Marker found for condition that causes numerous tumors

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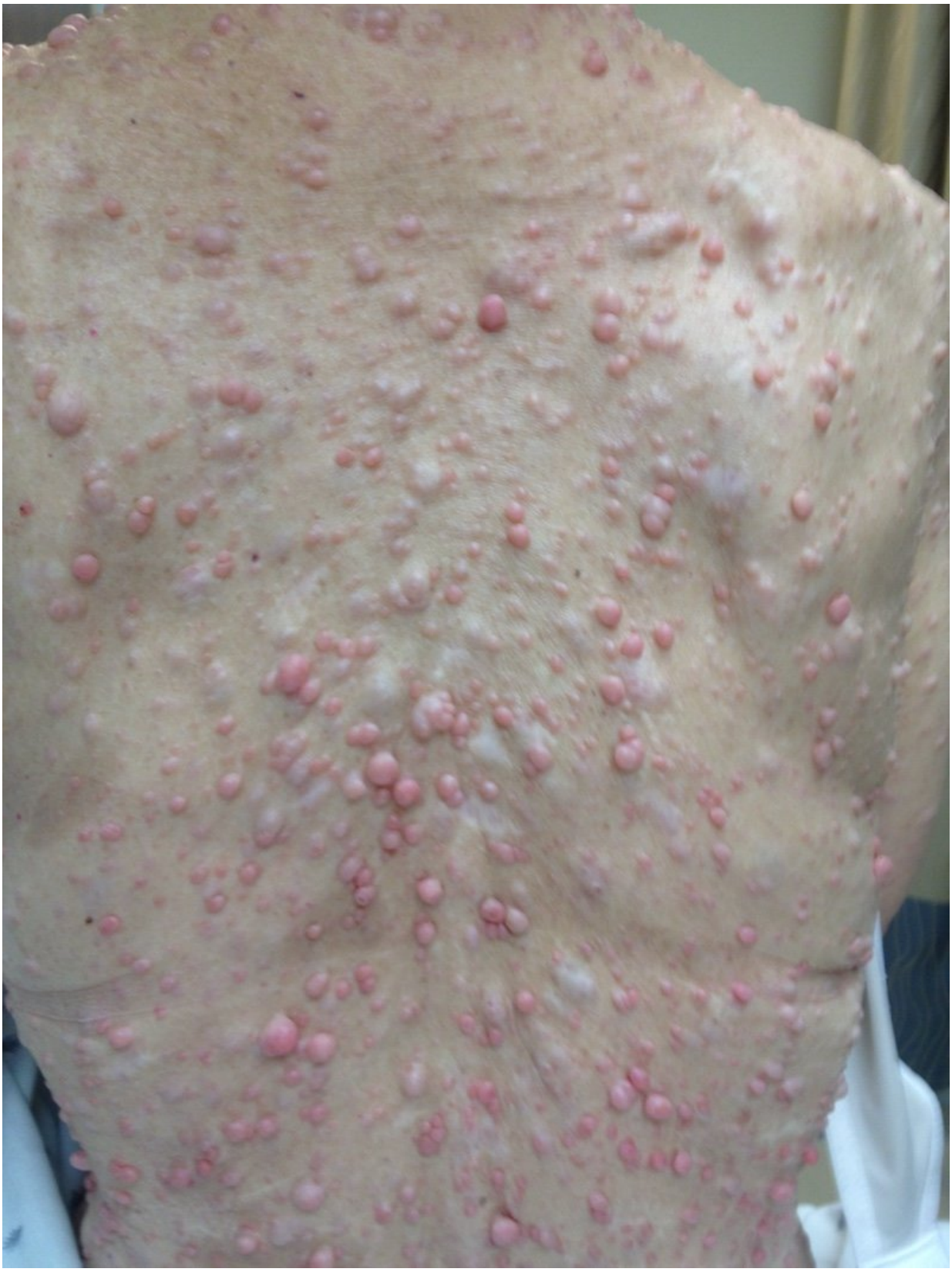

Cutaneous neurofibromas cover the back of a patient. Credit: UTSW

UT Southwestern researchers have made a major advance in uncovering the biology of how thousands of disfiguring skin tumors occur in patients troubled by a genetic disorder called neurofibromatosis type 1 (NF1). This scientific advance could slow the development of these tumors.

NF1, which affects 1 in 3,000 people, has a wide spectrum of symptoms that include malignant tumors, high blood pressure, and learning disorders. While the skin tumors, which are called cutaneous neurofibromas, are most often noncancerous, they can number in the thousands and cover much of a patient's body. They also can be painful or itchy, catch on clothing, bleed and become infected. Perhaps even more severe than the physical discomfort is the emotional distress. NF1 tumors can be severely disfiguring, like a layer of warts across the skin, and patients often dress to hide them.

Currently, the only treatment for neurofibromas is surgical removal of the most uncomfortable and most disfiguring of the skin tumors. It would be impossible to remove them all.

"NF1 causes significant morbidity, and an effective treatment for NF1 is long overdue," said Dr. Lu Le, an Associate Professor of Dermatology who holds the Thomas L. Shields, M.D. Professorship in Dermatology at UT Southwestern Medical Center.

"For the first time we have a mouse model that develops different types of neurofibromas inside the body and on the skin, just like in humans. Because of this model, we now know the exact origin of these two types of tumors. If you know where the tumor begins, and you know the end

result, then you can follow the steps in the occurrence of the tumor and figure out how to interrupt the development of the tumors," said Dr. Le, who treats NF1 patients as well as does research on the condition.

The researchers found that the protein Hox-B7 is a marker for the cell of origin for NF1 tumors. "It's like a GPS system in a car. By making the Hox-B7 cells light up, we can follow the development of the tumor. It's like branding," said Dr. Le, the senior author of the study and a member of the Harold C. Simmons Comprehensive Cancer Center.

Another key discovery is that a parallel pathway, the Hippo pathway, can modify growth and development of these tumors. This is particularly important because treatments are being developed to block the Hippo pathway. "If you can control the Hippo pathway, you should be able to slow the development of neurofibromas, specifically in NF1 patients who also have genetic changes in their Hippo pathway," Dr. Le said.

The research appears in the journal *Cancer Discovery*.

Other UT Southwestern researchers involved in this study were first author and Assistant Instructor Dr. Zhiguo Chen; postdoctoral researchers Dr. Juan Mo, Dr. Jean-Philippe Brosseau, Dr. Chung-Ping Liao, and Dr. Jonathan Cooper; research associates Tracey Shipman and Yong Wang of Dermatology; and Professor of Internal Medicine and Molecular Biology, Dr. Thomas Carroll. Dr. Carroll holds the NCH Corporation Chair in Molecular Transport.

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