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IMIM researchers have generated pancreatic cells with acinar phenotypes for the first time

Barcelona 8 October 2008 - A study directed by Anouchka Skoudy in which researchers from the **Municipal Institute of Medical Research** (IMIM-Hospital del Mar) and the **Department of Experimental and Health Sciences** (CEXS) at Pompeu Fabra University (UPF) took part, in collaboration with other European institutions, has enabled the generation of pancreatic cells with acinar phenotypes under controlled conditions for the first time.

Acinar pancreatic cells have an essential function in digestion given that they produce the necessary enzymes for breaking down food. The synthesis and secretion of these cells are closely regulated by the human body and alteration of these processes can lead to various pathologies of the exocrine pancreas, such as pancreatitis. In recent years, interest in this type of cell has been marked by the fact that **acinar cells can acquire a ductal phenotype and numerous pieces of evidence point to these as the possible origin of pancreatic ductal adenocarcinoma, the most common type of tumour of the pancreas and one of the most aggressive human tumours.**

Given that normal acinar cells do not maintain the properties differentiated in vitro, the main aim of this research was to produce cells from undifferentiated precursors so that new study models could be developed. Therefore, from embryonic stem cells that can be differentiated in culture from all types of embryonic cells, various strategies have been designed to force their differentiation to pancreatic cells, as spontaneously their capacity is very limited (< 1%).

Methodologically, the **study used sophisticated cell differentiation and isolation techniques.** Stem cell cultivation conditions capable of activating the necessary signals towards the differentiation of acinar pancreatic cells have been optimised. Through viral vectors that express transcription factors that are key for pancreatic development, the process of obtaining a sufficient amount of these cells has been amplified and, ultimately, a painstaking genetic selection and cell lineage purification has been assured for the study. Through the integration of these approaches, the isolation of highly efficient cells with acinar phenotype-functionally similar to acinar pancreatic cells- has been obtained. The importance of this study lies in its distinction from previous studies carried out using primary cultures: the cells generated do not display a ductal intermediary phenotype. This fact has made it so that a new model has been established, in vitro using non-tumour cells, for the acinar differentiation study, a deregulated process in many diseases of the exocrine pancreas.

The fact that cells with an immature phenotype have been generated gains relevance since it was demonstrated that immature acinar cells are more susceptible to oncogenic transformation than mature cells and therefore will serve as a base for understanding the nature of tumour precursors.

Reference article: "Murine Embryonic Stem Cell-Derived Pancreatic Acinar Cells Recapitulate Features of Early Pancreatic Differentiation", Meritxell Rovira, Fabien Delaspre, Mohammad Massumi, Selma A. Serra, Miguel Angel Valverde, Josep Lloreta, Marlène Dufresne, Bruno Payré, Stephen F. Konieczny, Pierre Savatier, Francisco X. Real, Anouchka Skoudy. **Gastroenterology** 135:1301-1310.e5, 2008.

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