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Titel des Beitrags:
Genetic association study identifies HSPB7 as a risk gene for idiopathic dilated cardiomyopathy.

Abstract:
Dilated cardiomyopathy (DCM) is a structural heart disease with strong genetic background. Monogenic forms of DCM are observed in families with mutations located mostly in genes encoding structural and sarcomeric proteins. However, strong evidence suggests that genetic factors also affect the susceptibility to idiopathic DCM. To identify risk alleles for non-familial forms of DCM, we carried out a case-control association study, genotyping 664 DCM cases and 1,874 population-based healthy controls from Germany using a 50K human cardiovascular disease bead chip covering more than 2,000 genes pre-selected for cardiovascular relevance. After quality control, 30,920 single nucleotide polymorphisms (SNP) were tested for association with the disease by logistic regression adjusted for gender, and results were genomic-control corrected. The analysis revealed a significant association between a SNP in HSPB7 gene (rs1739843, minor allele frequency 39%) and idiopathic DCM (p = 1.06 x 10^-7, OR = 0.67 [95% CI
0.57-0.79] for the minor allele T). Three more SNPs showed $p < 2.21 \times 10^{-2}$. De novo genotyping of these four SNPs was done in three independent case-control studies of idiopathic DCM. Association between SNP rs1739843 and DCM was significant in all replication samples: Germany ($n = 564$, $n = 981$ controls, $p = 2.07 \times 10^{-3}$, OR $= 0.79$ [95% CI 0.67-0.92]), France 1 ($n = 433$ cases, $n = 395$ controls, $p = 3.73 \times 10^{-3}$, OR $= 0.74$ [95% CI 0.60-0.91]), and France 2 ($n = 249$ cases, $n = 380$ controls, $p = 2.26 \times 10^{-2}$, OR $= 0.63$ [95% CI 0.50-0.81]). The combined analysis of all four studies including a total of $n = 1,910$ cases and $n = 3,630$ controls showed highly significant evidence for association between rs1739843 and idiopathic DCM ($p = 5.28 \times 10^{-13}$, OR $= 0.72$ [95% CI 0.65-0.78]). None of the other three SNPs showed significant results in the replication stage. This finding of the HSPB7 gene from a genetic search for idiopathic DCM using a large SNP panel underscores the influence of common polymorphisms on DCM susceptibility.