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## **Moving towards mitigating migraines Researchers identify new gene variants associated with the most common form of migraine**

For the first time researchers have identified variations in or around genes that increase a person's susceptibility to developing the most common form of migraine.

The team uncovered four new genetic variations that increase the risk of developing migraine without aura, where a migraine occurs without a sensory or motor disturbances signalling its onset.

Migraine affects approximately one in six women and one in twelve men, and up to two thirds of people with migraines have them without aura. It's estimated that migraine is the most expensive brain disorder in the EU and US, with the overall cost of the disorder comparable to that of diabetes.

"We wanted to look at the mechanisms behind this debilitating disorder and find common genetic variants that underlie migraine without aura," explains Verner Anttila, author from the Wellcome Trust Sanger Institute. "To accomplish this, we compared the genetic variations of more than 2500 people who have migraine without aura with a similar number of people who are migraine free."

The team found that both neural and vascular components seem to be important features in people predisposed to migraine without aura. They observed that genetic variations that produced disturbances to the transport of biological molecules across the nervous system seemed to be a crucial component of migraine predisposition. In addition, two of the variants identified have previously been linked to such vascular disorders as coronary heart disease.

"Studies of this kind are possible only through large-scale international collaboration - bringing together the wealth of data with the right expertise and resources. The identified genes open new doors to investigate how this devastating type of migraine comes about," says Dr Arn van den Maagdenberg, co-lead author from Leiden University Medical Centre.

The team found also that two of the variants identified as risk factors for migraine without aura were also linked with migraine with aura from previous studies. *TRPM8*, one of the genes associated with both migraine types, is associated with temperature related pain response. The researchers speculate this gene variant may contribute to pain sensitivity during a migraine headache. This is one of the few neurological diseases where a combination of variants contributing to the development of migraines is seen.

"The onset of migraines is made up of a cascade of cellular events," says Dr Aarno Palotie, co-lead author from the Wellcome Trust Sanger Institute. "Our research provides a new way of understanding these events that underlie migraines. Although the predisposition of migraines is still not fully understood, these studies reveal specific regions of the genome we can now focus on.

"The next step for our research is to compare susceptibility regions on the genomes of an even larger cohort of people to discover further variants involved. To allow us to determine the exact pathways involved in migraines and to identify treatment targets for this common disorder, we will need to carry out functional studies."

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## Notes to Editors

### About migraine

The World Health Organization (WHO) defines migraine as a headache disorder where pain-producing inflammatory chemicals are released around the nerves and blood vessels in the head. Migraine commonly begins in puberty and but tends to affect people aged between 35 to 45 years of age. People with migraines most commonly have an attack approximately once a month, but the frequency can range between once a year and once a week or even more often.

A migraine attack in an adult can last anywhere between a few hours to two to three days.

The pain is usually moderate to severe in intensity; it is typically unilateral (i.e. localized to one side of the head), with a throbbing character. Attacks are often accompanied by nausea, vomiting and sensitivity to normal levels of light and noise. Symptoms are typically aggravated by normal physical activity.

Migraine attacks in children are more likely to feature nausea or other abdominal symptoms and be shorter in duration.

### Sources for statistics

World Health Organisation Factsheet No 277. Headache disorders. Published March 2004.

Accessed August 2010. <http://www.who.int/mediacentre/factsheets/fs277/en/>

Hu XH, Markson L, Lipton R, Stewart W, Berger M; Association for Health Services Research. Meeting. Burden of migraine in the United States - disability and economic costs, a population based approach. *Abstr Book Assoc Health Serv Res Meet.* 1998; 15: 272-3.

### Publication details

Freilinger, T *et al.* (2012) Genome-wide association analysis identifies susceptibility loci for migraine without aura. *Nature Genetics.*

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### Participating Centres

A full list of participating centres can be found at the *Nature* website.

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<http://www.lumc.nl>

The **Institute for Stroke and Dementia Research (ISD)** was founded in 2009 and launched in 2010 thanks to the generosity and vision of Zygmunt Solorz-Żak and Malgarzata Żak. Their founding gift was intended to provide the resources necessary to allow the institute to maintain a high degree of flexibility within a rapidly moving field. Munich's pre-eminent University Hospital, the University of Munich, and the State of Bavaria shared the Solorz-Żak's vision and joined together with them as the founding partners of the Institute for Stroke and Dementia Research. The ISD is equally committed to comprehensive patient care and research. The ISD strives to provide the highest quality in preventing, recognizing and treating both stroke and cognitive decline thus offering the best service to patients, their families, and referring physicians.

<http://www.isd-muc.de>

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**End of Notes to Editors**