A large international study of migraine reveals new biological pathways for treatment

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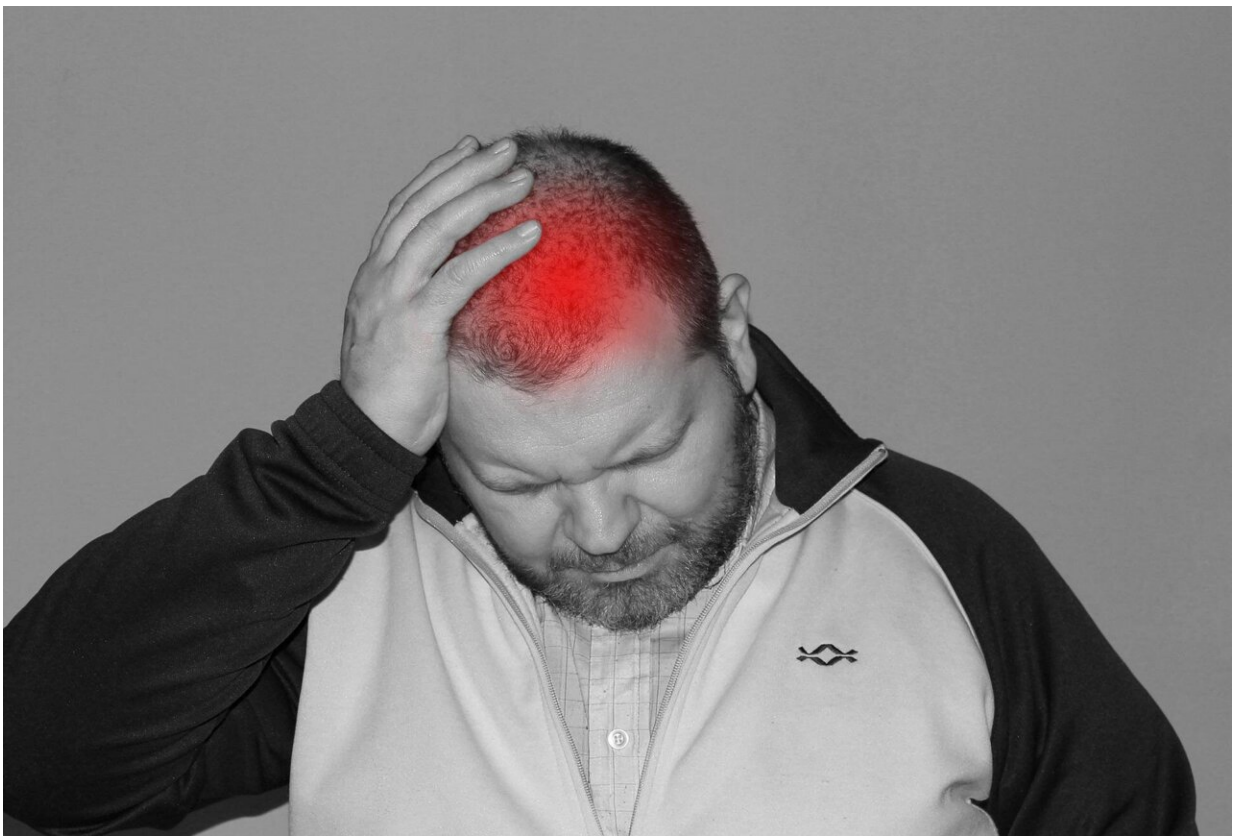

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A large international study led by deCODE Genetics on the genetics of migraine provides novel insights into the biology of migraine enabling

detection of rare variants protecting against migraine, opening an avenue for potential development of novel drug targets.

In a study published in *Nature Genetics* a group of international scientists led by deCODE Genetics in Iceland, a subsidiary of Amgen Inc, analyzed genetic data from over 1.3 million participants of which 80 thousand had migraine. The scientists focused on detecting sequence variants associated with the the two main subtypes of migraine: migraine with aura (often referred to as classical migraine) and migraine without aura.

The results highlight several genes that affect one of these migraine subtypes over the other, and point to new biological pathways that could be targeted for therapeutic developments.

Migraine is among the most common chronic pain disorders worldwide, with up to 20% of adults affected. Although recent advances have been made in studies of the genetics and underlying biology of migraine and new treatments recently developed that are effective for many migraine sufferers, they do not work for all types of migraine

The study revealed associations with 44 variants, 12 of which are novel. Four novel migraine with aura associations were revealed and 13 variants associated primarily with migraine 'without' aura. Of particular interest were three rare variants with large effects pointing to distinct pathologies underlying different types of migraine. Thus, a rare frameshift variant in the PRRT2 gene confers a large risk of migraine 'with' aura and with another brain disease, epilepsy, but not of migraine without aura.

In SCN11A, a gene known to play a key role in pain sensation, the scientists detected several rare loss-of-function variants associated with protection effects against migraine, while a common missense variant in the same gene is associated with modest risk of migraine.

Finally, a rare variant pointing to the KCNK5 gene, confers large protection against severe migraine and brain aneurysms, either identifying a common pathway between the two diseases or suggesting that some cases of early brain aneuryisms may be misclassified as migraine.

"What makes our study unique is that it includes large datasets from sequenced individuals enabling detection of rare variants protecting against migraine, potentially opening an avenue for development of novel drug targets," says Kari Stefansson CEO of deCODE genetics..

The joint effort of the international research team was led by scientists at deCODE genetics in Iceland and included collaborating scientists from the Copenhagen Hospital Biobank and Danish Blood Bank Study, the HUSK study in Norway, the Intermountain Health study in the US, and data generated by the large population-based studies from the UK Biobank and FinnGen.

More information: Rare variants with large effects provide functional insights into the pathology of migraine subtypes with and without aura, *Nature Genetics* (2023). DOI: 10.1038/s41588-023-01538-0

Provided by deCODE genetics

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