nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-022-28167-1 OPEN

Rare *SLC13A1* variants associate with intervertebral disc disorder highlighting role of sulfate in disc pathology

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Back pain is a common and debilitating disorder with largely unknown underlying biology. Here we report a genome-wide association study of back pain using diagnoses assigned in clinical practice; dorsalgia (119,100 cases, 909,847 controls) and intervertebral disc disorder (IDD) (58,854 cases, 922,958 controls). We identify 41 variants at 33 loci. The most significant association ($OR_{IDD} = 0.92$, $P = 1.6 \times 10^{-39}$; $OR_{dorsalgia} = 0.92$, $P = 7.2 \times 10^{-15}$) is with a 3'UTR variant (rs1871452-T) in *CHST3*, encoding a sulfotransferase enzyme expressed in intervertebral discs. The largest effects on IDD are conferred by rare (MAF = 0.07 – 0.32%) loss-of-function (LoF) variants in *SLC13A1*, encoding a sodium-sulfate co-transporter (LoF burden OR = 1.44, $P = 3.1 \times 10^{-11}$); variants that also associate with reduced serum sulfate. Genes implicated by this study are involved in cartilage and bone biology, as well as neurological and inflammatory processes.

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