# Cardiac stem cells are indispensable for heart homeostasis and repair

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Resident cardiac stem cells in embryonic, neonatal and adult mammalian heart have been identified by different membrane markers and transcription factors. It is likely that a number of these cell populations, especially in the adulthood, represent different developmental and/or physiological stages of a unique resident stem cell. However, despite a flurry of publications no consensus has been reached on the identity and actual regenerative effects of the adult cardiac stem cells. Concurrently, intensive research on the adult mammalian heart's capacity for self-renewal of its muscle cell mass has led to a consensus that new cardiomyocytes (CMs) are indeed formed throughout adult mammalian life albeit at a disputed frequency. The physiological significance of this renewal, the origin of the new CMs, and the rate of adult CM turnover are still highly debated. Myocyte replacement, particularly after injury, was originally attributed to differentiation of a stem cell compartment. More recently, it has been reported that CMs are replaced by the un-expected division of pre-existing post-mitotic CMs. These latter results, if confirmed, would shift the target of regenerative therapy toward boosting mature CM cell-cycle re-entry. The adult endogenous c-kit$^{pos}$ cardiac stem cells (c-kit$^{pos}$eCSCs or just eCSCs) participate in adaptations to myocardial stress, and, when transplanted into the myocardium, regenerate most cardiomyocytes and microvasculature lost in an infarct. Nevertheless, the *in situ* myogenic potential of adult c-kit$^{pos}$ cardiac cells has been questioned. To revisit the regenerative potential of c-kit$^{pos}$ eCSCs, we have recently employed experimental protocols of severe diffuse myocardial damage in combination with several genetic murine models and cell transplantation approaches showing that eCSCs are necessary and sufficient for CM regeneration, leading to complete cellular, anatomical, and functional myocardial recovery. Here we discuss the available data on adult eCSC biology and their regenerative potential placing it in the contest of the different claimed mechanisms of CM replacement. These data are in agreement with and have reinforced our view that CMs are replaced by *de novo* CM formation through the activation, myogenic commitment and specification of the eCSC cohort.