COUP-TFII EXPRESSION DEFINES TWO DIFFERENT SEPTUM TRANSVERSUM CELL COMPARTMENTS CRUCIAL TO CARDIAC SEPTATION AND COMPACT VENTRICULAR WALL GROWTH

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COUP-TFII encodes for an orphan nuclear receptor expressed by multiple embryonic tissues. COUP-TFII functions include the regulation of mesodermal progenitor differentiation and cell fate specification, and is required for completion of cardiovascular development as shown by the early death (E9.5) of COUP-TFII-null mice. In this study, we show that COUP-TFII, which is strongly expressed in the atrial myocardium, is also expressed in two different compartments of the *septum transversum* (ST, E9.5), a mesodermal folding adjacent to cardiac inflow myocardium. The first ST compartment is COUP-TFII^{+}/Isl1^{+}; cells in this compartment concentrate in the posterior part of the ST, overlap with SHF, and are continuous with the dorsal mesenchymal protrusion (DMP, also known as *spina vestibuli*). The second compartment is characteristically COUP-TFII^{+}/Isl1^{-}, and comprises the majority of proepicardial cells. To dissect the role of COUP-TFII^{+} ST cells in cardiac development, we conditionally deleted COUP-TFII in the ST using two different Cre constructs (Wt1Cre; G2-Gata4Cre). We show that COUP-TFII deletion in the ST is most severe in G2-Gata4Cre;COUP-TFII$^{-/-}$ mice, containing various cardiovascular progenitor lineages. Mutant mice display atrial septation and atrioventricular septal defects as well as a severe disruption of compact ventricular myocardial growth and coronary vascularization. We conclude that COUP-TFII plays critical, pleiotropic, tissue-dependent roles during cardiac septation, growth and vascularization.