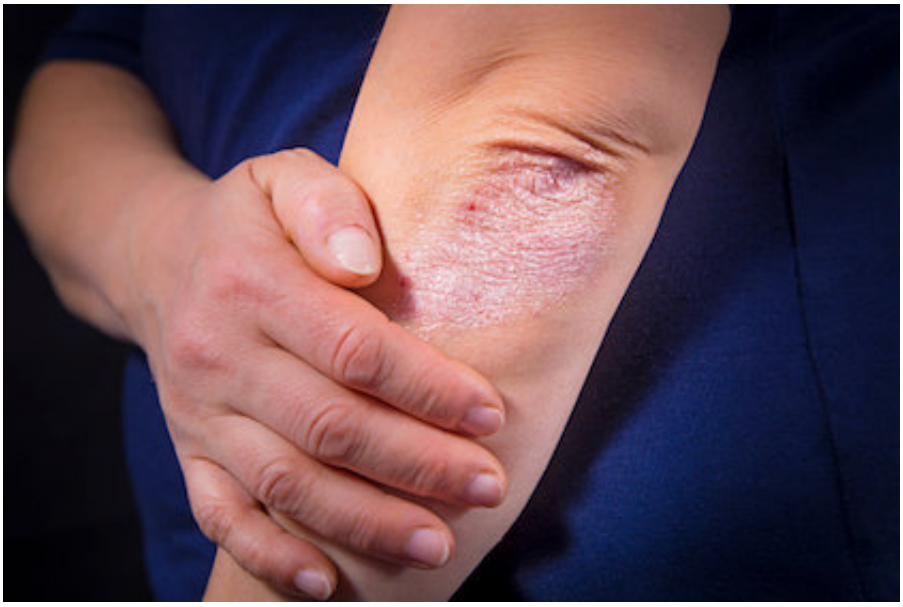
Medical Xpress

Insight into potential new strategy to target skin diseases like psorias

May 4 2018, by Patrick Wascovich



Psoriasis is a chronic autoimmune disease that affects more than 7 million people in the U.S. Credit: UT Southwestern Medical Center

Research at UT Southwestern has shown that targeting metabolism in growing cells holds promise for the treatment of skin diseases like psoriasis that are characterized by skin overgrowth resulting from excess cell division, known as hyperproliferation.

A research team led by Dr. Richard Wang, Assistant Professor of Dermatology, demonstrated in mice that inhibiting glucose transport may be a safe and effective treatment for these diseases. Actively dividing

cells, like those underlying psoriasis, are more dependent on glucose for their growth. By inhibiting glucose transport in those cells, disease -associated skin overgrowth and inflammation were reduced. Their findings were recently published in *Nature Medicine*.

"This study provides a window for the treatment of various diseases by specifically targeting the metabolic requirements of hyperproliferative skin diseases. It also broadens our understanding of changes in skin metabolism in response to physiological stressors," Dr. Wang said.

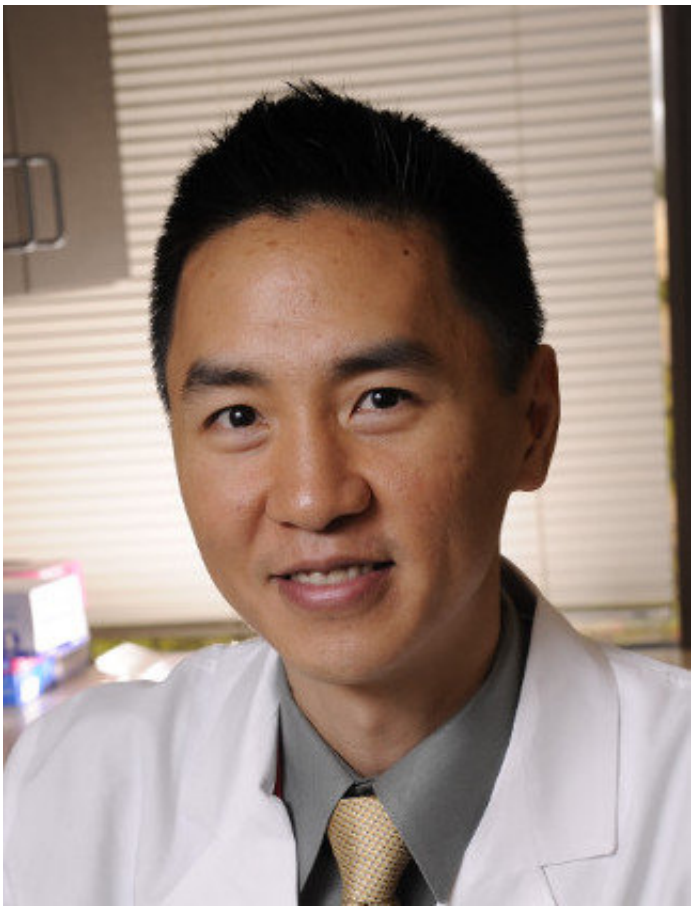
Most psoriasis therapies inhibit the immune cells that underlie the disease. They have been limited somewhat by side effects caused by broadly targeting the immune system, he said.

The study results, if proved effective in humans, may lead to development of new treatments for those with incurable skin conditions like psoriasis, a chronic autoimmune disease that affects more than 7 million people in the U.S., according to the Centers for Disease Control and Prevention. The condition manifests as patches of red skin with silvery scales typically found on the elbows, knees, scalp, lower back, face, palms, and soles of feet.

Recent studies have shown that people with psoriasis are at an increased risk for other inflammatory diseases, such as arthritis, heart disease/hypertension, diabetes, Crohn's syndrome, lupus, irritable bowel syndrome, depression, and obesity.

This trickle-down threat resulted in the World Health Organization (WHO) recognizing psoriasis under its umbrella of these four primary noncommunicable diseases: cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes. Affecting more than 125 million people worldwide, psoriasis has a direct causal linkage to several of these diseases. Although psoriasis alone rarely results in death, those with it

run a greater risk of various co-occurring diseases—including diabetes and cardiovascular disease—that can be fatal.



Dr. Richard Wang. Credit: UT Southwestern Medical Center

In the study, investigators successfully decreased skin overgrowth in mouse models of psoriasis-like disease by inactivating the transporter protein Glut1, either genetically or with drug-based inhibitors. These experiments did not compromise the skin's development or functionality. Glucose transport in skin cells called keratinocytes takes place through Glut1.

Researchers also were able to decrease inflammation with topical application of a Glut1 inhibitor. This inhibitor also had a remarkable effect on psoriatic human skin grown in a dish, suppressing both inflammation and the expression of disease-associated genes.

"Although I would still consider our findings preliminary, they have the potential to provide novel therapeutic approaches for inflammatory and neoplastic skin diseases," Dr. Wang said.

More information: Zhuzhen Zhang et al. Differential glucose requirement in skin homeostasis and injury identifies a therapeutic target for psoriasis, *Nature Medicine* (2018). DOI: 10.1038/s41591-018-0003-0

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