Lineage diversification of the multipotent cardiac progenitors

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While great progress has been made during the past 10 years in the analyses of the diversity of the cardiovascular lineages, our understanding of the cellular basis for the lineage diversification is still at its primitive stage. Recent studies have uncovered a diverse group of Isl1-positive cardiac progenitors derived from the second heart field that are central in controlling and coordinating the complex steps of cardiogenesis. Understanding the pathways that control their formation, renewal, and subsequent conversion to specific differentiated progeny forms the underpinning for unraveling the pathways for congenital heart disease and has direct relevance to cardiovascular regenerative medicine. Lineage tracing using Isl1-Cre mice revealed that Isl1-positive cardiac progenitors contribute to cardiac, smooth muscle and endothelial cells *in vivo*. Clonal culture on the feeder layer revealed that the early cardiac progenitors expressing Flk1/Isl1/Nkx2.5 give rise to three cardiovascular cell types, suggesting that a subset of Isl1-progenitors display multipotency at early stages. While endothelial competency is lost early during cardiogenesis, the cardiac and smooth muscle lineages stay closely related until later stages. Even until midgestational stages, a subset of late Isl1-progenitors maintain their bipotency to give rise to smooth muscle cells in vivo and in vitro. This cardiac-smooth muscle differentiation potential seems to be required for the formation of the boundary between the heart and great vessels that facilitate the dynamism of the central circulatory system. Together, Isl1-progenitors play an essential role during the formation of the cardiovascular system at multiple steps.