***TBX20* LOSS-OF-FUNCTION VARIANTS IN FAMILIES WITH LEFT VENTRICULAR NON-COMPACTION CARDIOMYOPATHY**

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*TBX20* encodes an essential cardiac-enriched transcription factor in which rare missense variants are associated with cardiac developmental anomalies, including atrial septal defects. Recent studies implicate loss-of-function *TBX20* variants with left ventricular noncompaction cardiomyopathy (LVNC), although clinical and genetic data in affected families is limited due to the rarity of these variants. We report four families with *TBX20* loss-of-function variants that segregate with LVNC. Genetic testing using genome or exome sequencing was performed in index cases from each family, variants were validated with Sanger sequencing, and cascade genetic testing was performed in affected family members. A multi-exon deletion (c.891-1260\_\*5103del), small deletion (c.710\_713del; p.Lys237ThrfsTer9), essential splice site variant (c.380+1G>C), and nonsense variant (c.374C>A p.Ser125Ter) in *TBX20* were found in four families. The index cases in two families were symptomatic children with LVNC who developed heart failure requiring heart transplantation. In one family, the child index case had LVNC and complex congenital heart disease, including atrial septal defects and aortic coarctation that required surgical repair. In the fourth family, the index case was a symptomatic adult female with LVNC. In all four families the variants segregated in relatives with isolated LVNC, or LVNC with congenital heart disease or cardiomyopathy. Family members displayed a wide clinical spectrum from asymptomatic individuals to those with severe presentations including restrictive cardiomyopathy and heart failure. Our data strengthen the association of *TBX20* loss-of-function variants as a rare cause of LVNC and support the inclusion of *TBX20* in genetic testing of LVNC.