

Research uncovers how UV light triggers immune activation and disease flares in lupus

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After sun exposure, people with systemic lupus erythematosus (SLE) frequently develop skin rashes, which often are accompanied by a flare of their overall disease. This connection between ultraviolet (UV) light and disease flares in lupus is well known, but the way in which UV exposure actually triggers the disease has been poorly understood.

In a new study being presented at ACR Convergence 2022, the annual meeting of the American College of Rheumatology, researchers from Hospital for Special Surgery (HSS) report that they have found an underlying mechanism that explains this association: decreased lymphatic drainage, which contributes to both photosensitivity and an [immune response](#) in the lymph nodes. The research also suggests that boosting lymphatic drainage may be an [effective treatment](#) for lupus photosensitivity and autoimmunity.

"When people with lupus have a systemic flare of their disease, it can affect any organ that is part of their disease," says senior author Theresa T. Lu, MD, Ph.D., who holds the St. Giles Chair for Research in the HSS Research Institute, is a faculty member in Pediatric Rheumatology and in Rheumatology at HSS and is a professor of microbiology and immunology and of pediatrics at Weill Cornell Medicine. "We wanted to look at why [sun exposure](#) at the level of the [skin](#) affects [internal organs](#) like the kidneys, heart and lungs."

"This study sheds some light on how sun exposure and UV light cause people with lupus to have more autoantibodies in their blood," adds first

author William Ambler, MD, a former fellow at HSS in Dr. Lu's lab who is now Metzger Scholar in Translational Medicine at the National Institute of Arthritis and Musculoskeletal and Skin Diseases at the National Institutes of Health.

The skin communicates with the immune system by sending cells and molecular signals via the [lymphatic vessels](#) to the lymph nodes, where immune responses begin. The signals that the skin sends to the lymph nodes control the type of immune responses that occur. Lymphatic vessels also serve the function of removing fluid and cells from the skin. If lymphatic vessels do not work properly to bring signals from skin to lymph nodes, there can be delayed resolution of skin inflammation, leading to faulty signals being sent to the lymph nodes.

Research in the Lu lab suggests that lymphatic flow from the skin to the draining lymph nodes is reduced in people with lupus. The investigators hypothesize that this decreased flow alters lymph node immune responses, making them more pathogenic. They decided to look more closely at this communication and how it impacts immune function. The current research employed both patient samples and mouse models of SLE.

The investigators studied skin biopsies from lupus patients as well as from healthy volunteers who served as controls. When they looked at the samples from the lupus patients, they found these more dilated lymphatic vessels compared with the healthy controls. This provided evidence that people with lupus have poor lymphatic flow.

They then studied mouse models of SLE, using a dye injected into the skin to visualize the flow of lymphatic fluid. They found that when lupus mice were exposed to UV radiation, more dye remained in the skin. This provided evidence that the lymphatics were not clearing the fluid as well as they should.

Importantly, the researchers then looked to see if they could improve certain hallmarks of disease in the mice by using manual lymphatic drainage techniques to manipulate the flow of lymph fluid. This type of therapy is used in people with certain types of cancer, especially breast cancer, to prevent lymphedema (fluid accumulation and swelling) after the surgical removal of lymph nodes. They found that performing lymphatic drainage in the mice reduced the numbers of plasmablasts and germinal center B cells, types of cells that are known to be important players in lupus.

Drs. Ambler and Lu are optimistic that manual [lymphatic drainage](#) may benefit lupus patients but emphasize that [clinical trials](#) in patients are needed to confirm it would be safe and effective.

The investigators note that this research is also important because it advances the broader field of understanding how skin and organs communicate through the [lymph nodes](#) and the immune system.

Provided by Hospital for Special Surgery

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