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Perturbation of the network regulating gene expression during cardiogenesis in mammals and man causes various congenital heart defects (CHDs) (1). The core unit of highly conserved transcription factor genes in this gene regulatory network is named cardiac kernel (2). Mutations in the cardiac kernel member genes, such as nkx2.5, tbx5 or gata4 form the basis for a range of CDHs with comparable pathologies (3-5). In particular, mutations in the nkx2.5 gene encoding a Nk2 class homeodomain transcription factor, causes a diverse range of clinical phenotypes such as ventricular and atrial septal defects, atrio-ventricular blocks and sometimes even tetralogy of Fallot (6, 7). Similar to these human cardiac defects, deletion of the nkx2.5 gene in mice leads to impaired progenitor specification in the second heart field and consequently blocks cardiac looping (8). Malformation of the ventricle in nkx2.5 null mice finally results in embryonic lethality (9) and even nkx2.5 haploinsufficiency attenuates cardiomyogenesis both in vivo and in vitro (10, 11).

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