Hamilton Scleroderma Group
Annual Progress Update

Prepared for

Scleroderma Society of Ontario

Prepared by

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FIRH
Firestone Institute for Respiratory Health
St. Joseph's Healthcare Hamilton
McMaster University Health Sciences

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1.0 Executive Summary

The Hamilton Scleroderma Group (HSG) was formed in 2009 in partnership with Mrs. Maureen Worron-Sauvé and the Scleroderma Society of Ontario (SSO). The HSG is a consortium of clinicians, scientists and educators who share an interest in improving the quality of care for persons affected by systemic sclerosis (SSc).

Through a 3 year grant of $456,000 from the SSO, innovative research, education and patient care provided by the HSG at St. Joseph's Healthcare Hamilton has been supported since 2011. With this contribution, the HSG has raised the profile of SSc within Hamilton and across Canada through patient research partnerships, community outreach and education. The multidisciplinary team meets thrice yearly to review, update and plan future initiatives.

The HSG has adopted the 3 following general objectives: to improve access to care for patients with SSc; to increase awareness of the disorder amongst family physicians, internal medicine residents, rheumatology trainees, allied health care professionals and medical students; and to expand basic science and clinical research.

Notable achievements since its inception include:

- several patient education sessions in conjunction with the SSO;
- the development of a patient help-line with a nurse fielding the calls;
- a CME program with speakers from many different medical disciplines, with physicians, nursing and allied health professionals along with undergraduate and post-graduate students in attendance;
- securing a visiting professor, Alan Tyndall, world expert in stem cell transplantation in scleroderma. He will give stem cell rounds, rheumatology rounds, rheumatology fellows teaching and 2 patient sessions in Hamilton and Toronto in April 2014;

- participation in chair of medicine grand rounds, family medicine rounds, allergy and immunology rounds and rheumatology rounds, all of which increase the awareness and education of physicians dealing with patients with systemic sclerosis;
- continuing research:
    - Canadian Scleroderma Research Group (CSRG). Hamilton has recruited 189 of the total of 1,465 patients across Canada and we continue to recruit actively
    - Clinical study to describe the impact of GI issues in patients with SSc (from the CSRG registry)
    - 4 basic science projects all of which are ongoing:
        1. Developing a mouse model for scleroderma (a PhD student is on track to complete this work in 2015)
        2. PBMC responses to HLA peptides
        3. T cell interactions with fibroblasts
        4. Peripheral blood fibrocytes in pulmonary fibrosis and nephritis

Future directions

It is anticipated that an application will be made for a pilot study of IL-5 inhibition in patients with scleroderma in association with Dr. Param Nair in respirology. In addition, Dr. Janet Poole is initiating a collaborative project with Toronto and HSG in splinting in patients with hand involvement in scleroderma.

The current clinical and basic science projects will continue.

There will be continuing association with family medicine, immunology and rheumatology for rounds and family practice residents teaching.

There is an opportunity to present scleroderma at the Farncombe rounds in gastroenterology. We anticipate the participation of Dr. Dinesh Khanna from the University of Michigan, who is a world-renowned expert in the GI manifestations of scleroderma.

In terms of clinical care, the HSG will continue to expand in other disciplines including psychiatry and psychology. With the upcoming visit from Prof. Alan Tyndall, we anticipate interest from the stem cell physicians at McMaster, and have a long term vision of developing a centre for stem cell therapy for patients with scleroderma.

2.0 HSG Executive Board

Dr. Maggie Larché continues to serve as the HSG's executive chair. Drs. Khalidi and Cox had served as interim chairs for the year 2011. A model of comprehensive care for patients with systemic sclerosis is continuing to grow, with the establishment of combined rheumatology/ respirology, rheumatology/immunology and rheumatology/respirology/nephrology clinics. The Board's strategic direction for 2014 is included in Section 7.0 of this Report.

The 2014 HSG Executive Board is comprised of the following members:
Gerard **Cox**, MB, FRCPCI, FRCPC, *Professor*, Div. of Respirology, Dept. of Medicine McMaster University, St. Joseph's Healthcare Hamilton

Nader A. **Khalidi**, MD, FRCPC, FACP, FACR, *Associate Professor*, Div. of Rheumatology, Dept. of Medicine, McMaster University, St. Joseph's Healthcare Hamilton

Martin **Kolb**, MD, PhD, Associate Professor, Div. of Respirology, Dept. of Medicine, McMaster University, St. Joseph's Healthcare Hamilton

Maggie **Larché**, MBChB, MRCP(UK), PhD, *Associate Professor*, Div. of Rheumatology, Depts. of Medicine & Pediatrics, McMaster University, St. Joseph's Healthcare Hamilton & McMaster Children's Hospital

Mark **Larché**, PhD, Professor, Div. of Clinical Immunology & Allergy, Dept. of Medicine, McMaster University

Peter **Margetts**, BSc, MD, PhD, FRCPC, Associate *Professor*, Div. of Nephrology, Dept. of Medicine, St. Joseph's Healthcare Hamilton

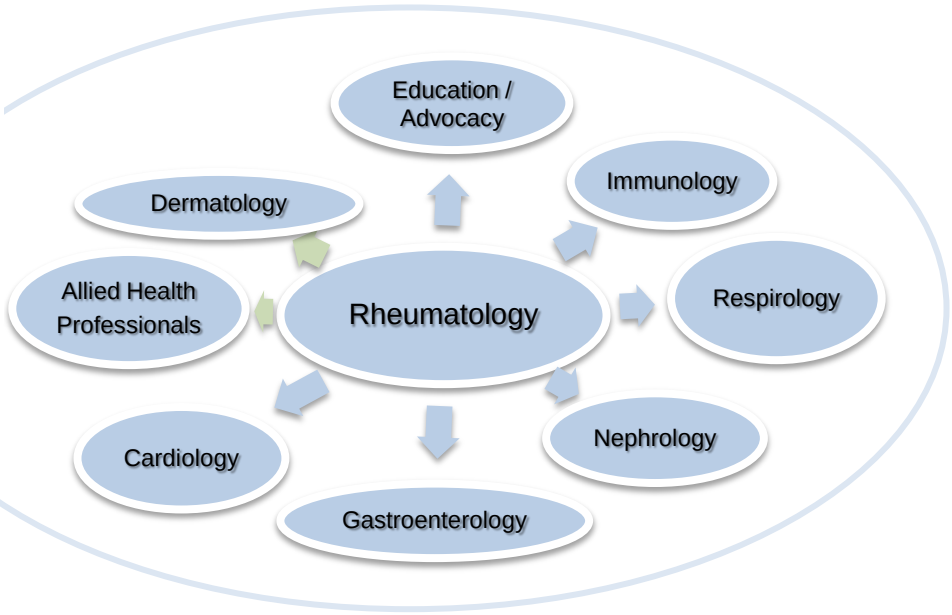
Sergio **Mazzadi**, MD Associate Professor, Division Gastroenterology, Depts. of Medicine & Pediatrics, McMaster University, St. Joseph's Healthcare Hamilton

3.0 Improving Access and Patient Care

Recruitment and consolidation of the HSG's circle of 'preferred specialist' care for patients with scleroderma is ongoing. To date we have representation from rheumatology (Dr. Nader Khalidi and Dr. Maggie Larché); respirology (Dr. Gerard Cox and Dr. Martin Kolb); nephrology (Dr. Peter Margetts); cardiology (Dr. Allan Kitching), dermatology (Dr. Peter Vigjnevic); gastroenterology (Dr. Sergio Mazzadi) and an immunologist (Dr. Mark Larché). At our recent meeting in February, we invited Helen Van DeMark from dietary services and Dr. Joe Pellizzari, psychologist, to join the HSG team. The role of patient advocate/educator/research coordinator has been filled by Ellen McDonald, Reg.N.

Dr. Maggie Larché has made preliminary contact with a world-renowned expert in wound healing, Dr. Sibbald. He has been invited to give rounds and advice (we will propose an afternoon of bringing in several patients with digital ulcers/necrosis) in 2013. Other sub-specialists (e.g. physio/occupational therapists) will be accessed, on an as-needed basis, depending on patients' needs.

Circle of Medical Care for Scleroderma Patients



The HSG has access to the Ontario Telehealth network. This is a videoconferencing system which allows clinicians to provide access to care for patients with scleroderma in every hospital and health care location across Ontario, including those from isolated rural communities. With the help of a local allied health professional or family practitioner, who facilitates the clinical examination, patients can be thoroughly assessed and monitored. The Telehealth network will also be used to facilitate delivery of distance education and meetings for health care professionals and patients.

4.0 Enhancing Scleroderma Education

A CME event was held prior to the Scleroderma Congress in September 2013, organised by a committee of participants from the SSO, SSC and HSG. During this CME event, clinical manifestations of scleroderma were discussed including Raynaud's, pulmonary, renal, cardiac and emergency room aspects of care. A panel of 5 specialists with an interest in scleroderma gave interactive talks. The event was attended by physicians, residents, fellows, nurses, students, respiratory therapists and physiotherapists. The remainder of the Congress targeted health care professionals and patients.

The role of the Scleroderma Educator Coordinator has facilitated patient education and continuing medical education relating to systemic sclerosis. This has been accomplished through the following key initiatives:

4.1 Patient Education and SSO Support Group Consultation

As the HSG's Education Coordinator, Susan Docherty-Skippen wrote / revised and compiled a collection of resource material intended to provide a framework that persons affected by scleroderma can use for the start-up and ongoing maintenance of Scleroderma Support Groups. Topics included in the manual were: Why the Need for Support Groups? ; What is a Support Group?; Newly Diagnosed; Grieving the Loss of the Healthy Body; Building Plan; Guidelines & Member Responsibilities; Confidentiality; Shared Leadership; Facilitation Skills. Ellen McDonald has been attending the support groups and is working on developing 2 patient-centred educational evenings with a world expert, Dr. Alan Tyndall in late April 2014 in Hamilton and in Toronto.

4.2 Education Partnership in Support of SSO Newsletters, SSO Web-site, Media & Fundraising & Public Awareness Events

In an attempt to improve awareness and boost recruitment in clinical trials, an article on patient's responsibilities as participants in a research study is underway.

Members of the HSG have provided scleroderma education support in partnership with Mrs. Maureen Worron-Sauvé and the SSO during the SSO Scleroderma Walk in the Park, the SSO Mississauga Gala, the Annual Scleroderma Walkathon and creation of a Needs Assessment Poster for the September Congress in 2013.

4.3 Patient Advocacy - Facilitating Care Access

As the "first port of call" for those seeking advice or health information regarding scleroderma, the HSG's Patient Educator/coordinator has been fielding telephone calls and providing guidance to patients, relatives and caregivers. This guidance has been

in consultation with the HSG clinicians. Through the SSO, a 1-888 telephone number and e-mail has been established so patients, their families, friends and health care professionals can access the HSG to receive up-to-date information about scleroderma support group meetings, access to patient care, educational events and conferences, entry into research studies, and health and wellness learning resources. Most recently, a website has been created for the HSG. The website provides easy access to all the resources described above and there are links to many resources and information. The website is currently live http://www.hamiltonscleroderma.org/. HSG members are continuing to build and update the site.

5.0 Expanding Basic Science and Clinical Research

The HSG plays an important role in a national research initiative through the Canadian Scleroderma Research Group (CSRG). The HSG rheumatologists have enrolled over 170 patients (the largest number of patients from a single centre) in this national cohort database. CSRG research studies include investigation of classification criteria, autoantibody profiles, fatigue, genetics and a disease activity index for application in scleroderma patient care and medical education.

The HSG has been engaged in a number of locally initiated basic science and clinical research projects. These are reviewed below:

5.1 Developing a mouse model of systemic sclerosis (Appendix 1)

Developing a model of scleroderma in the laboratory, we have previously hypothesized that scleroderma may be similar to graft versus host disease that is observed following bone marrow transplantation (BMT). In the latter, immune cells from the donor bone marrow attack the tissues of the host (the graft recipient) causing many symptoms that have similarities to scleroderma. Indeed, others have suggested that scleroderma might be related to a phenomenon called microchimerism. Microchimerism results from the survival of cells transferred through the placenta between mother and fetus such that most, if not all, of us still carry living cells in our bodies derived from our mothers and vice versa. We have attempted to create a mouse model of scleroderma by performing bone marrow transplants between two different strains of mice. If we can generate a model that resembles scleroderma in humans, we can test a vaccine therapy that has been developed in collaboration between our group and a group in

the UK. To date, we have results suggesting that we have been able to see evidence of lung fibrosis and some skin lesions in our mice. There is also a weaker signal for kidney disease, also often associated with scleroderma. We are currently investigating the nature of the lung fibrosis and during the next 6-10 months, we hope to begin experiments in which we will attempt to treat transplanted mice with the vaccine to see if established disease can be halted or slowed down.

5.2 Investigation of T lymphocyte responses to cryptic determinants in the α3 and transmembrane region of human leukocyte antigens in systemic sclerosis. (Appendix 2)

Analysis of white blood cell activation in scleroderma patients compared to rheumatoid arthritis patients and healthy control subjects.
We previously performed a study in which we tested the extent to which white blood cells from scleroderma patients become activated when they are exposed to certain proteins that define an individual's "tissue type" (the tissue type that is used to match donor and recipient for organ and bone marrow transplant). In the first study we showed that the response of scleroderma patients appeared to be more "pro-fibrotic" than that of healthy controls, since the scleroderma patients made more of a key fibrosis mediator called TGFbeta. More recently we have repeated this study with a new set of patients and controls. We also included a "disease control group". These were individuals with rheumatoid arthritis, another chronic disease. We wanted to see if differences we had observed between scleroderma patients and healthy controls were simply due to the fact that they had a chronic disease. The results of the second study did not support the findings in the first study. This does not mean that either study was "wrong", but rather that the results across the two studies were inconclusive with respect to the increased fibrosis signal. We are continuing to analyze the results to see if there are additional messages lying within the data.

5.3 Investigating the role of the fibrocyte in idiopathic and SSc pulmonary fibrosis rapidly progressive glomerulonephritis. (Appendix 3)

No new activities in the last year. Anything on this front with a biomarker perspective would be costly.
There is a plan to submit one or two research projects for funding within the next few weeks. Estimating $20K per project. The second project is straight forward and all methods are established (requirements are a small skin biopsy to derive the primary fibrocytess)

1. Interaction of Fc with Tregs (together with Mark), Ssc vs control.
2. Fibroblast cultures from skin biopsies and measurement of fibroblast activation. Comparing patients with Ssc with Raynauds who are treated with Ca channel blockers and patients who don't get these drugs; we have very interesting data from animal models showing that nifedipin has antifibrotic properties via Ca channels.

5.4 Fibroblast interactions with T cells.

Investigating differences in the way T cells talk to fibroblasts in scleroderma.
T cells are white blood cells that control immune responses to proteins from our own body and proteins from the world around us (including bugs, food, environmental proteins etc). Results of several large genetic comparisons of scleroderma patients versus healthy controls have suggested that a difference in T cell biology is strongly linked to scleroderma. We have chosen to test whether there is some difference in the

way T cells from scleroderma patients interact with fibroblasts (cells that seem to be overactive in scleroderma, resulting in fibrosis). To do this we have activated blood T cells from a cohort of scleroderma patients and a cohort of healthy control subjects. We have collected the secretions of the activated cells from each subject and we are about to add these secretions to cultured fibroblasts from the skin of a healthy control subject. After 24 hours we will isolate genetic material from the fibroblasts and measure the level of over 200 genes involved in fibrosis. By comparing the levels of these genes in scleroderma versus health, we will be able to determine whether there is an identifiable defect in the way T cells from scleroderma patients interact with fibroblasts, leading to excessive fibrosis. We expect to have the results of these experiments in the second half of 2014.

6.0 Highlights of Goal Accomplishments:

Goal	Target	Progress
1. Establish relationship with industry to sponsor outreach Continuing Medical Education (CME) program to primary care physicians and allied health.	Ongoing	Ongoing ✓ Several small grants have been awarded from industry for CME events and other educational initiatives such as the patient evening ✓ We continue the liaison with industry for ongoing educational projects.
2. Rollout CME program with annual events.	Ongoing	Ongoing ✓ A combined CME physician/healthcare and patient medical education conference was on September 24, 2011 in Hamilton, ON. 185 participants attended, of which 36 were medical professionals. ✓ Another combined CME physician/healthcare and patient medical education conference event was held in Hamilton with SSO, SSC, and HSG participating in September 2013 Followed by the Hamilton Scleroderma Congress. ✓ Medical Grand Rounds Jan 2014
3. Establish rolling visit program to LHIN.	Ongoing	This has been on hold for the past year as Dr. Cividino has taken the role of head of the Division. ✓ Comprehensive literature search pertaining to learning needs, learning performance outcomes and learning evaluation measures has been completed for the preparation of a didactic “Musculoskeletal Disorders Lecture Series for Family Physicians”.
4. Generation of educational	Ongoing	Ongoing Educational Materials for distribution and availability

Goal	Target	Progress
materials for distribution to primary care centers, LHIN and students.		to primary care centers, LHIN, and students include the following: ✓ SSO patient education brochures posted on St. Joseph's Healthcare web-site. ✓ John Hopkins "Living with Scleroderma" Patient Education Program posted on SSO web-site. ✓ A collection of educational resource material as part of the SSO web-site redevelopment. ✓ Medical lecture video series posted on SSO web-site. ✓ Hamilton Scleroderma Update 2011 CME Brochure distribution to over 4,984 health care professionals, 276 Scleroderma Society Members, and 300 Scleroderma patients from the clinics of Drs. Khalidi and Larché ✓ SSO "Supporting Persons with Scleroderma – AT HOME, WORK & SCHOOL" ✓ SSO "The Reporter" Quarterly Newsletter ✓ Hamilton Scleroderma Congress 2013 presentations uploaded on new HSG website. ✓ Creation of Newsletter article for patients role in research participation (in press)
5. Establish SSc educational evening for medical undergraduates	Beginning of Q1 2012 & annually thereafter	Ongoing ✓ Dr. Peter Margetts participated as a guest speaker at a "Careers Night" hosted by the Health Sciences Graduate Student Federation & Graduate Programs in Health Sciences on June 16th, 2010. Dr. Margetts will coordinate a Demystifying Medicine Rounds to inform the multidisciplinary medical community about scleroderma.
6. Begin actively enrolling patients in clinical studies as a CSRG Clinical Center.	Ongoing	Ongoing ✓ As of 19 February 2014, 189 scleroderma patients have been enrolled into the CSRG study through the clinics of Drs. Khalidi and Larché.
7. Establish a series of systemic sclerosis rounds at HHS / McMaster.	One every six months on a rolling basis.	Ongoing ✓ September 2012 – Clinical Immunology and Allergy rounds, McMaster University ✓ September 2012 – Family medicine rounds, St Joseph's Hospital ✓ January 2014 – Medical Grand Rounds, St Joseph's Hospital ✓ January 2014 – Family Practice Rounds, Stone

Goal	Target	Progress
		Church Medical Centre
8. First SSc grant submission to CIHR September 2011.	Aim for one each year for the following two years 2012/2013	Complete ✓ Drs. Margetts and Kolb have just received a $322,000 CIHR grant for their work on fibrocytes in glomerulonephritis which, although not directly related to systemic sclerosis, will improve knowledge in this disease.
9. Graduate 3 undergraduate students annually, each with four-month research thesis projects in systemic sclerosis.	Ongoing	Ongoing ✓ Two fourth year thesis students graduated in 2011 with 8-month research thesis in SSc. ✓ In Progress: Currently one 3rd year Biochemistry student involved with projects relating to SSc basic science ✓ One 3rd year BHSc student on target to start a summer studentship project on GI manifestations in SSc in April 2014.
10. Graduate one PhD scientist	2015	In Progress ✓ PhD candidate Jewel Imani on track to graduate in 2015.
11. Improve education of patients with scleroderma	2013	Complete ✓ "Needs Assessment" for congress attendees in 2013: ✓ Preparation of abstract and poster. ✓ Distribution of results to presenters to improve the direction of presentation to meet the stated needs of attendees. (see Appendix 5)

7.0 Strategic Direction / Future Plans 2014:

7.1 To promote ongoing graduate / medical education in the field of systemic sclerosis.

7.1.1 Jewel Imani, PhD Candidate continues his research into establishing a viable mouse model of scleroderma based on immune responses induced by bone marrow transplantation. This is particularly focussing on lung and kidney pathology.

7.1.2 Ongoing interactive sessions at rounds in rheumatology, immunology and family medicine.

7.1.3 Increasing presence in resident's teaching sessions.

7.1.4 Allied Healthcare professionals and students will be specifically targeted in order to foster interest and expertise in systemic sclerosis. Ellen McDonald will create a slide deck to present to nurses in areas where scleroderma patients are cared for in SJHH. Specifically, Out-patient clinic for patients receiving IVIG, In-patient areas: Nephrology, ICU and Cardiology.

7.2 Research:

7.2.1 Basic Science Research

7.2.1.a T cell activation, fibrosis, mouse models of disease. Determining interactions between fibrosis and T cell activation in patients with systemic sclerosis. These studies are ongoing and, by the end of 2014, we expect to have published our work in the interaction between T cells and fibroblasts.

7.2.1.b The mouse model of scleroderma is being developed currently with an emphasis on the pathological findings in the lung and the kidney. It is anticipated that this will be complete within the next 18 months to 2 years.

7.2.1.c Fibrocyte role in pulmonary fibrosis related to systemic sclerosis is ongoing.

7.2.1.d Investigation of T lymphocyte responses to cryptic determinants in the α3 and transmembrane region of human leukocyte antigens in systemic sclerosis.

7.2.2 Clinical Research:

7.2.2 a INDUSTRY SUPPORTED TRIAL Dr. Khalidi with Drs. Larché, Cox and Kolb have engaged in a study called The LOTUSS Trial: An Open-Label, Randomized, Phase 2 Study of the Safety and Tolerability of Pirfenidone When Administered to Patients With Systemic Sclerosis−Related Interstitial Lung Disease (SSc-ILD) (LOTUSS)

7.2.2.b NATIONAL COHORT STUDY CSRG: We continue to participate in the longitudinal national cohort, CSRG and in partnership with Dr. Khalidi and Dr. Larché. Sarah Fodor has stepped in to cover the project as the coordinator while Cathy Moreau is on Maternity leave. She will be focussing attention on coordinating this clinically relevant research. To date, HSG has enrolled 189 participants. There are 1,465 National participants.

7.2.2.c INVESTIGATOR INITIALED TRIAL In collaboration with Dr. Nair (respirology), Dr. Larché is currently preparing a protocol for a pilot study of antiIL-5 monoclonal antibody treatment in scleroderma to determine effect on lung function and skin scores.

7.2.2.d EPIDEMOLIGICAL STUDY Dr. Larché, in collaboration with Dr. Thabane, a biostatician, have secured a summer student for 2014 to explore analysis of the local CSRG database to answer clinically important questions pertaining to gastrointestinal features in scleroderma.

7.3 Clinical Care:

7.3.1 The "circle of care" of specialists and subspecialists with an interest in systemic sclerosis continues to be expanded. We have recently engaged a Dietitian at SJHH, Helen Van DeMark and a Psychologist, Dr. Joe Pellizzari. The Arthritis Society, along with the nursing schools and allied health schools at McMaster University will be petitioned to improve access to allied health professional care. In addition, patients attending the rheumatology clinics will be advised of the HSG website and the recently developed patient education material. http://www.hamiltonscleroderma.org

The HSG website has been linked with the McMaster Rheumatology and SSO websites.

7.3.2 Patients will be invited to attend specific educational sessions such as "navigating the health care system" "physiotherapy in systemic sclerosis"; "occupational therapy devices".

7.3.3 The HSG is sponsoring Dr. Alan Tyndall's visit to Hamilton. Dr. Tyndall has recently published his findings in Stem Cell research for patients who are living with scleroderma. He will review the protocol and present his work to clinicians and healthcare providers at a special rounds that will be held at the Juravinski Cancer Clinic and St. Joseph's Healthcare Hamilton. In addition, he will meet with patients/ families and allied healthcare providers to discuss scleroderma in Hamilton and in Toronto.

8.0 Budget.

8.1 Income of $152,000 per annum for 3 years has been received with an additional $152,000 committed for 2014. Additional income of $30,000 from the Around the Bay Road Race has also be allocated to the HSG Fund. The Fund balance as at March 31, 2014 is $301,944.

8.2 Proposed expenditures for 2014/2015

8.2.1 Seed funding for pilot data for basic research projects, it is proposed that researchers within HSG should be invited to submit small grant proposals to help with "seed funding" up to $10,000. These will be reviewed by the executive.

8.2.2 Developing workshops for patients such as "navigating the healthcare system".

8.2.3 Some running costs, e.g. stationary and rental of telephone line for the coordinator (maximum $1,000)

8.2.4 Summer students (up to 2) at a cost of $6,000 each.

8.2.5 Visiting professor costs – approx. $7,000

8.3 Current expenditure includes salary and running costs for PhD student Jewel Imani ($50,000 pa); salary and benefits for quarter-time coordinator ($30,000 pa); travel expenses for PhD Student and coordinator ($8,000 pa).Summer students (max of 3) up to $18,000pa. Fibrocyte role in pulmonary fibrosis, $30,000. Total projected expenditure for 2014/2015 fiscal year is $144,000.

8.4 Further funding after 2014: The SSO has committed another substantial grant for ongoing support of the HSG after 2013. This will facilitate continuing basic science and clinical research; improvements in clinical care; and ongoing educational programs. There may be an opportunity to create a "systemic sclerosis fellowship" for rheumatology fellows to continue their subspecialty training through the rheumatology program at McMaster University.

9.0 Strengths, Weaknesses, Opportunities and Threats (SWOT) analysis

Strengths

- A highly motivated multidisciplinary group with independently established interests in an underserved disease area.
- Significant advances in education in the Hamilton area through the combined efforts of Susan Docherty-Skippen, Maureen Sauvé and the medical and scientific faculty of HSG. Ongoing work now with Ellen McDonald.
- Pushing forward with collaborative work to explore new treatments for scleroderma.
- Positioned for primary educational role of students in undergraduate medical, science, nursing and allied health care and postgraduate students.
- Dedicated coordinator/patient-educator to facilitate access to health care and PhD student funded by SSO grant.
- Currently involved in CSRG.
- HSG has a local, regional and National reputation for excellence in Scleroderma healthcare and research.

Weaknesses

- Lack of adequate resources to facilitate basic science research and clinical trials.
- Current members of the group have competing commitments.

Opportunities

- Opportunity to strengthen undergraduate, allied health and postgraduate education, raising the profile of this disease in the scientific and medical community.
- Opportunity to engage local systemic sclerosis patients in clinical research studies.
- Increase physician resources by generating a systemic sclerosis fellowship program.
- Unparalleled opportunity to establish outreach educational program in LHIN and primary care for improved diagnosis and clinical care of patients with systemic sclerosis.

Threats

- Loss of momentum within the current group.
- Decay and fragmentation of the group.

10.0 Summary:

Through strategic research, education and patient care initiatives, the HSG has successfully achieved the primary objectives established at the onset of its formation in 2009. During the past 3-4 years, the educational agenda for the HSG has been developed, and will continue with a push to develop an integrated educational program including scleroderma through the LHIN. The basic research platform is continuing with activity in lung disease, renal pathology and in basic cellular biology. By the end of this year, it is anticipated that there will be published work relating to T cells and fibroblasts, and the development of a mouse model. Future work in the clinical field of scleroderma include the perfenidone trial in scleroderma, and the development of a pilot study of IL-5 inhibition in pulmonary fibrosis.
Engagement of new disciplines, such as dietetics and psychology and clinicians including emergency room doctors and respirologists with an interest in pulmonary hypertension to meet the needs of patients, has continued. A new HSG website has been launched to improve access to care for patients.
With the professional input and generous ongoing support of the Scleroderma Society of Ontario, along with leveraging funds through other funding organisations such as the CIHR, the HSG and its members look forward to continuing the collaborative research, clinical care and education in order to improve the lives of people living with scleroderma.

Appendix 1:

Developing a mouse model of systemic sclerosis

Introduction

Scleroderma or systemic sclerosis (SSc) is a rare heterogeneous disease. SSc is characterized as a dysfunction of the endothelium, fibroblasts and immune system, its pathogenesis is characterized by; vascular damage, activation of the immune system and deposition of collagen and extra cellular matrix proteins in the skin and internal organs including lung, kidney, and vascular system. While the etiology of this disease in unknown there is evidence that SSc may be linked to the presence of foreign immune cells in the patient, known as microchimerism. This phenomenon most commonly occurs during pregnancy during which cells from the fetus can across the placenta and enter the mother, known as fetomaternal microchimerism. Conversely maternal cells from the mother can also cross into the fetus; however this is appears to be rarer (6). The consequences of this phenomenon have yet to be fully elucidated; however it may lead to the development of chronic graft vs host disease (cGVHD). cGVHD occurs when immune-competent cells present in the bone marrow or other transplanted tissue from a donor reacts with the recipients surface antigens and the host must be incapable to mounting a response to the donor immune cells (3).

SSc and cGVHD have many similarities and SSc may represent a form of cGVHD and active fetal CD4+ T-cells have been found in the biopsies of lesional skin from SSc patients (1, 10). The skin and lung are involved in both diseases with prominent fibrosis (5), infiltration of immune cells is an early event and tissue damage is mediated by T-cells in both cases (7). Additionally, in one study anti-topo-1 antibodies were found in 32% of patients with cGVHD (2). Therefore it hypothesized that Scleroderma represents a form of chronic graft vs host disease brought on my presence of foreign cells in the patients originating from either previous blood transfusion/tissue transplants or fetal cells in the mother. Such an occurrence would offer an explanation for the increased incidence of SSc in older women than men. While the pathogenesis of GVHD also remains unclear, the presence of autoantibodies in GVHD patients would indicate that a response to auto antigen is occurring (11). Due to the rarity and heterogeneity of scleroderma; effectively studying this disease is difficult. The best alternative currently is studying mouse models of GVHD.

Objective

The objective of this project is the development and characterization of a mouse model of cGVHD as an analogue of Scleroderma. There are various mouse models of cGVHD, however most models employ a similar strategy of adoptively transferring bone marrow and/or spleen cells across major or minor histocompatibility antigen mismatched strains of mice. Our current study has adapted the B10.D2 -> BALB/c model as first described by Clark et *al* 1985(4), which utilizes the adoptive transfer of bone marrow and spleen cells from B10.D2 mice into sublethally irradiated BALB/c mice (4, 8, 12). In our study, BALB/c mice were irradiated with 650 RADs (6.5 Gy) and reconstituted with either donor B10.D2 (treatment) or BALB/c (control) RBC free $2x10^6$ splenocytes and $1x10^6$ bone marrow cells. Donor mice were euthanized through anaesthesia overdose and cervical dislocation. The femurs, tibias and humeri bones were harvested, placed in PBS and grinded using a mortar and pestle.

The cell suspension was passed through a 70 um filter and red blood cells were subsequently lysed. Spleen cells were recovered by physically rupturing the spleen in HBSS and filtering the cell suspension through a 40 um filter and subsequently lysing the red blood cells.

The two cells suspensions were mixed in PBS at appropriate concentrations and 200µl of the bone marrow and spleen cell suspension (13) was intravenously injected into the recipient mice under gaseous isoflurane anaesthesia. The recipient mice were monitored three times daily for signs of poor health, skin lesions, diarrhea, and weight loss, weighed on alternating days for 2 weeks after which they were monitored once daily until study endpoint. Acetaminophen was given to any animals displaying discomfort (under discretion of the animal facility staff). At the study endpoint; days 30, 60 and 90 groups of 5 mice were sedated, anesthetized and then euthanized; lung, kidney and skin tissues were then collected for analysis.

Results

Lung Physiology
Each Mouse was intubated with an 18g needle and placed on a “flexivent” mechanical ventilator while lung compliance (Fig 1a) and airway resistance (Fig 1b) measured were taken and analyzed by Flexivent 5.2 software. A lower compliance value indicates a lung which is stiffer. There is a significant difference in lung compliance between treatment and control groups at day *30 p=00002, **60 and ***90 p< 0.0001. There is also a significant increase in lung compliance from day 60 to 90 p<0.001 in the control groups and a significant decrease in lung compliance from day 30 to 60 and day 30 to day 90 p = 0.03 and p=0.02 in the treatment groups. A significant difference is seen between treatment and control groups on days *60 and *90 p=0.0005 and 0.008. There was no significant difference in airway resistance in the control groups between any days. There was however a difference between day 30 and 60 and day 60 and 90 in the treatment groups, p=0.0004 and p=0.007.

BAL
Two 250 µl volumes of PBS were injected with a 1 ml syringe while massaging the chest in between injections. The PBS was subsequently extracted and the cells were enumerated following a Modified Wright Giemsa Staining protocol for neutrophils, lymphocytes, eosinophils and macrophages. (Fig 2a-d). There is no significant difference in the control groups for any cell type at any time point. There appears to be an increase in all cell types in treated groups from day 30 to 60, however the number of cells returned within control levels by day 90. The only significant difference between treated and control groups is seen in neutrophils on days 30 and 60, p>0.001 and p=0.252.

Lung Histology
Mouse lungs were placed in 10% formalin for a minimum of 24 hours, the left lobe was dissected into superior, middle and inferior sections. The 3 sections were embedded in paraffin wax, cut into 4 µm sections and stained with picrosirius red (PSR) for collagen staining. Stained lung section images were captured at 100x using an Olympus BX40 camera. Three random sections of lung parenchyma were imaged and percent PSR stain area was using northern eclipse 5.2 image analysis software. The basement membranes of the major airways and blood vessels were intentionally excluded for analysis. There was no noticeable collagen staining present in the parenchyma of the lungs in both the control and treatment groups at any time points. (Data not Shown)

Skin Histology
Skin samples from the dorsum were shaven and excised. The skin was placed on filter paper to prevent the samples from shrinking or folding and placed in 10% formalin for a minimum of 24 hours.

Samples were processed and paraffin embedded. 4 µm sections were cut and stained with PSR for collagen. Skin sections images were captured at 100x using an Olympus BX40 camera. Skin collagen staining was calculated by selecting a band encompassing the dermis and subcutaneous layer (Fig 3b) and percent PSR stained area was calculated from 3 fields per samples using northern eclipse 5.2 image analysis software (Fig 3a). There is a negative difference between treatment and control group on day *30 p=0.003, however there is a positive significant difference between control and treatment groups at day **60 p=0.01. No difference is seen at day 90.

Kidney Histology
One kidney from each mouse was collected for histology. The kidney was placed in 10% formalin for a minimum of 24 hours. The samples were processed, paraffin embedded and 4um sections were cut and stained with Massons Trichrome. (Data not shown, In Progress)

Urine Analysis
Urine was collected every 3 weeks starting 21 days after cell transfer. Individual mice were placed in a metabolic cage and urine was collected for 8 hours. Urine protein (mg/L) and creatinine (µmol/L) levels were measured and proteinuria is expressed as a ratio of protein to creatinine (mg/µmol). Proteinuria was compared to syngeneic controls (Fig 4). There is significant difference between the treatment and control groups over 90 days p = 0.04 however no difference between treatment and control groups is seen at individual time points.

FACS
Shaved dorsal skin samples from each mouse was collected and digested in a media containing collagenase, hyalrundiase and DNase for 2 hrs at 37^{O}C. The cells were filtered through a 70 um filter and mononuclear cells were density separated using histopaque. Cells were then stained for CD4+ T-cells, CD8+ T-cells, and CD11b+ macrophages. (Data not shown, In Progress)

Discussion

BALB/c mice were irradiated with 650 RADs and reconstituted with $1x10^6$ bone marrow and $2x10^6$ spleen cells from donor B10.D2 mice. These two strains of mice are MHC matched but are mismatched at minor antigens MiHC. Donor lymphocytes should recognize and reject these minor antigens on the recipient's tissues, overtime this may lead to a chronic GVHD phenotype with disease manifestations in Lung, skin and kidneys. Previous work on this scleramatous GVHD mouse model has shown increased collagen I mRNA, macrophage infiltration and TFG- β in the skin by day 21 post cell transfer (4,8,12) lung alveolar space is reduced by day 21 and there is increased dermal thickening from day 21 to 75 (9). However no kidney involved was shown. In our current study, Groups of treated and control mice were euthanized on days 30, 60 and 90 and the previously mentioned tissues were analyzed. While we did not see any difference in lung collagen deposition in the treated groups, we did however see decreased lung compliance in the treated mice as early as day 30 which continued to decrease up to 90 days.

We also see increased airway resistance in the treated mice starting at day 60; this data complements the results from previous studies showing reduced alveolar spaces in these mice. The treatment mice also showed significantly increased skin collagen staining on day 60 and 90 (not significant). This is also consistent with previous findings showing increased collagen I mRNA in the skin of treatment animals (9).

There was an overall increase in proteinuria over 90 days in the treatment group compared to the controls. This may be caused by a dysfunction if glomerular filtration leading to increased protein in the urine an indicator of kidney involvement in our model GVHD. Most of the mice in the study tolerated the treatment protocol; however three mice from the day 90 treatment group had adverse reactions and were prematurely euthanized. Two mice on day 60 (data merged with day 60 group) and one mouse on day 85 (no data). These three mice may have had an acute GVHD response characterized by rapid onset weight loss and skin lessions. Solutions to decrease the chances of acute GVHD manifesting in future experiment may include reduced the radiation regiment and or reducing the number of transferred cells. While the skin cells remain to be analyzed by FACS and kidney histology still needs to be analyzed, the current data is suggestive that the mice are undergoing a GVHD type response, however the missing mice from the day 90 treatment group renders these data points unreliable and the study needs to be repeated.

Fig 1

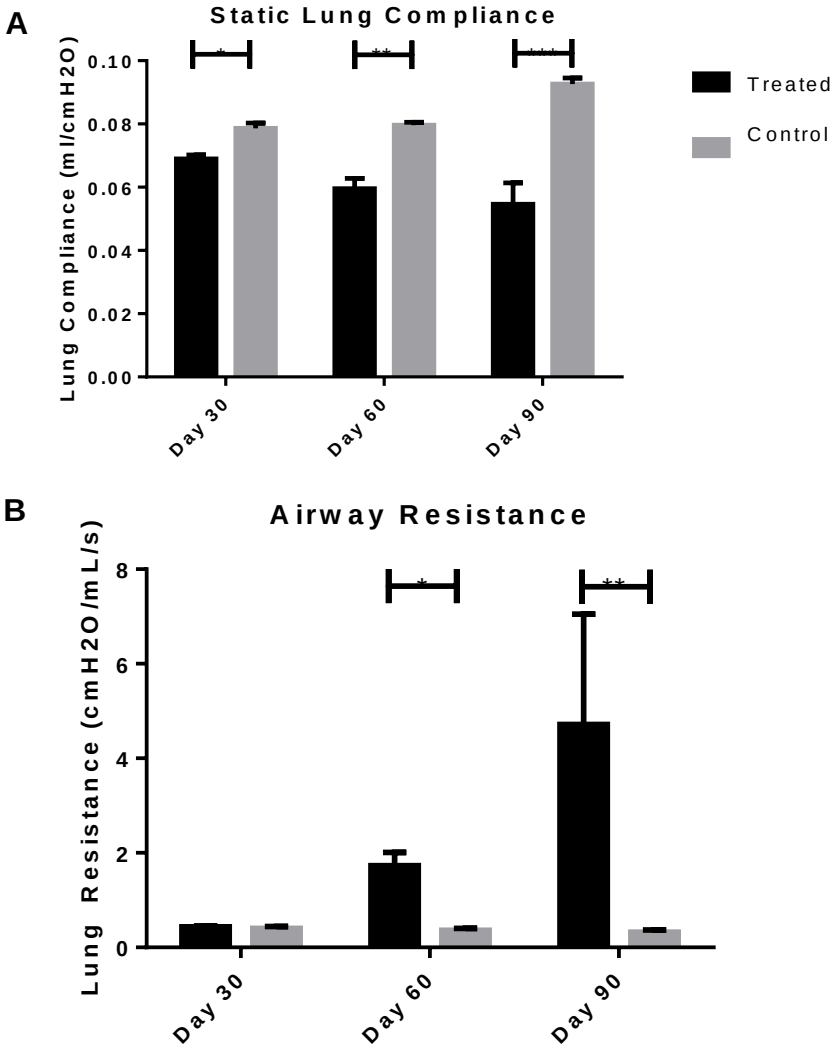


Fig 1. (A) Static lung compliance in BALB/c mice injected with Bone marrow and Spleen cells from B10.D2(treatment) or BALB/C (control) mice. A lower value indicates a "stiffer" lung. A significant difference in lung compliance between treatment and control groups at day *30 p=00002, **60 and ***90 p< 0.0001.Data analyzed using two tailed t-test. There is also a significant increase in lung compliance from day 60 to 90 p<0.001 in the control groups and a significant decrease in lung compliance from day 30 to 60 and day 30 to day 90 p = 0.03 and p=0.02 in the treatment groups. A significant difference is seen between treatment and control groups on days *60 and *90 p=0.0005 and 0.008. Data analyzed using one way ANOVA with uncorrected Fisher's LSD. (B) Airway resistance in BALB/c mice injected with Bone marrow and Spleen cells from B10.D2 (treatment) or BALB/C (control) mice. A greater value indicates increased resistance to airflow through the airways. No significant difference in airway resistance in the control groups between any days. A significant difference between day 30 and 60 and day 60 and 90 in the treatment groups, p=0.0004 and p=0.007. Data analyzed using one way ANOVA with uncorrected Fisher's LSD

Fig 2

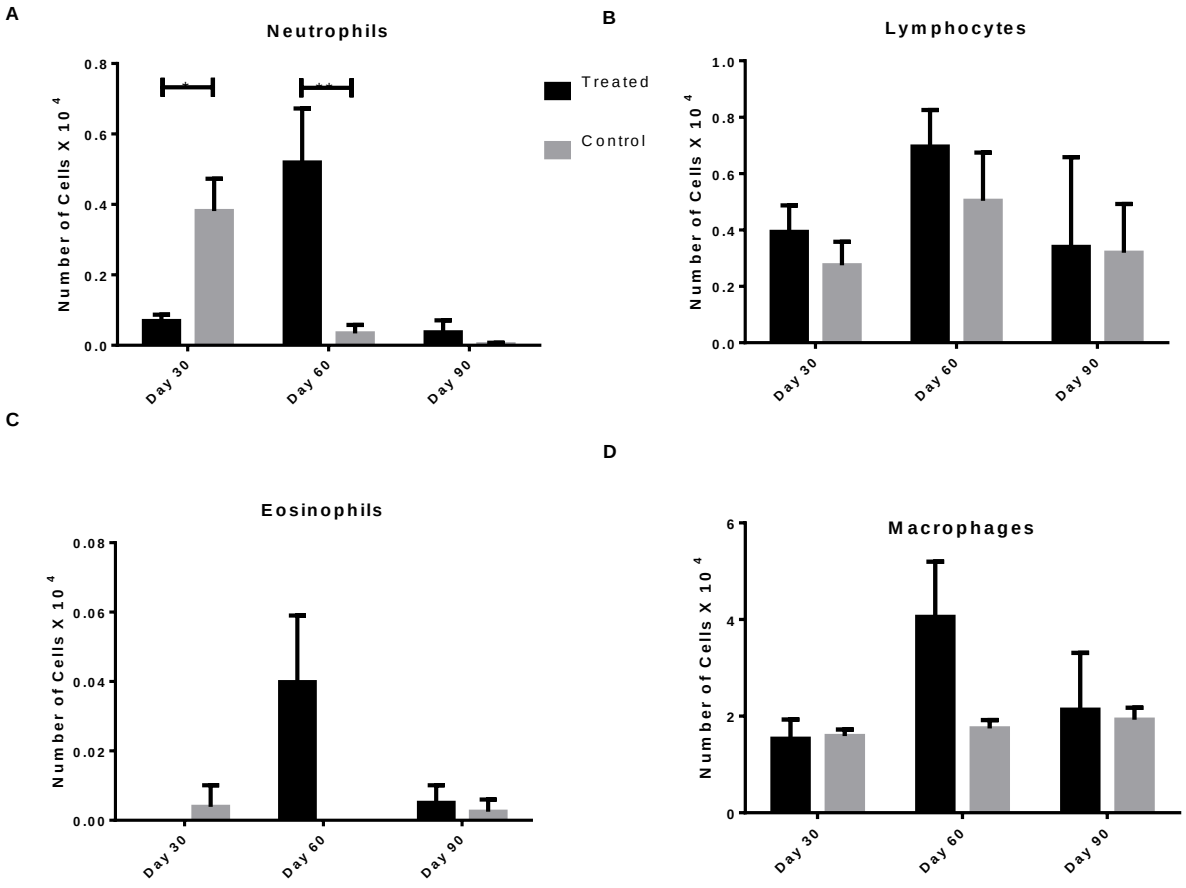


Fig 2 - 200 cells from each mouse was randomly counted twice, data represents median value of entire group per time point. Error bars indicate standard deviation of the mean. A significant difference in neutrophils is seen between treated and control groups on days 30 and 60 * p<0.0001 **p = 0.0252 respectively. Data was analyzed using two tailed t-test

Fig 3

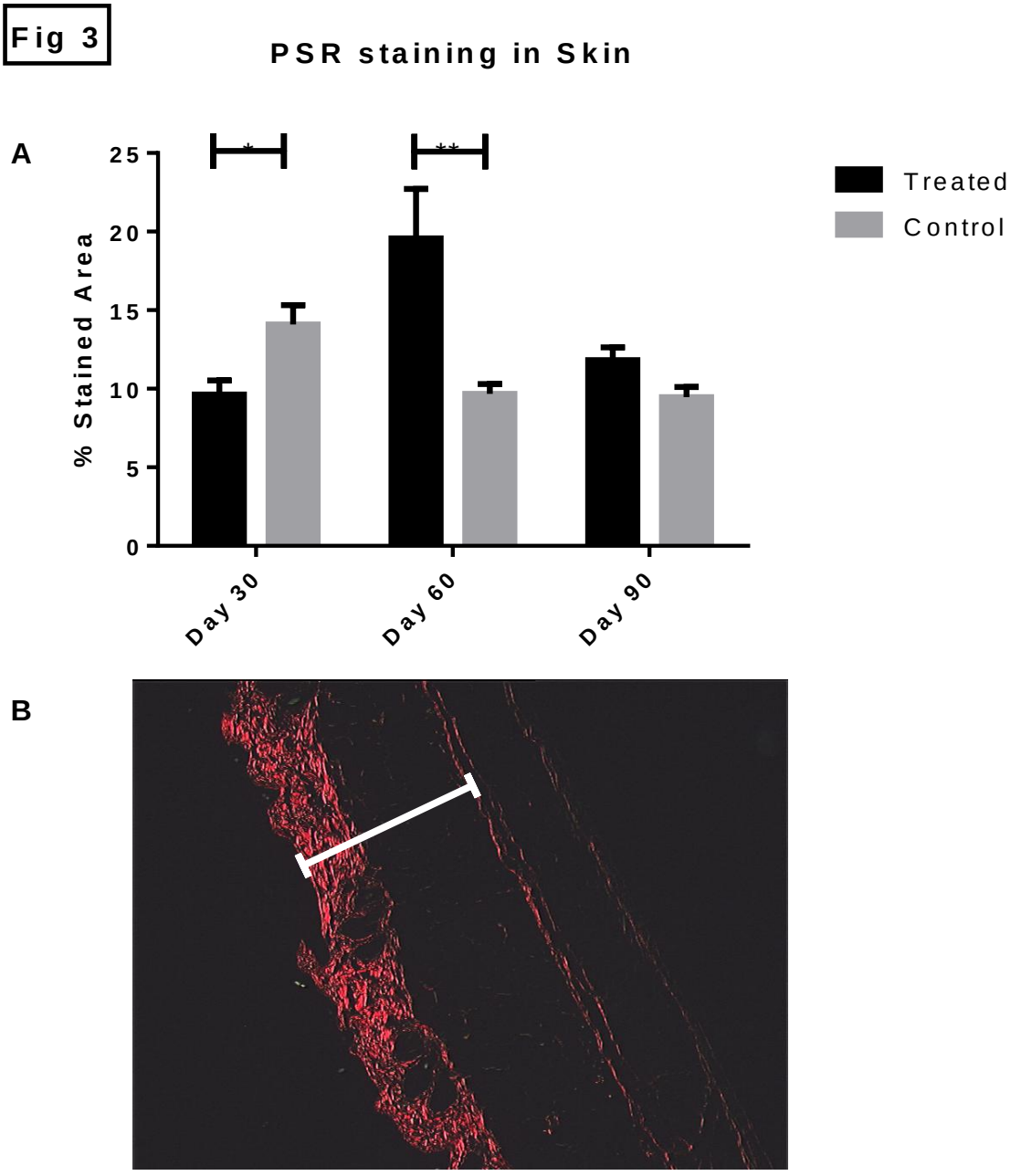


Fig 3. Skin sections were stained with PSR and imaged at 10X. A band encompassing the dermis to the subcutaneous layer interiorly was selected and the percent stained area was calculated. 3 random fields were sampled from each skin section. (A)There is a negative difference between treatment and control group on day *30 p=0.003. Significant difference between control and treatment groups at day **60 p=0.01. No difference is seen at day 90. (B) White line denotes measured area comprising dermis and subcutanous layer. Red areas represent collagen.

Fig 4

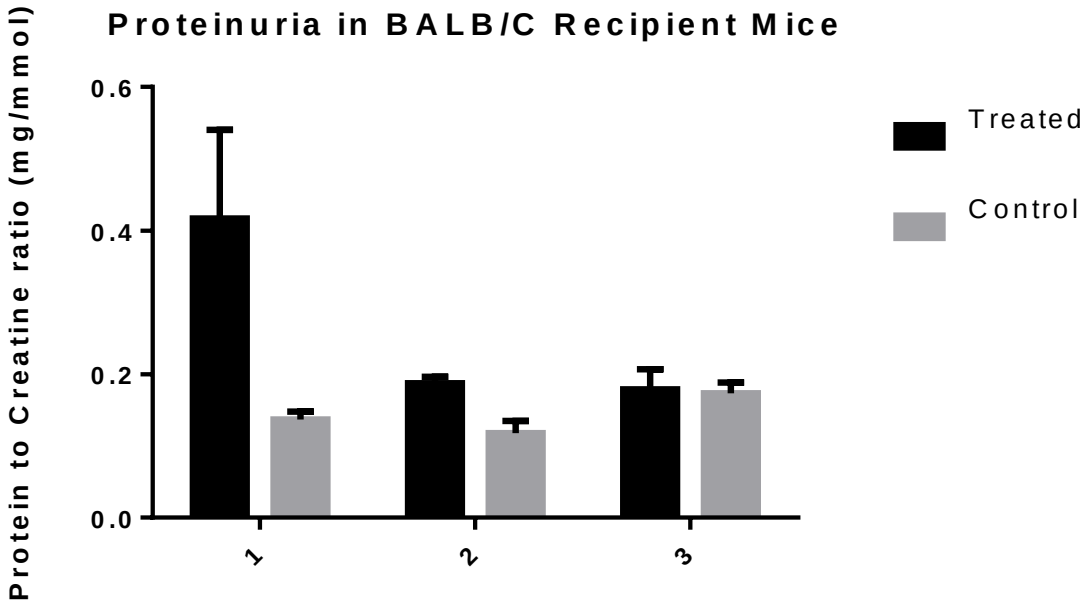


Fig 4 - Urine samples were collected from recipient mice every 3 weeks until day 90. Proteinuria is measured as urine protein to creatinine ratio (mg/mmol). A greater value suggests a dysfunction in glomerular filtration, an indicator of kidney failure. There is significant difference between the treatment and control groups over 90 days p = 0.04 however no difference between treatment and control groups is seen at individual time points. Data analyzed with two way RM ANOVA.

References

1- Artlett CM, Cox LA, Ramos RC, et al. Increased microchimeric CD4+ T lymphocytes in peripheral blood from women with systemic sclerosis. Clinical Immunol 2002;103:303–308.
2- Bianchi DW, Zickwolf GK, Weil GJ, et al.: Male fetal progenitor cells persist in maternal blood for as long as 27 years postpartum. Proc Natl Acad Sci USA 1996;93:705–708.
3- Brubaker DB: Immunopathogenic mechanisms of posttransfusion graft versus-host disease. Proc Soc Exp Biol Med 1993; 202:122–147.
4- Claman HN, Jaffee BD, Huff JC, Clark RA. Chronic graft-versus-host disease as a model for scleroderma. II. Mast cell depletion with deposition of immunoglobulins in the skin and fibrosis. Cell. Immunol 1985;94:73-84.
5- Jelaska A, Korn JH. Role of apoptosis and transforming growth factor-1 in fibroblast selection and activation in systemic sclerosis. Arthritis Rheum 2000;43:2230-9.
6- Kalogerou A, Gelou E, Mountantonakis S, Settas L, Zafiriou E, Sakkas L. Early T-cell activation in the skin from patients with systemic sclerosis. Ann Rheum Dis 2005;64:1233-5.
7- Korngold R. Lethal graft-versus-host disease in mice directed to multiple minor histocompatibility antigens: Features of CD8+ and CD4+T cell responses. Bone Marrow Transplant 1992; 9:355-364.
8- Korngold R, Sprent J. Lethal graft-versus-host disease after bone marrow transplantation across minor histocompatibility barriers in mice. Prevention by removing mature T cells from marrow. J. Exp. Med 1978;148: 1687-1698.
9- McCormick LL, Zhang Y, Tootell E, Gilliam, AC. Anti-TGF-beta treatment prevents skin and lung fibrosis in murine sclerodermatous graft-versus-host disease: a model for human scleroderma. J. Immunology 1999;163:5693-5699.
10- Sawaya HHB, Jimenez SA, Artlett CM: Quantification of fetal microchimeric cells in clinically affected and unaffected skin of patients with systemic sclerosis. Rheumatology 2004;43:965–968.
11- Spangrude GJ. Assessment of Lymphocyte Development in Radiation Bone Marrow Chimeras. Current Protocol Immunology 2008;81:4.6.1-4.6.9.
12- Zhang Y, McCormick LL, Gilliam AC. Latency-Associated Peptide Prevents Skin Fibrosis in Murine Sclerodermatous Graft-Versus-Host Disease, a Model for Human Scleroderma. The Journal of investigative Dermatology 2003;121:4.
13- Zhang C, Todorov I, Zhang Z, Liu Y, Kandeel F, Forman S, Strober S, Zeng D. Donor CD4+ T and B cells in transplants induce chronic-verus-host disease with autoimmune manifestations. Blood 2006;106:2993-3001.

Appendix 2

Investigation of T lymphocyte responses to cryptic determinants in the α3 and transmembrane region of human leukocyte antigens in systemic sclerosis.

Principal Investigators:

Dr. Mark Larché, Dr. Maggie Larché

Co-Investigators:

Dr. Derek Haaland, Dr. Elzbieta Kaminska, Dr. Nader Khalidi

Study Overview:
Key pathogenic components of SSc including immune activation, vasculopathy and fibrosis. Prognosis is poor and current therapeutic avenues are unsatisfactory. Sakkas and Plateau have summarized evidence favouring a central role for T cells in the pathogenesis of systemic sclerosis, with a TH2 skewed response. A number of studies have identified oligoclonal T cell expansion in this disease, but the relevant antigen(s) have yet to be identified. There are many apparent similarities between clinical manifestations of systemic sclerosis and those in graft versus host disease. The rationale for the current proposal is founded in earlier studies by the PI and collaborators in the United Kingdom, focusing on the loss of self tolerance to framework regions of major histocompatibility complex (MHC) molecules in patients awaiting renal transplantation or with graft versus host disease following renal and/or liver allograft (unpublished observations). The purpose of this study is to investigate autoimmune responses to framework (non-polymorphic) regions of MHC class I molecules and the loss of tolerance to self.

Study Update:

Based on initial findings, where TGF-beta responses were exaggerated to a) peptides from the HLA-A2 molecule and b) also to common recall antigens, we have been focusing on whether there is an increased TGF-beta response in patients with scleroderma to all antigens. To do this, we have recruited 10 patients with SSc and 10 control subjects (healthy volunteers). We will assess TGF-beta responses together with other disease-relevant

cytokines (MCP-1, MIP-1alpha, IL-6, IL-17 and IFN-gamma) in response to a variety of common antigens (bacterial, viral, food, airborne, skin) to account for why these patients have systemic fibrosis. Subsequently, we will perform co-culture experiments to determine whether enhanced TGF-beta responses from T cells cause fibrosis through activation of fibroblasts and myofibroblasts from cell lines. Both supernatants from peripheral blood mononuclear cells (PBMC) cultures and T cells from patients with scleroderma will be used and compared to healthy volunteer samples. We will determine fibrosis-related outcomes including measurement of collagen, extracellular matrix genes and myofibroblast numbers and activation. Genetic analysis using polymerase chain reaction (PCR) will be performed on the fibroblasts which had been co-cultured with T cells or with supernatant, and on the T cells from patients compared to healthy volunteers.

1) In patients with SSc, T cell responses to HLA peptides were associated with increased TGF beta and decreased MIP1alpha. In order to determine whether the response is HLA-specific , we did another T cell stimulation experiment in SSc vs controls using mitogen and recall Ags and showed that increased TGFbeta did not seem to be associated with these stimulants.

Now we are repeating the original study in a new independent cohort with HLA peptides and a disease control group (RA)

2) Another study has been designed to confirm whether HLA responses are disease-specific phenomenon. Exaggerated T cell responses to HLA may occur in a number of diseases other than SSc. We have therefore repeated this experiment with a disease control group (rheumatoid arthritis). We have completed patient recruitment (10 subjects with SSc, 10 age and gender-matched healthy controls and (additionally) 10 subjects with inflammatory autoimmune disease (RA)). We will determine whether

    i) increased TGFb responses are reproducible in a second independent study

ii) enhanced TGFb production to HLA peptides is a disease-specific phenomenon (observed in SSc but not RA)

We will then go on to use the supernatants to see if they induce profibrotic gene expression in fibroblasts.

3) Determining the effect of T cell supernatants on fibroblast cocultures

Principal Investigators: Dr Mark Larché ; Dr Martin Kolb, MD, PhD

During this study, T cells from patients with scleroderma and from healthy controls are cultured with a variety of stimulants. The supernatant is then co-cultured with fibroblasts to determine whether excess fibrosis occurs in the presence of scleroderma supernatants.

Update:

We have cultured 2 fibroblast cell lines with supernatants from PBMCs (stimulated or unstimulated) from healthy controls and subjects with scleroderma at 3 dilutions (25,75 and 5) to see whether supernatants from stimulated SSc T cells could induce enhanced ECM production by fibroblasts. Interestingly we found that supernatant of unstimulated SSc cells appeared to induce elevated expression of a number of ECM matrix genes compared to healthy control samples. These findings are being followed up.

Appendix 3

Role of the fibrocyte in rapidly progressive glomerulonephritis.

CIHR grant $322,000 over 4 years

Principal investigators: Dr Peter Margetts and Dr Martin Kolb

Rapidly progressive glomerulonephritis refers to a group of autoimmune renal diseases manifest by glomerular inflammation. These diseases are associated with a significantly increased risk of mortality and progression to end stage renal disease. Effective immunosuppressive therapy reduces these outcomes, but also exposes patients to important risks of infection and malignancy. Progression to end stage renal disease is associated with kidney function at the time of renal biopsy, but also correlates with the extent of fibrosis evident in the biopsy material. The cause of this tubulointerstitial fibrosis is not clear, but may be related to the recruitment of bone marrow derived fibrocytes.

Fibrocytes were first described by Bucula and colleagues in 1994. This is a circulating peripheral blood cell identified by surface progenitor markers (ie CD34) and markers of mesenchymal phenotype (intracellular pro-collagen). It has been hypothesized that fibrocyte mobilization from the bone marrow occurs in the setting of injury; these cells then home to the injured tissue and play a reparative role. It is further hypothesized that organ fibrosis represents an aberrant healing response, and that fibrocyte recruitment may play a deleterious role in this process.

Hypothesis: We hypothesize that peripheral blood fibrocytes will be increased in patients with acute glomerulonephritis and patients with more circulating fibrocytes will have worse renal outcomes.

Methods: PEXIVAS is an ongoing multicentered study randomizing patients with anti-neutrophil cytoplasmic antibody (ANCA) positive glomerulonephritis to 2 different treatment regimens. We will use the infrastructure developed in this study to recruit 150 patients. A

blood sample will be taken at enrollment, 2 weeks and 3 months. We will measure the number of circulating fibrocytes using flow cytometry. From the patients who have a renal biopsy (80%), we will use dual immunofluorescence to assess the tissue presence of fibrocytes. Tissue and serum will be assayed for the chemokines stromal derived factor -1, monocyte chemotactic protein -1 and secondary lymphoid tissue chemokine – all associated with mobilization and recruitment of fibrocytes. Clinical data will be gathered at enrollment and at 1 year. The primary outcome will be the change in glomerular filtration rate after diagnosis and we will compare the number of circulating and tissue fibrocytes with this change. We will further compare chemokine expression in serum and tissue with mobilization of fibrocytes and recruitment to renal tissue. In s subgroup of patients, we will grow fibrocytes from peripheral blood and compare the gene expression of these fibrocytes compared to fibrocytes derived from healthy volunteers.

Impact: Glomerulonephritis is a potentially fatal renal disease. Treatment is effective, but is highly toxic. Prognostic indicators help with treatment decisions and quantification of circulating fibrocytes may provide important additional prognostic information that can guide therapy and possibly improve patients' outcomes. Our research will also answer important basic questions about fibrocyte recruitment and function that will open further avenues of investigation. By quantifying circulating and tissue fibrocytes, and comparing this with clinical outcome, we will be able to answer whether fibrocytes are associated with disease progression and how this interaction occurs. With this knowledge, further treatment options that alter fibrocyte recruitment can be envisioned as adjunctive therapy in this serious kidney disease.

Appendix 4

Fibrocytes in Idiopathic Pulmonary Fibrosis and Scleroderma Pulmonary Fibrosis

Principal Investigator: Dr Martin Kolb

Previous work has shown that circulating fibrocytes are increased in patients with pulmonary fibrosis. Studies are ongoing to determine whether this finding also pertains to fibrosis associated with systemic sclerosis.

Appendix 5

Needs Assessment of Patients with Scleroderma Attending an Educational Congress

E. McDonald, M. Kho, M. Larché, M. Sauvé, A. Takaoka, D. Cook, G. Guyatt

Background
Scleroderma is a complex, multifaceted disease with large impact on quality of life. Optimal care involves assessing the needs of patients, their families, and clinicians.

Objective
Our objective was to understand the learning needs of scleroderma patients, their families and their clinicians.

Methods
1) Document Review and Domain Generation
We conducted a textual analysis of 94 Scleroderma Congress evaluations from 2011, focused on issues that addressed participants' learning needs.

2) Survey of Importance Ratings
We asked patients attending the Hamilton Scleroderma Support Group to rate the importance of each of the 9 domains generated by congress evaluation form review using a 4 point Likert scale (1=least important to 4=most important). Respondents added additional items that they believed were important.

Results
Congress Evaluations: of 185 attendees at the prior Scleroderma Congress, 94 (50.8%) completed evaluations. We summarized their comments in 9 domains.

Support Group Survey: At the Hamilton Spring 2013 support group meeting, 12 patients with scleroderma (mean duration 10.3 years) completed the questionnaire and chose "signs and symptoms" and "research" as the highest ranking domains and "psychosocial concerns" and "stories/ testimonials" as the lowest.

Conclusions
We used 2011 Scleroderma Congress evaluations and 2013 support group importance survey results to develop a patient-centered congress. 4 domains (signs and symptoms, research, lab results and disease) were rated as $\geq$ 3.5 (between important and very important). There is a need to address these issues with patients, families, and healthcare providers. Results were provided to speakers to assist with their congress presentation.