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Summary

WHOLE EXOME SEQUENCING REVEALS NOVEL SUSCEPTIBILITY GENETIC VARIANTS FOR GASTRIC CANCER RISK AND PROGNOSIS

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Whole exome sequencing in 100 Spanish gastric cancer patients and 100 matched controls identified 16 novel SNPs significantly associated with gastric cancer risk and 8 SNPs associated with overall survival.

KEY POINTS

- 16 SNPs were significantly associated with gastric cancer risk after multiple testing correction ($p<1.0\times10^{-4}$), with the strongest associations found for rs6598758 (OR:0.23; p=3.84E-08), MAP2K3 rs62057727 (OR:0.26; p=4.84E-07), DNAJC30 rs1128349 (OR:0.35; p=4.48E-06), and KCNJ12 rs62049521 (OR:3.95; p=1.86E-06).
- 8 SNPs (rs313710, rs1137288, rs440279, rs2404773, rs12910991, rs17603986, rs1641728, and rs3765044) were significantly associated ($p<10^{-5}$) with variations in overall survival across four time points (1.5, 3, 5, and 10 years).
- Gene ontology and pathway enrichment analyses highlighted roles of identified variants in immune response and surveillance, DNA repair efficiency, xenobiotic transport, and structural cell integrity.
- The study used whole exome sequencing (NovaSeq 6000 platform, Twist Exome 2.0 panel) with SNP filtering based on read depth ≥10X, genotyping quality ≥50%, MAF >5%, and HWE p-value $>1.0\times10^{-4}$.
- Further internal and external validation will be conducted to corroborate the relevance of newly identified genetic variants, including a planned replication study in 800 gastric cancer patients and 800 controls from Spain.

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