UKE Paper of the Month May 2012

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Localization of Islet-1–Positive Cells in the Healthy and Infarcted Adult Murine Heart

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ABSTRACT: Rationale: The transcription factor Islet-1 is a marker of cardiovascular progenitors during embryogenesis. The isolation of Islet-1–positive (Islet-1+) cells from early postnatal hearts suggested that Islet-1 also marks cardiac progenitors in adult life.
Objective: We investigated the distribution and identity of Islet-1+ cells in adult murine heart and evaluated whether their number or distribution change with age or after myocardial infarction.
Methods and Results: Distribution of Islet-1+ cells in adult heart was investigated using gene targeted mice with nuclear β-galactosidase inserted into the Islet-1 locus. nLacZ-positive cells were only present in 3 regions of the adult heart: clusters in the interatrial septum and around the pulmonary veins, scattered within the wall of the great vessels, and a strictly delimited cluster between the right atrium and superior vena cava. Islet-1+ cells in the first type of clusters coexpressed markers for parasympathetic neurons. Positive cells in the great arteries coexpressed smooth muscle actin and myosin heavy chain, indicating a smooth muscle cell identity. Very few Islet-1+ cells within the outflow tract expressed the cardiomyocyte marker α-actinin. Islet-1+ cells in the right atrium coexpressed the sinoatrial node pacemaker cell marker HCN4. Cell number and localization remained unchanged between 1 to 18 months of age. Consistently Islet-1 mRNA was detected in human sinoatrial node. Islet-1+ cells could not be detected in the infarct zone 2 to 28 days after myocardial infarction, aside from 10 questionable cells in 1/13 hearts.
Conclusions: Our results identify Islet-1 as a novel marker of the adult sinoatrial node and do not provide evidence for Islet-1+ cells to serve as cardiac progenitors

STATEMENT: *The current study addressed the intensively discussed question whether cells that express Islet-1 might constitute a progenitor cell population in the adult heart, as the identity of a cardiac progenitor cell population in the adult heart has not been clearly established.Our study has two main results. It provides strong evidence against the idea that Islet-1^{+} cells could serve a progenitor role in the adult heart. Furthermore it is the first study to identify Islet-1 as a specific marker of sinoatrial node pacemaker cells. This work was performed as collaboration between different groups within the cardiovascular research center of the UKE*.

BACKGROUND: This study was performed at the Institute of Experimental Pharmacology headed by Prof. Thomas Eschenhagen. It was part of the medical doctoral thesis of Dennis Mehrkens in the group of Florian Weinberger. Florian Weinberger is a MD currently participating in the MD/PhD-program of the medical faculty. The group´s research is focused on different strategies for cardiac regeneration. This work was supported by the Leducq Foundation and Dennis Mehrkens holds a scholarship of the Werner Otto Stiftung.