have any history of psoriasis, and 91 (12%) were reported to have concomitant psoriasis. Of those 21 had psoriasis at their baseline visit and 70 developed psoriasis in the course of follow-up. AS patients with psoriasis were followed for 5.4 years and those without were followed for 3.5 years. Patients with AS were youger at diagnosis compared to those with PsA with or without axial disease. There were more males among AS patients, and they were more likely to have HLA-B*27 than those with PsA, even those with axPsA. Patients with PsA had more actively inflamed joints, and there was no difference between the group with axPsA and pPsA. Back pain was more common among patients with AS than those with both axPsA and pPsA. Enthesitis and dactylitis were more common among the PsA patients while iritis was more common in the AS patients. However, patient global assessment of disease activity was similar and ASADS-ESR was also similar. One of the advantages of our cohorts over other cohorts described in the literature is that our patients have been followed longitudinally. We were able to compare these variables over time and showed that the differences were maintained over time. We then used a logistic regression with the outcome being AS with psoriasis or axPsA. We demonstrated that HLA-B*27 was associated with AS with psoriasis whereas active arthritis was associated with axPsA. BASMI was higher in AS patients with psoriasis than in axPsA. The severity of sacroiliitis was higher in AS with psoriasis than in axPSA. Use of biologic agents was similar. We concluded that AS patients with or without psoriasis are different demographically, genetically, clinically and radiographically from axPsA patients suggesting that axPsA is a distinct entity.

Other Studies

A study of liver disease in PsA and found that Independent factors associated with liver abnormalities were higher body mass index (BMI), daily alcohol intake, higher damaged joint count, elevated C-reactive protein, and use of methotrexate, leflunomide, or tumor necrosis factor inhibitors (2).

We have also studied remission in PsA and demonstrated that defining remission as having no evidence of clinical activity at all and having the patient reported outcome at the level of minimal disease activity definition 18% of the patients achieved remission at least once, and almost 10% achieved a sustained remission for a year. Patients treated with biologic agents are more likely to achieve remission (3).

We recently demonstrated that the levels of chemokine CXCL10, which was initially identified as a gene overexpressed in PsA patients compared to psoriasis without arthritis (PsC), and is increased in patients with PsC destined to develop PsA, actually drops once PsA is diagnosed and continue to fall after the diagnosis. This may suggest that there is honing of CXCL10 and the cells producing it into the synovium (4).

Publications:

1. *Feld J, Ye JY, Chandran V, Inman RD, Haroon N, Cook R,* ***Gladman DD****. Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis? Rheumatology (Oxford) 2020;59:1340-1346.*

2. *Pakchotanon R, Ye Y, Cook RJ, Chandran V,* ***Gladman DD****. Liver Abnormalities in Patients with Psoriatic Arthritis. J Rheumatol 2020;47:847-853.*

3. *Al Harbi S, Lee Ker-Ai, Chandran V, Cook R,* ***Gladman DD.*** *Remission in psoriatic arthritis: Definition and predictors. Semin Arthritis Rheum. Online 2020/02/03.*

4. *Abji F, Lee K, Math M, Pollock RA, Machhar R, Cook RJ, Chandran V,* ***Gladman DD****. Declining levels of serum CXCL10 over time are associated with new onset of psoriatic arthritis in patients with psoriasis: A new biomarker? British Journal of Dermatology. Online 2020/02/09.*

(A report by Dr. Vinod Chandran, SPARCC Co-Investigator, Co-Director –Psoriatic Arthritis Program, UHN - Toronto Western Hospital)

Metabolomics in PsA

Metabolomics refers to the systematic identification and quantification of the small (<1500 Da) molecule metabolic products (the metabolome) of a biological system at a specific point in time. While genomics studies the genetic basis of phenotype, and transcriptomics and proteomics study the products of these genes, metabolomics seeks to identify the downstream effects caused by the action of these enzymes and proteins as well as the influence of environmental exposures in the context of metabolic activity.

We used a novel sample preparation protocol based on solid-phase microextraction (SPME) to prepare serum samples obtained from: 1) individuals with psoriasis, some of whom develop psoriatic arthritis (n=20) and 2) individuals with varying PsA activity (mild, moderate, severe; n = 10 each). Metabolomic fingerprinting of the obtained extracts was performed using reversed phase liquid chromatography coupled to high resolution mass spectrometry. We demonstrated that psoriasis patients who developed PsA had similar metabolomic profiles to patients with mild PsA and were also indistinguishable from patients with psoriasis who did not develop PsA.

Elevated levels of selected long-chain fatty acids (e.g., 3-hydroxytetradecanedioic acid) that are associated with dysregulation of fatty acid metabolism, were observed in patients with severe PsA. In addition, 1,11-undecanedicarboxylic acid – an unusual fatty acid associated with peroxisomal disorders – was also identified as a classifier in PsA patients vs. healthy individuals. Furthermore, S-aminomethyldihydrolipoamide, related to serine and threonine metabolism, pathways previously reported to be affected in psoriasis patients, was also tentatively identified. Thus, we employed a global metabolomics approach to analyze the serum metabolome of patients with psoriasis, PsA, and healthy controls in order to examine potential differences in the biochemical profiles at a metabolite level. A closer examination of circulating metabolites may potentially provide early markers of disease conversion and PsA activity.

Publication:

Looby N, Roszkowska A, Reyes-Garcesa N, et al. Serum metabolic fingerprinting of psoriasis and psoriatic arthritis patients using solid-phase microextraction – liquid chromatography – high-resolution mass spectrometry. Metabolomics 2020 (submitted)

Various SPARCC On-going Initiatives and Sub-studies on SpA

(A report by Ms. Laura Passalent, ACPAC Physiotherapist, Spondylitis Program, UHN-Toronto Western Hospital)

Advancing Models of Care for the Early Detection of Axial Spondyloarthritis

The Toronto Western Hospital has continued to operate its Spondylitis Screening Clinic receiving referrals from primary care providers and through the Ontario Ministry of Health's Rapid Access Clinics Low Back Pain Programs across the Greater Toronto Area (GTA). The screening clinic has successfully pivoted to a virtual platform since the onset of the COVID-19 pandemic. In addition, the Toronto Western Hospital Spondylitis Program has received an investigator initiated unrestricted grant from UCB Canada to run a pilot axial spondyloarthritis screening program beyond the GTA out of St. Joseph's Health Care in London, Ontario, with Dr. Sherry Rohekar and Dr. Tristan Boyd as co-investigators. This is in collaboration with the South Western LHIN's Rapid Access Clinic Low Back Pain program, located at London Health Sciences Centre.

Physical Activity and Exercise in Axial Spondyloarthritis

The Spondylitis Program at Toronto Western Hospital was awarded a CIORA grant in 2019 for the project entitled, "physical activity (PA) in axial spondyloarthritis (axSpA): development and implementation of an evidence-based health technology approach to improve adherence to recommended guidelines. This project includes co-investigators from the Department of Physical Therapy, Faculty of Medicine at the University of Toronto, the Arthritis Program, Krembil Research Institute and collaboration with the Canadian Spondylitis Association. Phase 1 of this project was recently completed and focused on key informant interviews of SPARCC registered patients regarding: axSpA patients' definition of PA; identification of facilitators and barriers to PA participation and exploration of the importance of PA in the context of axSpA. In addition, key informant interviews also aimed to understand the role of technology to increase PA engagement amongst patients with axSpA with respect to: smartphone habits; technology design; electronic reminders; performance feedback and virtual support. Abstracts have been submitted for peer review to the CRA/AHPA Annual Scientific Meeting, 2021. Phase 1 results will inform the development of the Phase 2 e-health intervention to increase PA uptake in patients with axSpA to be evaluated via randomized control trial with SPARCC registered patients. It is expected the development of a patient-centered intervention that utilizes existing technology will positively affect the uptake of PA in patients with axSpA and thereby improve disease-related outcomes and quality of life in this patient population.

Education update

SPARCC investigators from Toronto (Laura Passalent, Dr. Robert Inman and Dr. Nigil Haroon), Montreal (Dr. Michel Zummer, Dr. Nicolas Richard) and Vancouver (Dr. Jon Chan), in collaboration with the Canadian Spondylitis Association, were awarded a 2020 SPARCC pilot grant to revise the current web-based patient e-learning module on axial spondyloarthritis (axSpA) originally launched in 2016 (www.wegotyourbackTWH.ca). Revisions will reflect up-to-date evidence regarding assessment and management of axSpA, incorporate links to national organizations to enhance the self-management strategies of the e-learning module and translate all content to French to ensure accessibility to both English and French speaking Canadians. After the completion of these revisions, we aim to conduct a pan-Canadian randomized controlled trial to examine the effectiveness of the updated e-learning module on self-efficacy, exercise behaviour, disease activity, function, and health status in adult patients diagnosed with axSpA in both official languages.

Other educational projects in the pipeline include the exploration of a 4-week a national SPARCC Physiotherapist Preceptorship. The overarching goal of this project is to improve access to interdisciplinary care for patients

with axial spondyloarthritis (axSpA) within an academic tertiary care facility with global leaders in spondyloarthritis. The aim would be to create a national network of axSpA physician specialists working in collaboration with competent physiotherapists in the assessment and management of axSpA. The preceptorship would be designed to meet a growing demand for registered physiotherapists looking to advance their knowledge in the treatment of patients with axSpA and to further expand their inter-professional rheumatology network. The preceptorship would draw from existing and newly developed internal and external resources to explore the theoretical and practical skills essential to develop the level of practice required for physiotherapists to provide evidence-based care for this unique patient population. We are currently exploring funding options for this initiative.

Publication:

Passalent L, Hawke C, Lawson DO, Omar A, Alnaqbi KA, Wallis D, Steinhart H, Silverberg M, Wolman S, Derzko-Dzulynsky L, Haroon N, Inman RD. Advancing Early Identification of Axial Spondyloarthritis: An Interobserver Comparison of Extended Role Practitioners and Rheumatologists. J Rheumatol. 2020 Apr;47(4):524-530. doi: 10.3899/jrheum.180787. Epub 2019 May 1. PMID: 31043543.

SPARCC Pilot Projects

Since 2009, SPARCC provides seed funding annually to support research proposals aligned with its primary objective for the advancement of SpA-related research. For 2019, SPARCC funded the following 3 pilot project initiatives and their progress reports to date for these projects are appended below:

Progress Reports – 2019 Awardees

1. **Awardee**: **Dr. Akihiro Nakamura**, Krembil Research Institute, Division of Genetics and Development; Spondylitis Program, UHN-Toronto Western Hospital; Award: $25,000

   Project Title: ***Macrophage Migration Inhibitory Factor induces abnormal new bone formation through endochondral ossification originated from GDF5-positive osteo-chondroprogenitor cells in AS mouse models***

   Background: We recently discovered that serum levels of macrophage migration inhibitory factor (MIF) are significantly elevated in Ankylosing spondylitis (AS) patients compared to healthy controls and that it is higher in AS patients with rapid compared to slower radiographic progression. However, the pathogenic role of MIF in abnormal new bone formation (NBF) following inflammation and mechanical loads (mechano-inflammation) is largely unknown.

   Methods: Curdlan (β-glucan; 3 mg/mouse) or MIF-plasmid (EEV, 5ug/mouse) treated SKG mice (8-10 weeks) were used as AS mouse models. Arthritis and NBFs in ankle joints were weekly observed until 8 weeks post-treatments (n=7 mice/group) and assessed by histopathology and µCT. MIF antagonist (MIF098; 40mg/kg, twice/day, i.p.) or MIF knockout (KO) SKG mice were also assessed for arthritis and NBF after curdlan. Endochondral ossification (ECO) markers were assessed by qPCR and immunoblotting in GDF5+ osteo-chondroprogenitor cells (OCPs) treated with MIF. Tail suspension system was applied to curdlan-treated SKG mice until 4 weeks post-curdlan.

   Results: Curdlan or MIF-plasmid treatment induced the development of arthritis and NBF in ankle joints over 8 weeks. Mean weekly arthritis scores (maximum 13) were 0 at baseline, 2.28 at 1-2 weeks, 4.78 at 3-4 weeks, 6.21 at 5-6 weeks, and 10.21 at 7-8 weeks post-curdlan. NBFs were observed in 0% at baseline, 0% at 1-2 weeks, 42.9% at 3-4 weeks, 71.4% at 5-6 weeks, and 85.7% at 7-8 weeks post-curdlan. MIFKO SKG mice and MIF098 treatment significantly reduced the severity of arthritis and NBF at 7-8 weeks in curdlan-

treated SKG mice. Gene expression of ECO makers (Sox9, Runx2, Col2a1, Acan, Ocn, Alp) were significantly increased in ankle joints of curdlan-treated SKG mice compared to controls. Tail suspension system remarkably suppressed the severity of arthritis and NBF after curdlan treatment in-vivo.

Conclusion: These results indicate that MIF is a crucial regulator of mechano-inflammation-induced NBF in AS. The rest of the data to fully address the questions in the funded proposal will be ready by the time of final report.

2. **Awardee**: **Dr. Cheryl Barnabe and Dr. Ryan Lewinson**, University of Calgary; Award: $25,000

Project Title: Investigating the relationship between biomechanics and inflammation in psoriatic disease

Background: Psoriatic disease represents a spectrum of chronic systemic inflammatory processes manifested by skin involvement (psoriasis) and musculoskeletal involvement as psoriatic arthritis (PsA) in up to 30% of cases. The reasons why some psoriasis patients develop PsA remain unknown; however, one possible trigger may be mechanical loading (i.e. Koebner phenomenon). Unfortunately, biomechanics has received very little attention in psoriasis and PsA, thus the mechanisms relating biomechanics to subsequent inflammation and musculoskeletal involvement are not known. Understanding this process has the potential to provide insight on instigating factors for PsA development, and potentially identify new patient subgroups and avenues for therapeutics.

Objectives: To incorporate inflammatory, imaging and biomechanical data from psoriasis and PsA patients into computational models to identify key interacting variables that relate to clinical phenotype, and gain understanding on how systemic inflammation interacts with biomechanics to produce musculoskeletal involvement in psoriatic disease.

Methods: To do this, we planned to recruit patients with psoriasis and PsA to complete a series of tests including clinical evaluation, serologic assessment of inflammatory markers, clinical CT of the foot and ankle for assessment of bone architecture, and ankle isokinetic dynamometry with concurrent dynamic ultrasound to assess Achilles tendon function. The variables would be interpreted together using a variety of machine learning approaches.

Progress to date: COVID-19 has significantly impacted our study. With limitations in patient recruitment, social distancing, and recruitment of trainees due to the pandemic, our research has been delayed. In the interim, we have conducted three separate scoping reviews on the links between biomechanics and inflammation in psoriasis and other Koebnerizing diseases that are currently under journal review or in preparation for submission. Our hope is to initiate in-person testing as soon as possible.

3. **Awardee**: **Dr. Sayaka Nakamura**, Krembil Research Institute, Division of Genetics and Development; Spondylitis Program, UHN-Toronto Western Hospital; Award: $24,875

Project Title: ***T Cell Receptor (TCR) motifs in different T Cell Phenotypes in ankylosing spondylitis***

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, characterized by inflammation in the spine and sacroiliac joints. Although the disease etiology remains unclear, previous studies indicate that T cells play an important role in AS. Mitochondria are the powerhouse of the cell, providing energy for the cellular biochemical reactions. It has been shown that T cell activation, proliferation, and survival are also intimately linked to the mitochondrial activity. This study aimed to profile the mitochondrial activity in

T cells in AS using mitochondrial membrane potential (MitMP), a parameter of mitochondrial activity.

Methods: Fresh peripheral blood mononuclear cells (PBMCs) from AS patients (n=11) and healthy donors (n=4) were used for analyses. PBMCs were stained with antibodies followed by incubation with Mitochondrial dye and analyzed by flow cytometry. Mitochondrial membrane potential in each subset of CD4+ and CD8+ T cells were assessed. The Spearman rank correlation test was applied to test correlations.

Results: MitMP of naive CD8+ T cells showed moderate positive correlations with AS disease activity (BASDAI; r=0.61), ESR (r=0.697) and CRP (r=0.65). On the other hand, MitMP of all the subsets of CD4+ T cells showed strong positive correlations (r=0.78 to 0.83) with disease duration.

Conclusion: CD4+ T cells and CD8+ T cells showed distinct correlations with MitMP. Our data suggest that MitMP in CD4+ T cells is related to disease chronicity, while MitMP in CD8+ T cells is related to disease activity and inflammatory markers. Further study with larger sample number needs to be performed.

2020 SPARCC Pilot Project Program Awardees

In 2020, SPARCC awarded the following 4 meritorious pilot project initiatives:

Project Title	Principal Investigator	Affiliation	Award
DEEP CELLULAR IMMUNE PROFILING IN PSORIATIC ARTHRITIS: A STEP TOWARDS INDIVIDUALIZED THERAPY	**Dr. Lihi Eder, PI** Co-Investigators: Dr. Vinod Chandran; Dr. Kun Liang; Dr. Igor Jurisica	Women's College Research Institute, Women's College Hospital, Toronto, Ontario	$25,000
METABOLOMIC PROFILING IN RESPONDERS AND NO-RESPONDERS TO TUMOR NECROSIS FACTOR INHIBITOR AND INTERLEUKIN-17 INHIBITOR THERAPY IN PSORIATIC ARTHRITIS	**Dr. Ashish Jacob Mathew, PI** Co-Investigators: Dr. Vinod Chandran; Dr. Proton Rahman; Dr. Vathany Kulasingam	Psoriatic Arthritis Program, UHN – Toronto Western Hospital	$25,000
WE GOT YOUR BACK, VERSION 2.0: PAN-CANADIAN IMPLEMENTATION AND EVALUATION OF AN E-LEARNING PATIENT EDUCATION PROGRAM IN AXIAL SPONDYLOARTHRITIS – A PILOT STUDY	**Laura Passalent PT, PI** Co-Investigators: Dr. Robert D. Inman; Dr. Nigil Haroon; Dr. Michel Zummer; Dr. Nicolas Richard; Dr. Jonathan Chan; Alaina Cyr; Daeria Lawson	Spondylitis Program – UHN-Toronto Western Hospital	$24,965
MIF-MEDIATED TREG CONVERSION INTO TH17 CELLS IN ANKYLOSING SPONDYLITIS	**Dr. Akihiro Nakamura, PI** Co-Investigators: Dr. Nigil Haroon and Robert Inman	Krembil Research Institute, Division of Genetics and Development; Spondylitis Program, UHN-Toronto Western Hospital	$24,500

A summary of these projects will be presented during the upcoming scientific virtual meeting on October 30th.

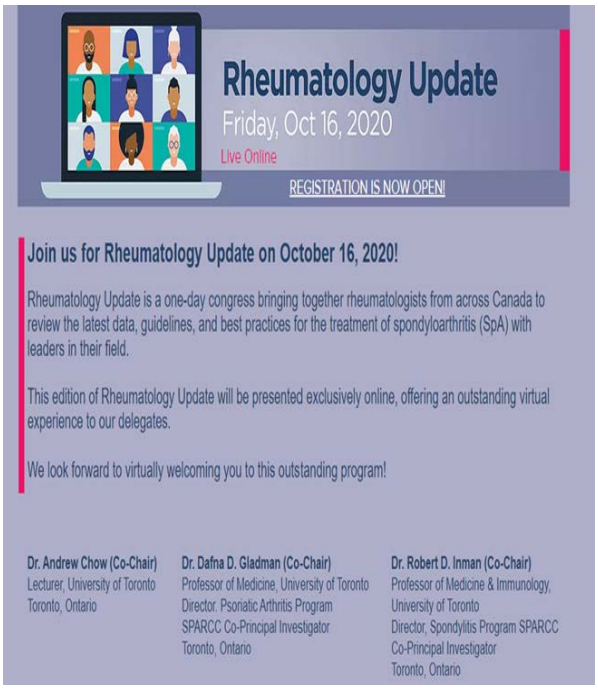
SPARCC Continuing Medical Education (CME) Workshops for Practicing Rheumatologists

Background and Past Events

Since 2015, SPARCC has been conducting a SpA Update for practicing rheumatologists across Canada; the first was held in Montreal, Quebec, whereby 60 rheumatologists and selected nurse practitioners in SpA participated from across Quebec. The event was conducted bilingually and spearheaded by Dr. Michel Zummer, our SPARCC Montreal site and member of the SPARCC Executive Committee. The Quebec event also illustrated the value of strategic partnerships, as the Quebec Division of the Arthritis Society and the Canadian Spondylitis Association worked closely with SPARCC in the successful program. Succeeding CME workshops followed in the other provinces as follows:

Year	Event Particulars
2016	This event was held in Vancouver, British Columbia at the Sheraton Vancouver Wall Centre on April 30, 2016, spearheaded by Dr. Kam Shojania (University of British Columbia) and Dr. Jonathan Chan, a SPARCC Collaborator from ARTUS Health Centre
2017-2018	We conducted this event in Calgary through the University of Calgary and hosted by SPARCC Collaborator - Dr. Dianne P. Mosher. The event took place on November 17th, 2017 at the HRIC Atrium, University of Calgary, and participated by over 70 rheumatologists and allied health practitioners in the province of Alberta.
2019	Our Montreal collaborating site once again, spearheaded by Dr. Michel Zummer, hosted the bilingual event held at the LOEWS Hotel Vogue in Montreal on October 25, 2019, and participated by about 50 rheumatologists and allied health practitioners in the province of Quebec, New Brunswick and Ottawa.

2020 CME Event Update



RHEUMATOLOGY UPDATE ON SPONDYLOARTHRITIS (SpA)
October 16, 2020
PROGRAM

Time	Particulars	Speakers
7:30 – 7:40	Welcome and Opening Remarks; Program Overview	Dr. ANDREW CHOW Assistant Professor, McMaster University; Lecturer, University of Toronto
7:40 – 8:20	Overview of the SPARCC Research Program Diagnosis and Classification of SpA and Early Detection Treatment Goals & Medical Therapy in Ankylosing Spondylitis	Dr. ROBERT D. INMAN Professor of Medicine & Immunology, University of Toronto; Director, Spondylitis Program SPARCC Co-Principal Investigator
8:20 – 9:00	Advances in management of Psoriatic Arthritis (PsA) and related enthesitis Treatment Goals & Medical Therapy in PsA State of the Art in PsA screening, imaging and diagnosis including ultrasound	Dr. DAFNA D. GLADMAN Professor of Medicine, University of Toronto; Director, Psoriatic Arthritis Program SPARCC Co-Principal Investigator
9:00 – 10:00	Role of Imaging in the Diagnosis and Management of SpA X-ray/MRI reading and scoring	Dr. RAKESH MOHANKUMAR Assistant Professor, Dept.of Medical Imaging, University of Toronto, Toronto Joint Department of Medical Imaging, UHN, Sinai Health System & Women's College Hospital
10:15 – 10:50	Role of IL17 in SpA Early Detection; indication for non-radiographic; symptoms MRI – when to do it? Gender differences When to use a biologic and profiling the patient cases	Dr. NIGIL HAROON Associate Professor Department of Medicine, University of Toronto, University Health Network; Co-Director, Spondylitis Program SPARCC Co- Investigator
10:50 – 11:25	Biomarkers for the management of Psoriatic Disease- current status and vision for the future? Co-Management, combined Derm/Rheum Clinic	Dr. VINOD CHANDRAN Associate Professor, Department of Medicine, University of Toronto, University Health Network; Co-Director, Psoriatic Arthritis Program; SPARCC Co- Investigator
11:25 – 12:00	Non-pharmacologic treatment in AS Screening Pathway	Ms. LAURA PASSALENT ACPAC Physiotherapist, Spondylitis Program, UHN-Toronto Western Hospital
	Extra Articular Manifestations of SpA: Interdisciplinary Collaboration	
1:00 – 1:35	Current Concepts in Uveitis Panel Discussion/ Q&A	Dr. LARISSA DERZKO-DZULYNSKY Ophthalmologist; Assistant Professor, University of Toronto; Chief of uveitis Service, Dept.of Ophthalmology & Vision Sciences
1:35 – 2:10	Current Concepts in Psoriasis Panel Discussion/ Q&A	Dr. RONALD VENDER Associate Clinical Professor, Div. of Dermatology, Dept. of Medicine, McMaster University
2:10 – 2:45	Current Concepts in Inflammatory Bowel Disease (IBD); Co-Management with Rheum – when to refer Panel Discussion/ Q&A	Dr. MARK SILVERBERG Professor of Medicine, University of Toronto; Division of Gastroenterology, Mount Sinai Hospital - Inflammatory Bowel Disease Centre
2:45 – 3:00	Evaluations Closing Remarks; Acknowledgments	Dr. ANDREW CHOW Assistant Professor, McMaster University; Lecturer, University of Toronto

For **2020**, SPARCC has modified its approach to this workshop and collaborated with Dr. Andrew Chow who is affiliated with the Credit Valley Rheumatology, to conduct a similar initiative to capture practicing rheumatologists, allied health professionals and SpA nurses in West and Central Ontario. The event is entitled "**RHEUMATOLOGY UPDATE ON SPONDYLOARTHRITIS"** originally scheduled in May 2020, but due to COVID-19, has been moved to October 16, 2020 in **virtual** format. Accreditation has been extended by the Canadian Rheumatology Association (CRA). Over 180 participants participated in this event and a full report on the outcome of the event will be disclosed during the SPARCC scientific meeting scheduled for October 30, 2020. Above is a copy of the online invite, along with the program for the full day event.

SPARCC Training for Fellows

Since 2012, SPARCC has been conducting a training workshop for research fellows in rheumatology, and held at the Toronto Western Hospital, spearheaded by Drs. Robert Inman and Dafna Gladman. This event is participated by more than 20 rheumatology fellows from across Canada annually who are nominated by the program directors in their respective provinces. The purpose of this program is to provide rheumatology fellows across Canada who treat SpA with up-to-date information on early diagnosis and optimal intervention (including the use of biologic agents) to improve outcomes, and share the strategies used by SPARCC in the institutions involved to treat patients with severe forms of AS and PsA. In 2019, this workshop was conducted on May 3, 2019.

For 2020 however, in view of COVID-19, SPARCC is unable to conduct this training workshop due to suspension of initiatives of this nature at UHN and across the province. As there is a hands-on component to this initiative, a virtual format in lieu of an in-person approach will not be suitable. We will revisit our options in 2021 when hopefully, this pandemic will be done and over with.

Canadian Spondylitis Association (CSA)

In a collaborative effort with SPARCC, SpA patients from across Canada have developed the Canadian Spondylitis Association, a national non-profit patient association formed in April 2006 to support and to advocate for those suffering from AS, PsA, and SpA-related diseases. The CSA's officers and directors are comprised of individuals who understand what kind of support and advocacy is needed, because they struggle with spondylitis in their own lives as well. The mission of the CSA is to provide the most current information and resources for people with AS, PsA and related diseases. In this regard, we therefore will continue the annual joint SPARCC-CSA patient symposiums across Canada which aims to provide the latest updates and new discoveries related to SpA, including updates on medical treatment of AS and PsA. The integration of patient-consumers into the research planning is a cornerstone of the phase research plan of SPARCC. The annual SpA Patient Forum, jointly conducted by SPARCC and CSA, is an example of this partnership. Since 2008, these forums rotate in the various sites. Examples are listed below:

Year	Event Particulars/Venue/Hosts
2008	Edmonton (Fantasyland Hotel): Host: Dr. Walter Maksymowych
2009	Montreal (Delta Centre-Ville Hotel); Host: Dr. Michel Zummer
2010	Toronto (Delta Chelsea Hotel); Hosts: Drs. Robert Inman and Dafna Gladman
2011	Three (3) separate In-Campus SpA forums in 1) Edmonton (Stanley Milner Library Theatre) hosted by Dr. W. Maksymowych, 2) St. John's (Health Science Centre Main Auditorium, Memorial University of Newfoundland) hosted by Dr. Proton Rahman, and 3) Toronto (UHN – Toronto Western Hospital Main Auditorium) hosted by Drs. Robert Inman and Dafna Gladman

2012	Two (2) Separate SpA forums in 1) Toronto (Courtyard Marriott Hotel) hosted by Drs. Robert Inman and Dafna Gladman, and 2) Vancouver (Metropolitan Hotel Vancouver) hosted by Dr. Cathy Flanagan
2013/2014	Toronto – AS Patient Forum (UHN – Toronto Western Hospital Auditorium); Hosts: Dr. Robert Inman and Nigil Haroon
2015	Montreal (Marriott Montreal Chateau Champlain, 1 Place du Canada, Montreal); Host: Dr. Michel Zummer
2016	Vancouver (Sheraton Vancouver Wall Centre); Hosts: Dr. Jonathan Chan and Dr. Kam Shojania
2017	Calgary (WINSPORT Multi-Purpose Room, Olympic Road); Hosts: Drs. Dianne Mosher and Ola Ziouzina
2018	Toronto – AS Patient Forum; BMO Education & Conference Centre, Krembil Discovery Tower, UHN, Toronto Western Hospital (Live streamed on You Tube); Hosts: Drs. Robert Inman and Nigil Haroon
2019	Montreal, QC – LOEWS Hotel Vogue, Montreal, October 26, 2019; Hosts: Drs. Michel Zummer and Nicolas Richard

In 2020, amid COVID-19, we are unable to conduct another SpA patient forum. In lieu however, SPARCC and the CSA once again jointly collaborated and conducted "**The COVID-19 and Rheumatic Arthritis Update"**, an evening **Webinar** on May 19th, 2020.

The focus for this year's event shifted towards managing SpA diseases (focusing on AS) during the pandemic which was a more appropriate theme under the present global crisis. Our Toronto Core Site team from the Spondylitis Program spearheaded by Drs. Robert Inman and Nigil Haroon were keynote speakers, along with Ms. Laura Passalent, PT and Dr. Gillian Fitzgerald, Clinical Fellow. The CSA orchestrated the event, managed the invites as well as the webinar logistics.

This is the program invite for this event.

INFRASTRUCTURE

The SPARCC Network: The organizational structure of SPARCC has been led by the Executive Committee responsible for the overall policy and direction of SPARCC. The incumbent officers elect from **November 1, 2019 to hold office for one (1) year or until October 30, 2020** are:

President	:	**Dr. Dafna D. Gladman**
Vice President	:	**Dr. Proton Rahman**
Secretary	:	**Dr. Sherry Rohekar**
Treasurer	:	**Dr. Robert D. Inman**
Director-at-Large	:	**Dr. Michel Zummer**

The new officers elect holding office from November 1, 2020 to October 31, 2021 will be announced during the SPARCC Scientific Meeting on October 30th.

The core sites in the SPARCC network are:

- **University Health Network** - Toronto Western Hospital, Toronto, ON (Drs. Robert D. Inman and Dafna Gladman as PIs; Drs. Nigil Haroon and Vinod Chandran as Co-Is.)
- **Memorial University of Newfoundland** – St. John's, NL (Dr. Proton Rahman)
- **University of Western Ontario, St. Joseph's Healthcare**, London, ON, (Dr. Sherry Rohekar; Dr. Tristan Boyd as Co-I)

The SPARCC collaborating sites nationwide have expanded significantly over the years as follows:

- **CH Maisonneuve Rosemont**, Montreal, QC (Dr. Michel Zummer; Dr. Nicolas Richard)
- **The Arthritis Program Research Group Inc**., Newmarket, ON (Dr. Carter Thorne)
- **University of Saskatchewan**, Saskatoon, SK (Dr. Bindu Nair)
- **The Hospital for Sick Children**, Toronto, ON (Dr. Shirley Tse)
- **University of Calgary**, Calgary, AB (Dr. Dianne Mosher & Dr. Olga Ziouzina)
- **McGill University Health Science Center**, Montreal, QC (Dr. Alexander Tsoukas & Dr. Michael Starr)
- **ARTUS Health Centre**, Vancouver, BC (Dr. Jonathan Chan)
- **McMaster University**, Hamilton, ON (Dr. Raj Carmona)
- **University of Alberta,** Pediatrics (Dr. Dax Rumsey)
- **University of Ottawa** (Dr. Sibel Aydin)
- **Women's College Hospital** (Dr. Lihi Eder)
- **West Island Rheumatology Research Associates (WIRRA)** (Dr. Michael Starr, Dr. Mary-Ann Fitzcharles, and Dr. Martin Cohen)
- **CHU De Quebec, Université Laval** (Dr. Karen Adams, Dr. Paul Fortin, and Dr. Lois Bessett)

At present, SPARCC is funded by multi-industry support from **ABBVIE, AMGEN, NOVARTIS, UCB, PFIZER, ELI LILLY**, **JANSSEN.**

CONTACT INFORMATION

Address: SPARCC Research Program, University Health Network (UHN) - Toronto Western Hospital, 399 Bathurst Street, East Wing, Rm. 412a, Toronto, Ontario M5T 2S8 CANADA

Website: www.sparcc.ca

Ms. MARIA T. MORALES, National Administrative Coordinator
Email: maria.morales@uhnresearch.ca
Tel. No. 416-603-5800 ext. 5093; Cell# 416-710-1361; Fax No. 416-603-9387

Mr. STEVE RAMKISSOON, Database Manager
Email: Steve.Ramkissoon@uhnresearch.ca
Tel. No. 416-603-5800 ext. 3197; Fax No. 416-603-9387

Ms. JULIE GAGNIER, Biobanking Technician
Krembil Discovery Tower, Toronto Western Hospital, 60 Leonard Ave, Room 5KD 429C
Toronto, Ontario M5T 2S8; Phone: (416) 603-5800 ext 5123; or (647) 633-6948
Email: Julie.gagnier@uhnresearch.ca

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THANK YOU!