MedicalXpress

Hereditary swellings caused by defective blood protein

July 20 2015

Oedema, or tissues becoming swollen due to fluid retention, is a common symptom in a number of pathologies such as allergies or kidney and heart diseases. The swelling is caused by blood vessels leaking fluid into the surrounding tissue. In hereditary angioedema (HAE), the leakage, and hence the swelling, is primarily caused by the hormone bradykinin.

HAE is a serious disease with painful episodes of swelling typically involving the skin and gastrointestinal tract. The attacks can be life-threatening since the airways may become obstructed due to the swelling. The most common variants of the disease are called HAE type I and II, and the cause of these are well known.

"HAE type III was discovered just recently. If we want to treat the disease, we must first understand the underlying mechanism", says Dr Jenny Björkqvist at the Department of Molecular Medicine and Surgery, Karolinska Institutet, one of the researchers behind the study.

The researchers already knew that patients with HAE type III have a mutation in the blood protein factor XII - but they didn't know why this would cause swellings. In the current study, the researchers discovered that a single sugar was missing in the mutated factor XII in HAE type III patients. The mutated factor XII was found to be overactive. This caused an excess of bradykinin production, resulting in vessel leakage and swelling.

There are natural inhibitors in blood that normally prevent factor XII from becoming activated. These inhibitors can also bind to and inhibit the mutated factor XII, but this is not enough to completely stop the overactivation.

"We realised that we had to find substances that could block factor XII more effectively. We have previously made an antibody that can inhibit factor XII, and shown that this antibody blocks factor XII driven blood clot formation. In the current study, we demonstrate that the same agent prevents oedema in mice", says Dr Thomas Renné at the Department of Molecular Medicine and Surgery, Karolinska Institutet, principal investigator of the study.

The researchers hope that the study results can be used to establish the first treatment for patients with HAE type III - with the potential for use in a broad array of other types of swelling diseases.

More information: 'Defective glycosylation of coagulation factor XII underlies hereditary angioedema type III', Jenny Björkqvist, Steven de Maat, Urs Lewandrowski, Antonio Di Gennaro, Chris Oschatz, Kai Schönig, Markus M. Nöthen, Christian Drouet, Hal Braley, Marc W. Nolte, Albert Sickmann, Con Panousis, Coen Maas and Thomas Renné, *Journal of Clinical Investigation*, online 20 July 2015, DOI: 10.1172/JCI77139.

Provided by Karolinska Institutet