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Role of cardiac stem cells in the formation of adult heart and the maintaining its homeostasis: New experimental data and hypotheises

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Despite numerous studies on mammalian cardiogenesis, the mechanism of self-renewal of cardiac muscle cells and the causes of limited regenerative potential of adult heart are still an enigma. Considering this, the possibility of dedifferentiation of pre-existing cardiomyocytes and transdifferentiation of hematopoietic stem cells into cardiomyocytes is discussed. However, these data are inconclusive. The impact of resident cardiac stem cells (CSCs) on myocardium self-renewal is generally recognized, although the mechanism of the development of mature cardiac cells from cardiac stem cells is not fully understood. In addition, passive involvement of resident CSCSs into myocardium regeneration is unexplainable as well [Leri et al., 2015]. The discovery of the phenomenon of intracellular development of mammalian resident CSCs within mature cardiac cells via "cell-in-cell structure" generation both *in vitro* and *ex vivo* allowed to hypothesize about the significant role of this mechanism in the maintenance of homeostasis of healthy heart during the whole life cycle. Moreover, the presence of considerable amounts of closed and opened "cell-in-cell structures" (CICSs) in neonatal rat heart by the time of birth and their significant decrease by the end of the first week of life allow to hypothesize that embryonic CSC-CICSs deliver transit amplifying myocytes (TAMs) into neonatal myocardium. TAMs are actively involved into neonatal heart development. The presence of CSC clones and CSC-CICSs in adult and elderly mammalian myocardium demonstrates that myocardium self-renewal occurs during the whole life. However, resident CSC switch to intracellular development under hypoxia and acidosis (ischemia, myocardium infarction) accounts for their inactivity under pathological conditions. Hence, we suggest that free resident CSCs of several types as well as TAMs released from "cell-in-cell structures" immediately after the birth greatly contribute to neonatal heart development and its regeneration in the first days of life. These findings conflict with previous data published by Porello et al. [2011]. These authors claim that in the first days of life damaged heart regenerates by the division of pre-existing cardiomyocytes and deny the role of resident CSCs in this process. However, age-related decrease in resident CSCs and the blockade of their activity in acute pathology significantly reduce their involvement in damaged myocardium regeneration. We hope that the progress in the study of CSC intracellular generation in the damaged myocardium will promote a new strategy for the development of novel targeted drugs stimulating myocardial regeneration in cardiovascular diseases.

Biography

Galina Belostotskaya was born in 1947 in St. Petersburg (former Leningrad), graduated from Leningrad State University in 1970 and defended her thesis in 1984 on a specialty "Radiobiology". From 1986 to the present day she is working in the Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian academy of sciences as a senior researcher and the Head of Cytoanalysis center. In recent years, she has been studying the resident muscle stem cells and published more than 10 papers in Russian Journals and 2 articles in "Cell Cycle" (2014) and Bioelectromagnetics (2014). Being the head of investigations she released 7 specialists and 2 graduate students. The works have been supported by the 10 Russian grants

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