

Atrial Appendage Derived Progenitor Cells Generate Early Cardiomyocytes via Cell Fusion and Asymmetric Division

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Background:

We recently identified two distinct cardiac progenitor cell populations from the left atrial appendages of adult murine hearts. One of these progenitor cell populations expresses CD45 and c-kit and is located in the epicardial region of the appendages. Our objective was to further analyze the genetic profile of this progenitor cell population and the mechanism of spontaneous cardiomyogenic differentiation observed in vitro.

Methods:

To analyze the transcriptomes of progenitor cell populations, we performed whole-genome expression array experiments to cell sorted samples from the CD45+ cell population before and after spontaneous differentiation. We investigated the differentiation process using repeated flow cytometry and live microscopy experiments. The cells were also investigated using confocal microscopy and transmission electron microscopy.

Results:

The CD45 expression in the progenitor cell population was stable (~90% of the cells) up to five passages. After the fifth passage a rapid decline of CD45, c-kit and Flk-1 expression was observed. In live microscopy formation of giant Sca-1+ and Gata-4+ cells by cell fusion of CD45+ cells was first seen, followed by asymmetric division of these cells, which created smaller CD45- cells (Figure 1-4, in chronological order). These smaller cells were positive for myosin heavy chain, sarcomeric actinin and atrial natriuretic factor. The transcriptome was significantly skewed toward a cardiomyocyte phenotype with the spontaneous differentiation, although this differentiation was not complete, as seen by electron microscopy. The partially differentiated cell population could be grown for at least 65 passages.

Conclusion

Our study describes a novel mechanism of immature cardiomyocyte formation from adult cardiac progenitor cells. Currently this mechanism is observed in vitro only, but in future in vivo studies using lineage tracing will be performed.

