When injured muscles mistakenly grow bones

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For hundreds of thousands of people, injuring a muscle through an accident like falling off a bike or having surgery can result in a strange and serious complication. Their muscles start growing bones.

No one understood what caused the abnormal bone growth, so there was no treatment. But now, research from Northwestern University Feinberg School of Medicine and the Perelman School of Medicine at the University of Pennsylvania shows that a neuropeptide in the brain called Substance P appears to trigger the formation of the extraskeletal bone. Eliminating Substance P prevents the bone growth.

The discovery -– in human and animal tissues -- offers a molecular target for drugs to potentially prevent and treat the abnormal bone growth, which is called heterotopic ossification.

"Patients who have it become very uncomfortable, and there is no way to make it go away," said Jack Kessler, M.D., chair of neurology at Northwestern's Feinberg School, a neurologist at Northwestern Memorial Hospital and the senior author of the paper, which was published in the *Journal of Cellular Biochemistry*. "This explains why it happens and gives us a way to develop a therapy to potentially treat it."

Lixin Kan, research associate professor at Feinberg and lead author of the paper, found that Substance P is dramatically increased in newly damaged tissue of patients who have the more common heterotopic ossification as well as a rarer and debilitating genetic disease. In the

genetic disease, connective tissue begins to ossify and turn into bone. It's called fibrodysplasia ossificans progressiva (FOP).

In the paper, Kan reports that knocking out Substance P in animals prevented the development of the extraskeletal bone in an animal model.

"This work establishes a common mechanism underlying lesion induction for nearly all forms of heterotopic ossification including brain and spinal cord injury, peripheral nerve injury, athletic injury, total hip replacement and FOP," said paper co-author Frederick Kaplan, the Isaac & Rose Nassau Professor of Orthopaedic Molecular Medicine at Penn's Perelman School. "These novel findings usher in a new era in understanding of these complex disorders."

Provided by Northwestern University