The piRNome of adult cardiac/progenitor cells: a novel procardiogenic piRNA promotes their specification and differentiation in cardiomyocytes in vitro

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Recent evidence demonstrates that PIWI interacting RNAs (piRNAs) are also expressed in somatic cells within the cardiovascular compartment, like the cardiomyocytes (CMs) but also in cardiac progenitor/stem cells (CSCs) postulating a potential role for piRNAs in the function of these cells and in regeneration events, possibly through genome rearrangement and epigenetic programming. We evaluated the potential role of piRNAs in CSC function and their myogenic commitment. Data obtained from piRNA expression profile (piRNome) in multipotent cloned CSCs were matched with those obtained from pluripotent mouse ESCs (ESCs) as a prototypical model system for cell differentiation in vitro. We compared their piRNome during myogenic differentiation identifying a set of piRNAs differentially expressed. We focused on myo-piRNA-1, as promising putative target to foster endogenous CSCs activation because we found it typically expressed in CSC-derived CMs and ESC-derived CMs. To investigate whether myo-piRNA-1 is relevant in cardiomyogenic differentiation in vitro, we overexpressed a mimic for myo-piRNA-1 in both the ESCs and the CSCs in vitro. myo-piRNA-1 overexpression fostered myocyte cell differentiation in both ESCs and CSCs. We performed loss of function assays by transfecting both ESCs and CSCs with a specific myo-piRNA-1 inhibitor. Interestingly cardiac-specific gene levels were significantly reduced in the inhibitor-transfected cells compared to scramble transfected cells and treated cells show poorly defined sarcomeric structures. Overall, gain and loss of function experiments modulating myo-piRNA-1 expression in ESCs and CSCs demonstrated that this piRNA is directly involved with myogenic commitment having an essential procardiogenic role in the acquisition of the CM phenotype.