MICHIGAN MEDICINE

Scleroderma Research and Patient Care

University of Michigan Scleroderma Program
2017-18 Highlights

June is Scleroderma Awareness Month. As I reflect on my time at the University of Michigan and our mission to provide local, national and international leadership to advance the treatment of scleroderma and related conditions, through excellence in clinical care, teaching and research, I am excited for what we've accomplished. Together, with your support, we are transforming care for patients with scleroderma.

Scleroderma means hard skin. This rare and unpredictable disease is usually diagnosed in the prime years of life, between the age 30-50 and can cause hardening of the skin, damage to the blood vessels and internal organs, including the heart and lungs. Everyday people diagnosed with scleroderma navigate the challenges that come with this disease.

With autoimmune disorders like scleroderma, the immune system reacts to normal body tissues that it would normally ignore. What causes the immune system to no longer tell the difference between healthy body tissues and foreign antigens in unknown. Here at Michigan, we have built one of the largest clinical and research programs with a team of clinicians and scientists who, everyday are working tirelessly to stop and reverse the features of the disease that affect patients' quality of life and threaten their health.

I am pleased to share the following updates and accomplishments over the past year in the Scleroderma Program in the Division of Rheumatology at Michigan Medicine. We are:

- **Leading the way and partnering with the National Institutes of Health and pharmaceutical companies to design and conduct clinical trials and studies in scleroderma:** We are embracing an unprecedented period of progress and hope in science - the opportunities for launching new scientific endeavors, for creating partnerships for innovative projects and advancing the pace of drug discovery are boundless. Scientists in the lab are investigating the causes of scleroderma from a basic science level looking at genetics and environmental effects that active an immune response. We are studying promising compounds and discovering new ways to intervene and interrupt this pathway to flip the "off" switch of the disease or slow the process. In addition, scientists in our labs have discovered a novel protein that is elevated in some patients with early scleroderma—paving a way to personalized therapy. We are also looking at the interplay between the genetics and environment and how it can cause scleroderma.

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  - **Evaluation of Tofacitinib (Xeljanz ®, approve for rheumatoid arthritis) in early diffuse cutaneous systemic sclerosis**- (funded by Pfizer)
  - **Scleroderma Lung Study – Phase III –** comparing Pirfenidone [Esbriet®], approved for IPF (funded by Genentech/Roche)
  - **Riociguat (Adempas ®) in scleroderma digital ulcers** (funded by Bayer)
  - **Trial for Abatacept (Orencia®), an FDA approved drug for RA,** (funded by BMS)
  - **Novel Rehabilitation Strategies to improve function in patients with Scleroderma**- (Partnership with Dr. Murphy in occupational therapy)
  - **University of Michigan/Michigan State University partnership.** A collaborative project with **Dr. Dinesh Khanna, Dr. David Fox, Dr. Scott Larsen and Dr. Richard Neubig** at Michigan State University to develop new treatments/drugs for scleroderma. Over the past few years, we have improved our compounds so that they aren't cleared from the body so fast in mouse studies. Also, we have discovered how the compound works. We found a protein that the compound binds to and that has let us more rapidly improve the potency of our compounds by computer-aided drug design. Our

next major step is to pick a compound to move toward clinical trials – that is a clinical candidate. We hope to do that late this year or early next and in clinical trials in approximately 2 years.

- **Investing in Medicine's Best and the Future of the Field:** Only with a great team can the Scleroderma Program fulfill its commitment to making significant advances in scleroderma. We have secured two new remarkable faculty members, and honored another with the appointment of an endowed professorship in efforts to further strengthen the research, education and individualized clinical care.

    - **Vivek Nagaraja, MD**, Clinical Assistant Professor, works in partnership with Dr. Khanna in clinical trials in scleroderma. He is interested in assessing impact of lung fibrosis in scleroderma and how pulmonary rehabilitation can help them.
    - **Amber N. Young, MD,** Clinical Lecturer and Research Fellow, is involved in clinical research with a focus in pulmonary arterial hypertension. She is currently assessing on how to detect and treat scleroderma-related pulmonary arterial hypertension, a leading cause of mortality.
    - **Eliza Tsou, PhD**, was inaugurated as the first holder of the Edward T. and Ellen K. Dryer Early Career Professorship in Rheumatology on April 9, 2018. Dr. Tsou's research focuses on examining the pathogenesis of systemic sclerosis.
    - **Rafael Contreras, PhD**, is a post-doctoral researcher at UM who has made exciting discoveries in his lab. Some patients with scleroderma aberrantly produce antibodies that interact with chromosomes, microscopic thread-like structures inside our cells that carry genetic information. Specifically, the antibodies recognize the centromere, the middle region of each chromosome. The centromere is very important to cells, as it is the location at which chromosomes are pulled apart to be equally divided to nascent daughter cells during cellular division. Defects in centromeres can thus lead to unequal distribution of chromosomes, creating cells with incomplete genetic information that can become diseased. We have seen that skin fibroblasts have centromere defects and have abnormal numbers of chromosomes. We are investigating the role of centromere defects seen in Scleroderma patients in the development of skin and other organ lesions.

- **Stronger through our Partnerships:** We find inspiration in those we serve. Your gifts, of time; volunteering as a Peer Mentor, treasure; contributing to research, talent and advocacy; hosting an event and generating awareness through social media and word of mouth, empower us to pursue promising ideas and lay the foundation for continued progress.

Thank you again for your support, and for helping us get to this point. For all of our patients and their families, the promise you are fueling is immeasurable. We look forward to keeping you aware of the progress we are making.

Sincerely,

Dinesh Khanna M.D., M.Sc.
Frederick G.L. Huetwell Professor of Rheumatology
Professor of Internal Medicine, Division of Rheumatology
Director, University of Michigan Scleroderma Program

If you would like to learn more about how you can help, please contact my development partner:

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