Clonal analysis unravels the Second Heart Field as a source of epicardial-like cells

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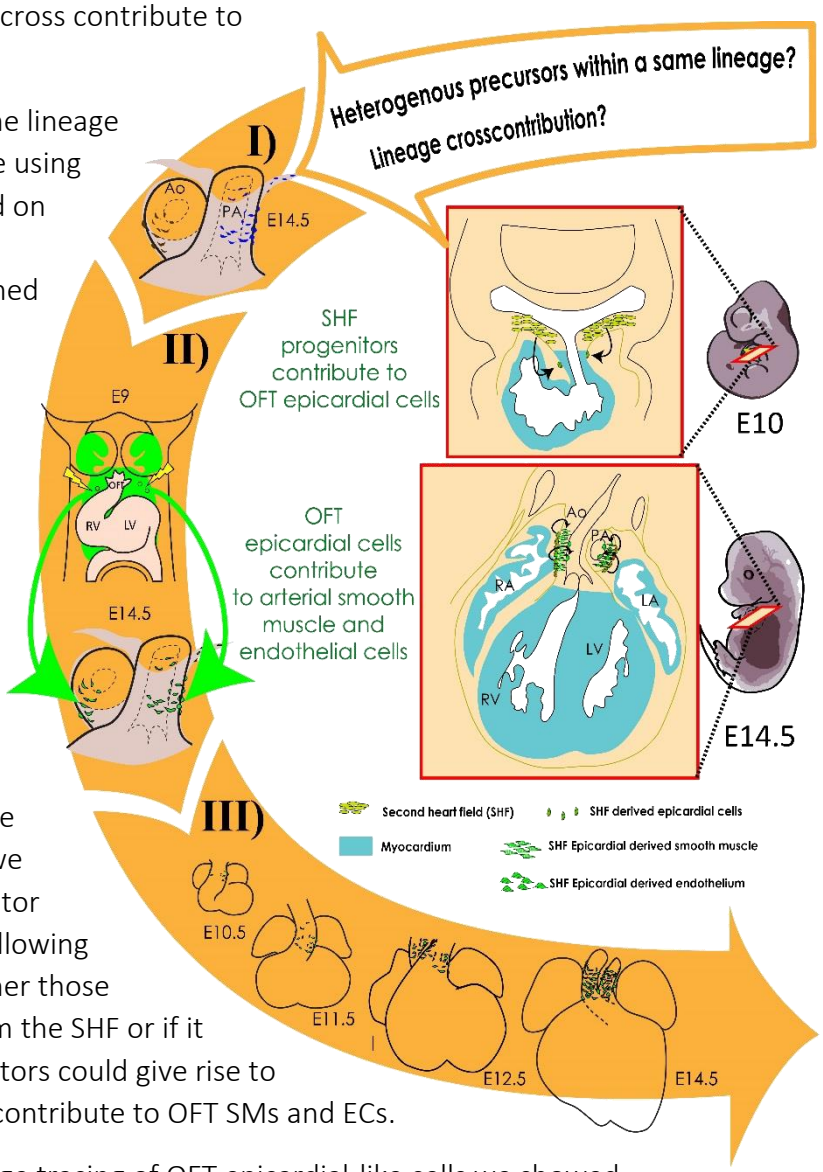
Congenital heart defects are the most common birth defects, it is thus of importance to understand the lineage tree of heart development. So far, four main populations of heart progenitor cells have been identified in the early embryo: the first and second heart field (SHF), the proepicardium, and the neural crest cell population.

However it is not known how plastic are these progenitors in terms of fate and to which extent different lineages cross contribute to identical cell types.

I) We aim at deciphering the lineage tree of heart progenitors in Mouse using retrospective clonal analysis based on the random labeling of heart precursors. Cell labeling is performed with a ubiquitous Tamoxifen-inducible Cre recombinase triggering the expression of a LacZ and EYFP reporter. By labeling heart precursors around Embryonic day 9 (E9), we provided evidence of a common progenitor for Pericardium, epicardium, smooth muscle (SM) and endothelial cells (ECs) of the Outflow Tract OFT .



II) Using subsequent lineage tracing with SHF cre driving lines we showed that this common progenitor belongs to the SHF lineage. The following question we addressed was whether those OFT clones derive all together from the SHF or if it is a two-step process: SHF progenitors could give rise to OFT epicardium which ultimately contribute to OFT SMs and ECs.

III) Interestingly using lineage tracing of OFT epicardial-like cells we showed that, those cells remain multipotent as they substantially contribute to OFT smooth muscle and endothelium. We will now study how such cells are affected in mutants presenting a truncated OFT to further our knowledge on the cellular basis of such defects.