

Biochemists target relief for crippling condition

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Research led by Surgery and Biochemistry professor Dr. David O'Gorman has discovered a potential new therapeutic treatment for Dupuytren's disease, a debilitating condition that causes hand tissues to contract and fingers to curl permanently onto the palm of the hand. Credit: Paul Mayne, Western News

(Phys.org) —A molecule nobody thought to explore may unlock a potential therapeutic target for a debilitating connective tissue disorder, according to Western-led research.

Western professor Dr. David O'Gorman and PhD student Christina Raykha have identified a possible new focus for the treatment of Dupuytren's disease, a hereditary condition causing hand tissues to contract and fingers to curl permanently onto the palm of the hand.

The Surgery and Biochemistry researchers, who are also researchers at Lawson Health Research Institute, are the first to demonstrate insulin-like growth factor-II (IGF-II) can help cells in Dupuytren's disease to contract tissues. The finding was recently published in the scientific journal *Biochimica et Biophysica Acta-Molecular Basis of Disease*.

O'Gorman said IGF-II is an odd molecule in that increased levels are found in other connective tissue diseases (such as Frozen Shoulder Syndrome), and people with Dupuytren's disease often suffer from this or other [connective tissue](#) conditions.

IGF-II also induces the growth of cancers, and people who have Dupuytren's disease often have higher risk of cancer than the general population. Dupuytren's disease is much more prevalent in the diabetic than in the non-diabetic population and, again, IGF-II levels are increased in type-2 diabetes.

What makes this research important is IGF-II had not been previously suspected as a link between these diverse diseases.

"It's a bit of a paradigm shift for the field because no one was looking at this molecule as a potential target," O'Gorman said. "However, in retrospect, there is a lot of complimentary information about IGF-II that now makes a lot of sense."

Affecting almost 7 per cent of the world's population, the disease can be found in both sexes and all ages, but is most common in white males over 65 (90 per cent of cases). Being closely linked with diabetes, if you consider it in the context the type-2 diabetic epidemic in North America, O'Gorman argues it is going to get more common in years to come.

Currently incurable, the 'gold standard' treatment for Dupuytren's disease is surgery, which for many only provides temporary relief, with 1 in 3 seeing the disease returning within five years.

"Dupuytren's disease is a common and problematic condition for surgeons because the scar-like 'cord' that forms inside the hand often wraps around the adjacent tissues," said O'Gorman, who co-directs research in the Roth McFarlane Cell and Molecular Biology laboratory, located at St. Joseph's Health Care London, along with Dr. Bing Siang Gan.

"Your hand is full of small nerves and blood vessels. So, removing this contractile cord tissue without damaging these surrounding structures makes this a difficult operation."

One of the latest treatment options is collagenase clostridium histolyticum, an enzyme injected into the hand in an attempt to dissolve the scar tissue. Brand new in Canada, the jury is still out on the treatment, plus with a cost of \$1,000 per shot (with three needed), it is financially out of reach for many.

O'Gorman worked on some of these molecules in his postdoctoral studies in developmental biology and again while pursuing his PhD in cancer research.

"So when we did a blind analysis and up popped this molecule I was like, 'You have to be kidding me, what are the chances?'" he said.

To the point where patients have come in after multiple operations asking to simply cut their fingers off – stating amputation being a better option than living with the disease – O'Gorman realizes the significance of a therapeutic treatment to so many patients.

"At the end of the day, we would like to come up with a therapeutic intervention that could block the signaling pathways activated by IGF-II, in hopes that it might be useful as an adjunct to surgery," O'Gorman said. "By doing this, we might delay, or even stop, the recurrence of this disease.

"That would make a huge difference in the lives of these patients."

More information: Christina Raykha, Justin Crawford, Bing Siang Gan, Ping Fu, Leon A. Bach, David B. O'Gorman. "IGF-II and IGFBP-6 regulate cellular contractility and proliferation in Dupuytren's disease." *Biochimica et Biophysica Acta* (BBA) - Molecular Basis of Disease, Volume 1832, Issue 10, October 2013, Pages 1511-1519, ISSN 0925-4439, [dx.doi.org/10.1016/j.bbadis.2013.04.018](https://doi.org/10.1016/j.bbadis.2013.04.018).

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