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DEVELOPMENTAL BIOLOGY

Formation of hybrid myocardial zone

Left ventricular noncompaction cardiomyopathy is characterized by the presence of excessive recesses in the trabecular network that can result in heart failure, arrhythmia, and thromboembolism. Using genetic lineage tracing, Tian and colleagues found that inhibition of Hey2$^+$ cell expansion results in the formation of a noncompacted hybrid myocardial zone. These findings were published in *Nature Communications*.

The way in which trabeculations that make up the inner ventricular walls of the developing heart aggregate to form the compact myocardium seen in the mature ventricular wall remains unclear. Two theories of morphogenic transformation have been proposed: the first involves expansion of the compact myocardium into the trabecular layer, whereas the second model predicts the coalescence of trabecular muscles by themselves. To address this hypothesis, Tian *et al.* used *Nppa* and *Hey2* as markers of the trabecular and compact layers of the ventricular myocardium in the postnatal heart, respectively.

The luminal segments of the initial trabeculations were shown to develop in the subendocardial segment of the ventricular wall. The middle portion of the mature ventricular wall was found to be composed of portions of the trabecular myocardium of the embryonic heart; the fetal compact myocardium expanded and combined with the trabecular myocardium to form this hybrid myocardial zone. Inhibition of Hey2$^+$ cell expansion resulted in a noncompacted hybrid zone, suggesting that expansion of fetal compact myocardium is critical for formation of the hybrid myocardial zone.

"Most studies have suggested that noncompaction is persistence of excessive trabeculation rather than reduced resolution of compaction," explain the investigators. "Our study now suggests that, in addition to potential excessive trabeculation, there is a specific morphogenic process that may be perturbed, which then recapitulates the phenotypic features."

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ORIGINAL ARTICLE Tian, X. *et al.* Identification of a hybrid myocardial zone in the mammalian heart after birth. *Nat. Commun.* **8**, 87 (2017)