HEART INJURY AND REPAIR: HOPES AND HYPES OF CELL THERAPIES AND BIOMATERIALS

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During myocardial infarction about a billion of cardiomyocytes (CMs) is lost and the human heart is healed by fibrosis, leading often to heart failure being recently a world-wide epidemics. The lack of regenerative capacity of adult human heart is caused by the property of CMs, which are terminally differentiated cells. However, it has been demonstrated that some CMs can undergo divisions which in adult human heart is estimated to reach 1% of CMs per year. It is considered that this feature is a remnant of effective proliferation of fish and amphibians CMs or the CMs of new-born mammals, which like mice can efficiently heal the heart within first week of life. Accordingly, it is considered that this repairing capacity, lost with adulthood, can be exploited for the purpose of regenerative medicine.

Uncritical belief in the (omni)potency of stem cells (SCs) (or in fact any cell named as "stem" cells), combined with the lack of understanding of the SCs features resulted initially in application of bone marrow-derived cells for treatment of myocardial infarction and then developing heart failure [1]. The results of these first studies, although very much advertised and acclaimed, have been, however, refuted and it has been demonstrated that bone marrow-cells do not have the capacity to differentiate to CMs. However, this did not stop the clinical trials which have been initiated without confirmation of the pre-clinical experiments. This resulted in numerous applications of BM-derived autologous or allogeneic cells which are injected into the failing heart [1,2]. However, accumulating evidence clearly demonstrate that the effectiveness of such a treatment is transient and limited, if any [1]. The refuted claims of differentiation capacity have been then replaced by the paracrine hypothesis, suggesting that the injected cells release the substances which stimulate endogenous heart repair mechanisms. Meanwhile, the persistence of the injected cells in the heart is very limited what questions also the humoral effect.

Nevertheless, these doubtful approaches do not exclude the possibility (although maybe very limited) for stimulating the regeneration of damaged heart. It can be considered that some molecules, active in the early periods of heart development, when human CMs are still capable of division, can be used for stimulation of the proliferation of heart CMs after myocardial infarction. To this end the efficient overexpression of such molecules can activate CMs divisions. Moreover, the pluripotent stem cells, able to differentiate to CMs, are tested for application in heart regeneration. Embryonic SCs (ESC) or induced pluripotent SCs (iPSCs) can now be easily differentiated not only to CMs but also endothelial cells, raising the possibility of effective stimulation of heart regeneration [3-5]. However, achieving real clinical effectiveness will require overcoming the problems of electrical incompatibility of beating CMs and the heart, what creates the danger of arrhythmia after the cells' injection into the organs. This can be potentially solved by delivery of not differentiated CMS, but their precursors, isolated during ESCs or iPSCs differentiation to CMs. However, even if such progenitors or CMs will be generated in the sufficient numbers, they will still face the rapid elimination from the heart after the injection. To this end different scaffolds are being tested, opening the possibility for various biomaterials to be used both for immobilization of the injected cells in the heart and improving their regeneration potentials.

The promise for the future of the regenerative medicine in heart diseases is possible. However, one has to balance the expectations and the possibilities, not offering the hype which are not linked to scientific rationale and experimental evidence.

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