Ischemic infarctions account for the majority of infarction-related injuries (~87% of strokes and ~70% of heart attacks), with incidence rates continuing to rise alongside growing interest in prevention and treatment. The *ASIC1* gene encodes the ion channel isoform ASIC1a, for which animal model studies show that inhibition markedly reduces infarct volume and improves survival. However, human genetic evidence linking ASIC1 to relevant phenotypes remains limited, with only two prior studies, one involving fewer than 200 participants and the other lacking follow-up analyses. Here, we present the first systematic genetic investigation of *ASIC1*, examining associations with ischemic-related phenotypes (stroke and myocardial infarction), common clinical and psychological measures, and across the phenome to identify previously overlooked traits.

Using the latest European-ancestry meta-analyses and Neale-Lab summary statistics, we performed phenome-wide association analyses, followed by functional follow-up using tissue-specific and whole-blood eQTL data to test whether *ASIC1* expression exerts a causal effect on these phenotypes. We further annotated the cis-regulatory region encompassing *ASIC1* to characterise potential functional variants.

We identified over 30 phenotypes associated with *ASIC1* ($p \leq 1.296 \times 10^{-5}$), with three blood pressure traits showing the strongest evidence of association. Functional follow-up suggested that *ASIC1* whole-blood expression may causally influence blood pressure, although conditional F-statistics indicated potential weak instrument bias. Variant annotation revealed multiple Bayesian credible sets, with most variants located in regulatory regions.

Our findings provide the most comprehensive human genetic evaluation of *ASIC1* to date, suggesting a previously unrecognised role in blood pressure regulation. These insights may inform future studies on ASIC1a inhibition, including potential on-target cardiovascular side effects and therapeutic relevance for ischemic injury.