Bone Marrow Cells Regenerate Infarcted Myocardium

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Literature Reviews—Cell

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D. Orlic, J. Kajstura, S. Chimenti, I. Jakoniuk, S. M. Anderson, B. Li, J. Pickel, R. McKay, B. Nadal-Ginard, D. M. Bodine, A. Leri, and P. Anversa

Nature 2001;410:701-5.

Stem cell plasticity is certainly one of the most fascinating recent discoveries in biology and medicine. In addition, when experiments are described that have almost immediate clinical promise, the fields of clinical medicine and basic science come to a long-awaited synergy that cannot but generate sincere enthusiasm.

In this article by Orlic et al., myocardial infarction induced in mice is treated with perilesional administration of bone marrow stem cells, with remarkable improvement in the histological appearance and functional performance of the heart. The authors sorted lineage-negative bone marrow cells from transgenic mice expressing green fluorescent protein. Shortly after coronary ligation, the sorted cells were injected in the myocardial area immediately surrounding the infarct. Donor-derived myocytes and vascular structures occupied more than 60% of the infracted area 9 days after implant. Most important, functional performance of the treated hearts was significantly improved over that of control hearts. This approach represents a possible novel therapeutic tool for the treatment of coronary disease.

Transplantation of islets of Langerhans for the treatment of diabetes faces the sizable problem of scarce availability of human donors, vis-à-vis the recent success of clinical trials. Alternative sources of insulin-producing tissue must be defined. These recent 2 articles report exciting data on the derivation of insulin-producing cells from stem cells.

Insulin-Secreting Cells Derived from Embryonic Stem Cells Normalize Glycemia in Streptozotocin-Induced Diabetic Mice

B. Soria, E. Roche, G. Berna, T. Leon-Quinto, J. A. Reig, and F. Martin

Diabetes 2000;49(2):157-62.

Embryonic stem cells have been shown to possess the ability to differentiate in vitro into a variety of lineages. Spontaneous differentiation into insulin-producing cells, on the other hand, has been postulated to be exceedingly rare. Using a cell-trapping system, the authors of this article obtained an insulin-secreting clone from undifferentiated mouse stem cells. The selection strategy was based on the use of a transgene coding for a selectable marker under the control of regulatory regions of the insulin gene. The rare cells spontaneously expressing insulin could therefore be effectively selected in culture. One of the clones obtained was characterized and shown to produce a sizable amount of insulin and to display insulin secretion in response to selected secretagogues. Importantly, implants of cell clusters derived from this clone in diabetic mice led to reversal of hyperglycemia and weight gain. Metabolic testing of the recipient mice showed a normal oral glucose tolerance, whereas the response to an intraperitoneal challenge was altered. This data could potentially have a great impact in the quest for alternative sources of insulin-producing tissue for transplantation.

Differentiation of Embryonic Stem Cells to Insulin-Secreting Structures Similar to Pancreatic Islets

N. Lumelsky, O. Blondel, P. Laeng, I. Velasco, R. Ravin, and R. McKay

Science 2001;292:1389-94.

Mouse embryonic stem (ES) cells were cultured in sequential steps under strictly controlled conditions to generate three-dimensional structures that resembled islets. The steps included removal of LIF, culture in serum-free medium, mitogen stimulation, and the addition of nicotinamide. The islet-like structures, containing not only beta but also alpha and delta cells, showed glucose-regulated insulin secretion, albeit with insulin secretion and content that were lower than those of normal islets. Transplantation of these islet-like structures in diabetic mice allowed for longer survival of the recipients, when compared with nontransplanted subjects. However, it did not lead to diabetes reversal. Explanted islets were stained brightly for insulin and showed host-derived vascularization. These data define for the first time a successful in vitro culture procedure that leads to the ontogeny of insulin-producing cells from undifferentiated ES cells. The potential influence of this finding on islet transplantation is evident.

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