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Differentiation of Mesenchymal Stem Cells towards an insulin-releasing phenotype after co-culture with Pancreatic Islets

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Transplantation of pancreatic islets has become a promising clinical option to treat patients with type 1 diabetes, alternative to the standard therapy with insulin injections. Islet transplantation is a minimally invasive therapeutic approach, and it allows a better metabolic control and a long-term insulin independence in more than 80% of patients (Ryan et al., 2002). However this therapeutic treatment has some side effects, such as the poor yield of pancreatic islet explants and even more the immune graft rejection, which have as a consequence the very limited lifespan of transplanted pancreatic islets. To avoid these side effects several strategies have been proposed and, besides the treatment with immunosuppressive drugs, promising results have been obtained with the use of Mesenchymal Stem cells (MSCs), already known in literature to be able to support the survival of many cell types (Scuteri et al., 2006). Several in vivo studies have demonstrated that the concurrent transplantation of pancreatic islets with MSCs reduces the number of islets required to achieve glycemic control in diabetic rats, but the mechanisms of these encouraging results are still unknown (Figliuzzi et al., 2009). For these reasons in this in vitro study we characterized the effect of co-culture of rat MSC on survival and functioning of rat pancreatic islets, by evaluating for 4 weeks: i) MSC adhesion to pancreatic islets; ii) viability of pancreatic islets co-cultured with MSCs; iii) the expression of insulin after co-culture; iv) the ability of co-cultured pancreatic islets to correctly adjust insulin release after variation of glucose concentration. Our results demonstrated that MSCs are able to adhere to pancreatic islets, but to increase only partly the pancreatic islet survival, which retain the ability to express and correctly release insulin after glucose variation in medium culture. Noteworthy that the insulin level in the medium of co-cultured pancreatic islets is always higher with respect to medium of pancreatic islets alone. The immunofluorescence analysis reveals that also MSCs (and not only pancreatic islets) are able to express insulin, but only in co-culture. These results, which justify the in vivo observation reported above, suggest that MSCs undergo to differentiation into a insulin-releasing phenotype after co-culture with pancreatic islets. We are now evaluating the molecular mechanisms which drive this effect, by analyzing the role of soluble factors and of proteins able to induce insulin expression.

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