1. Avian embryonic coronary arterio-venous pattering requires the contribution of different endothelial cell populations

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Coronary blood vessels irrigate the heart muscle and are crucial to late embryonic and adult heart function. Despite the developmental significance and clinical relevance of coronary vasculature, the embryonic origin as well as the cellular and molecular regulation of coronary arterio-venous patterning remains obscure. It has been reported that the mammalian coronary vascular network develops from, at least, three different cell sources: the sinus venosus endocardium, the ventricular endocardium and derivatives of the septum transversum. However, it remains unclear how the venous and arterial components of the coronary system integrate into a complex functional coronary tree. In this work, we revisit the avian embryo, a classical animal model in the study of coronary blood vessel development, to dissect the ontogenetic origin and morphohenesis of coronary arteries and veins. Our results, which benefit from the use of experimental techniques (quail-to-chick chimeras, intravascular lectin injections, recombinant fibrin grafting), show that at least three different endothelial populations need to assemble in a coordinated manner for proper coronary vascularization. Our data also confirm that sinus venosus endocardium sprouts and proepicardial angioblasts grow simultaneously into the developing heart, growing towards a VEGF source. Prospective venous and arterial coronary endothelium remain disconnected during the first part of coronary development, so that arterio-venous shunts form just before prospective coronary arterial vessels connect to the aortic root. In summary, our study reveals that the coronary vascular system is a developmental mosaic, formed by the interaction of various vascular populations of different embryological origins.