Researchers link gene to common spinal disease

Lack of gene associated with collagen tissue may produce painful lumbar disc herniation

Medical specialists have long been mystified over why the bony discs of the spinal column of some people begin to badly deteriorate, leading to excruciating pain and sometimes paralysis. There has been no apparent cause and in advanced cases the cure can require surgery.

Now a team of Japanese medical researchers believes it has traced the reason for the disease, or at least the susceptibility to develop it, to the relative lack of a gene associated with the collagen tissue that helps hold the spine together.

Lumbar disc herniation, or LDH, is one of the most common musculoskeletal diseases that can affect people at any age but becomes more common in older people. A herniated lumbar disc can press on the nerves in the spine and cause pain, numbness, tingling or weakness of the leg.

In this disease, the connective collagen fiber that ties the spinal column together as well as providing flexibility and shock-absorption begins to deteriorate and can lead to disc compression and rupture. Although deteriorating discs can be treated with physical therapy, bed rest and painkillers, in the worst cases delicate surgery is often required to insert synthetic discs, "freeze" the spine with metal pins, and perform other invasive procedures to relieve pain and restore mobility.

Researchers affiliated with RIKEN’s SNP Research Center in Yokohama, in collaboration with Keio University, have found that for a number of sufferers of LDH, there tends to be less expression of a particular type of gene associated with "type XI collagen" that makes up a healthy spinal column. This collagen is one of several types of connective tissue that are present in human bone, cartilage and joints.

The researchers found that less of the "healthy collagen" gene, known as COL11A1, was expressed in the DNA from blood samples of 881 patients with LDH. Lab tests showed that those with the worst disc degeneration tended to show the lowest-level expressions of the gene. All research subjects had reported back pain for at least three months, with most ultimately undergoing corrective surgery.

Surgical biopsies further underscored the genetic component, the researchers reported.
Normal discs were found to have a highly uniform structure with intense immunostaining, indicating strong expression of type XI collagen. In degenerative discs, however, the researchers observed weak immunostaining of the collagen. A correlation was found as well between weak immunostaining and low levels of the marker gene. This indicates that the difference of one base in the gene COL11A1 that forms type XI collagen causes the slipped lumbar vertebrae. It has been known that abnormality in the type XI collagen, which occurs uniquely in the intervertebral disks, causes denaturation of the vertebra. The researchers compared the various types of COL11A1 between individuals unrelated to the patient and the statistical occurrence of the disease in the Japanese population, and found that certain types of the gene correlated strongly with occurrence of slipped disks. In fact, it appears that people who carry multiple types of the gene are 1.4 times more likely to suffer a slipped lumbar disk.

The authors of the report expressed a hope for "a better understanding of the pathogenic mechanisms of LDH and promising targets for a novel treatment strategy." This could hold out the prospect that a simple blood test might help doctors predict the likelihood of acquiring the debilitating condition and whether it might worsen. A genetic test could also help assess the need for corrective surgery, which is typically resorted to only after a painful waiting period of several months while other treatments are attempted.

Original work:

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