DEVELOPMENT

FGF8 — you're making my heart!

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> …provide important insights into the molecular mechanisms that control cardiogenesis.

Heart morphogenesis is a complex process that involves the perfect orchestration of cell specification, differentiation, proliferation and migration. Park *et al.* and Ilagan *et al.* now investigate the roles of the secreted signalling protein fibroblast growth factor-8 (FGF8) during heart development in the mouse embryo and provide important insights into the molecular mechanisms that control cardiogenesis.

Mice that carry *Fgf8* hypomorphic alleles are known to have cardiac defects, although the underlying mechanisms have been unclear. The heart originates from two populations of cells: the primary heart field (PHF) gives rise to the left ventricle, whereas the anterior heart field (AHF) contributes to the right ventricle and the outflow tract. Using reporter transgenes, Park *et al.* and Ilagan *et al.* found *Fgf8* expression in the AHF; Park and co-workers also reported low *Fgf8* expression in a subset of the PHF cells.

Using *Cre*-mediated recombination, the two groups then examined the phenotypes caused by *Fgf8* deletion in subsets of cardiac progenitor cells. Although they observed slightly different results, which can be explained by the different experimental setup and the *Cre* drivers that were used, both groups reached similar overall conclusions: *Fgf8* deletion in the AHF leads to severe truncations of the right ventricle and the outflow tract.

Further transgenic analysis and immunostaining experiments revealed that autocrine FGF8 signalling is required in the AHF to promote cell proliferation and survival. Ilagan *et al.* showed that the *Ets* transcription factor *Pea3*, a known FGF8 target, is downregulated in the absence of FGF8, possibly owing to reduced MAPK signalling. Park *et al.* showed that loss of FGF8 resulted in decreased expression of the FGF8 target gene *Erm*, and identified the transcription factors *Isl1* and *Mef2c* as probable effectors of FGF8 signalling in the AHF. Therefore, it seems that FGF8 promotes cardiogenesis by activating transcriptional networks that are required for cell division and survival.

Mouse strains generated in these studies constitute an important tool with which to study the pathology of human syndromes that are characterized by severe heart problems. The results already provide important insights into the roles of FGF8 during heart morphogenesis. It will be interesting to see whether FGF8 is also involved in cardiac cell migration, as FGF proteins can activate cell motility, and cell-migration defects could explain the heart defects that are observed in FGF8-deficient AHF.

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ORIGINAL RESEARCH PAPERS Park, E. J. *et al.* Required, tissue-specific roles for Fgf8 in outflow tract formation and remodeling. *Development* **133**, 2419–2433 (2006) | Ilagan, R. *et al. Fgf8* is required for anterior heart field development. *Development* **133**, 2435–2445 (2006)