GENETICS

Meta-analysis identifies variants in 22 loci associated with QRS duration

Genetic variation at 22 loci influences the duration of the QRS interval, a large international collaborative study published in *Nature Genetics* has shown.

People with long QRS intervals are at increased risk of sudden death, mortality, and heart failure. Smaller-scale studies have identified several loci associated with QRS duration. Sotoodehnia *et al.* performed a meta-analysis of 14 genome-wide association studies including 40,407 individuals of European descent to identify single nucleotide polymorphisms (SNPs) significantly associated with QRS duration. The investigators genotyped an additional group of 7,170 individuals to increase the statistical power of their findings and discover additional loci.

The analysis revealed genetic variation in 22 loci to be significantly associated with QRS duration ($P < 5 \times 10^{-8}$). Further studies of a group of 12,804 people with normal conduction and 519 people with ventricular conduction defects

provided evidence that the cumulative presence of genetic determinants of prolonged QRS interval was associated with the risk of these defects. In addition, blocking the function of *SCN10A*, a candidate gene at the most-significant locus identified in the study, prolonged QRS interval duration in a mouse model.

Some of the loci identified are near or in genes that encode proteins involved in pathways with known links to ventricular conduction, but some are close to genes with no previously known role in cardiac electrophysiology. Further research is needed to clarify the potential usefulness of these findings for patient screening and drug development.

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Original article Sotoodehnia, N. *et al.* Common variants in 22 loci are associated with QRS duration and cardiac ventricular conduction. *Nat. Genet.* **42**, 1068–1076 (2010)