Genes reveal which patients will benefit from scleroderma drug

April 10 2013

Systemic sclerosis, also known as scleroderma, is a rare autoimmune connective tissue disorder that's difficult to treat. However, thanks to new research at Northwestern University Feinberg School of Medicine and Dartmouth's Geisel School of Medicine, doctors may be able to treat some patients more effectively.

Characterized by thickening of the skin, scleroderma can also cause significant complications in the joints and internal organs—particularly the esophagus, lower gastrointestinal tract, lungs, heart and kidneys. There is no cure—and the one drug commonly used to treat the disease, mycophenolate mofetile (MMF) does not work for all patients. In the absence of a biomarker to inform therapeutic medical decisions, patients are exposed to ineffective and potentially toxic medications.

In the first study of its kind in scleroderma, Monique Hinchcliff, M.D., assistant professor of medicine at the Feinberg School, associate director of the Northwestern Scleroderma Program, and a physician at Northwestern Memorial Hospital, and Michael Whitfield, associate professor of genetics at the Geisel School of Medicine, together have shown that gene expression signatures can accurately identify patients who will positively respond to a particular therapy.

The paper was recently published electronically in the *Journal of Investigative Dermatology*.

"There is the potential for adverse reactions including death with

scleroderma therapies, and delay in initiating appropriate therapy can be harmful," Hinchcliff said. "Selecting effective treatment for each patient is the major issue facing physicians treating scleroderma patients."

Whitfield's and Hinchcliff's findings revealed that patients whose conditions improve with MMF therapy all share a particular gene expression pattern in skin.

During the clinical trial, patients who improved during MMF therapy were classified in the inflammatory gene expression subset, while patients who did not improve were classified in the normal-like or fibroproliferative gene expression subsets. This fits the initial hypothesis since MMF impairs lymphocyte proliferation.

An MMF response gene expression signature was also identified—the signature was composed of genes whose expression changed significantly during MMF treatment in patients that improved, but was absent in patients that did not improve.

The results of these experiments suggest that analysis of gene expression in skin may allow targeted treatment in patients with scleroderma.

While this is a small pilot study, it represents an important step forward in approaching complex rare diseases, such as scleroderma, where existing therapies show little or no efficacy, notes John Varga, M.D., the John and Nancy Hughes Professor at the Feinberg School and a physician at Northwestern Memorial, who also participated in the study.

If validated in a larger patient cohort now underway, the results will have significant impact on the development of effective treatment strategies for patients with systemic sclerosis.

More information: The research paper is titled, "Molecular Signatures

in Skin Associated with Clinical Improvement During Mycophenolate Treatment in Systemic Sclerosis." It can be found at: www.nature.com/jid/journal/vao … abs/jid2013130a.html

Provided by Northwestern University