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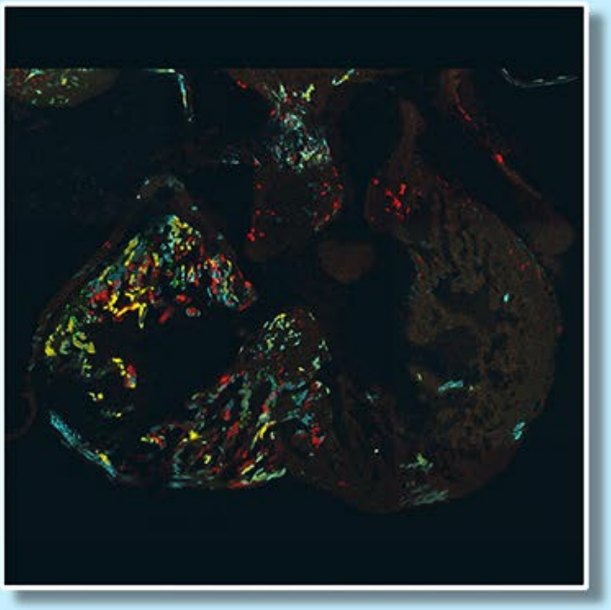

Isl1$^{cre/+}$*; R26R*$^{conf/+}$ e13.5 embryonic heart
(colors: second heart field derived clones)

Identifying a Cellular Mechanism of Cardiac Interventricular Septal Formation

Congenital heart disease (CHD), defined as any abnormality of the heart's anatomical structure present at birth, comprises almost one third of all major abnormalities at birth with 1.35 million babies born worldwide with lethal CHD each year. One third of CDH cases involve ventricular defects, occurring when the interventricular septum (IVS) does not fully develop. The morphological events surrounding formation of the IVS are well known, as current evidence supports a model where a muscular septum grows up from the myocardial wall and involves the interactions between two populations of cells, called the first and second heart fields. However, the molecular processes governing the integration and contribution of these two populations of cells to the septum and the role of the transcription factor CASZ1 are unknown. The Cre Recombinase system, driven by heart field specific promoters, and a novel mechanism of cell fate mapping in a reporter mouse line were used to elucidate the location of second heart field cells in mice on day 13.5 of embryonic development. Analysis of confocal microscopy Z-stack images of immunostained and sectioned heart tissue revealed that in wild-type *Casz1* mice, cells originating from the second heart field are found uniformly throughout the septum. In contrast, there was a marked reduction in the number of second heart field derived cells in the IVS of *Casz1* heterozygous and null mice in addition to sequestering of those cells to the right half of the septum. Additionally, *Casz1* knockout mice exhibited noticeably smaller hearts. Identifying contributing cells to the IVS and the impact that CASZ1 has on the integration of those cells will lead to a deeper understanding of the mechanism by which the IVS forms in the hopes that this could be manipulated in future treatment options for CHD.