

# Irritable bowel syndrome can have genetic causes

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Irritations of the bowel can have genetic causes. Researchers at the Institute of Human Genetics at Heidelberg University Hospital have discovered this correlation. The causes of what is known as irritable bowel syndrome (IBS), one of the most common disorders of the gastrointestinal tract, are considered unclear – making diagnosis and treatment extremely difficult. The results from Heidelberg, which were published in the prestigious journal "*Human Molecular Genetics*", improve the outlook for an effective medication against a disease that is frequently played down as a functional disorder.

In Germany, approximately five million people are affected by IBS, women about twice as often as men. But only around 20 percent of these people even consult a physician. Many patients suffer from constipation, others from severe diarrhea, or a combination of both. The illness affects the general condition and quality of life of these patients and often lasts for months or even years.

## Modified receptors lead to overstimulation of the bowel

Serotonin plays an important role in the complex processes in the digestive tract– just as it affects sleep, mood, and blood pressure. Various types of receptors are located in the intestine, to which serotonin attaches according to the lock and key principle and thus transmits cellular signals.

"We have determined that patients who suffer from irritable bowel syndrome with diarrhea show a higher frequency of certain mutations ", explains Dr. Beate Niesler, who investigates the genetic causes of complex diseases with her team in the Department of Human Molecular Genetics (Director: Prof. Gudrun Rappold) at the Heidelberg Institute of Human Genetics. These mutations appear to cause changes in the composition or number of receptors on the cell surface. "The signal transduction in the digestive tract may be disturbed and this may lead to overstimulation of the intestine. Resulting disturbances in fluid balance could explain the occurrence of diarrhea", says Johannes Kapeller, a PhD student in the team.

## **Medication blocks serotonin receptors**

The serotonin receptor blocker Alosetron is only approved in the US where it is effectively used in the treatment of women suffering from diarrhea-predominant IBS, but can only be prescribed with strict limitations due to its side effects. Alosetron inhibits the serotonin receptors in the intestinal tract and thus slows the movement of the bowels.

"Currently, patients with irritable bowel syndrome are treated on a trial and error basis", explains Dr. Beate Niesler. The Heidelberg data could contribute to development and prescription of specific medications for certain genetic mutations in patients.

## **Correlation with depression and pain**

Research of the serotonin system shows interesting correlations – serotonin receptors are located on neural transduction pathways involved in pain perception and influence them – which could explain why patients with irritable bowel syndrome often complain of severe pain although no

pathological changes such as infections or tumors are present. It has also been noted that persons with modified receptors suffer more frequently from depression.

Reference: J. Kapeller et al., First evidence for an association of a functional variant in the microRNA-510 target site of the serotonin receptor-type 3E gene with diarrhea predominant irritable bowel syndrome, *Human Molecular Genetics*, 2008, Vol.17, No.19, 2967-2977.

Source: University Hospital Heidelberg

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