Dissecting progenitor cell contributions to the developing heart: a potential role of *Hes1*

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Cardiac progenitor cells of the second heart field (SHF) contribute to the poles of the elongating embryonic heart. Perturbation of SHF development leads to a spectrum of congenital heart defects. Recent evidence suggests that distinct regions of the heart are pre-patterned in the SHF. In particular, the myocardium at the base of the aorta and pulmonary trunk were shown to be prefigured in the outflow tract. For example the dell22q11.2 or DiGeorge syndrome gene *Tbx1* is required in the SHF for development of the inferior wall of the embryonic outflow tract, giving rise to subpulmonary myocardium. By characterizing the expression of an enhancer trap transgene at the *Hes1* locus, encoding a transcriptional repressor, we have identified a complementary Notch-dependent $Hes1^{+}$ $Tbx1^{-}$ subpopulation of SHF cells giving rise to future subaortic myocardium. Using transcriptomic analysis on superior and inferior outflow tracts, we have characterized the distinct genetic signatures of future subaortic and subpulmonary myocardium and identified peroxisome proliferator activated receptor gamma (*Pparγ*) among the genes enriched in future subpulmonary myocardium. We have also shown that *Pparγ* acts as an upstream regulator in the cross-circuitry operating in superior and inferior OFT walls and plays a role in SHF cell addition to the OFT. Our genetic and explant analyses have revealed that *Hes1*, as a downstream target of Notch signaling pathway, controls the molecular signature of future subaortic myocardium through direct transcriptional repression of *Pparγ*. Altogether, our study reveals distinct genetic regulatory networks controlling different progenitor cell contributions to the developing heart and identifies a crucial role of *Hes1* in the regulation of cardiac progenitor cells fate.