The article will be published in the April edition of the Gastroenterology journal

A new molecular mechanism which participates in the cell proliferation and invasion of pancreatic cancer has been discovered

Barcelona, 1 April 2009 - A study conducted by the research group investigating molecular mechanisms involved in tumourigenesis at the **Municipal Institute of Medical Research** (IMIM-Hospital del Mar), together with researchers from the Department of Experimental and Health Sciences (UPF) and in collaboration with other national and European institutions, **has identified a new molecular mechanism connected with the proliferation and invasion of tumour cells in pancreatic ductal adenocarcinoma**, the most common type of pancreatic cancer (90% of all cases). Pancreatic cancer is one of the most lethal tumours and the fourth leading cause of cancer death worldwide.

Tissue plasminogen activator (tPA) is a protein which is naturally secreted by the cells that line the blood vessels in the presence of a clot in order to dissolve it. However, when the production of tPA is disturbed, this protein can carry out harmful functions on the body. Previous studies by this group have discovered that while **tPA** is absent in healthy pancreatic cells, **high levels of the protein are present in tumour cells of pancreatic ductal adenocarcinoma**, where it **plays an important role in cell proliferation, migration and invasion**. In order to carry out these functions, tPA must unite with proteins in the tumour cell membranes, i.e. its "receptors". In recent years, the objective of the **group led by Pilar Narvarro** has focused on the search for these receptors and their participation in tPA functions in pancreatic cancer.

In this study, the group identified a **new tPA receptor**: **a protein called Galectin-1**, which is also secreted in high levels in pancreatic tumours. The authors have used methodological strategies, such as surface plasmon resonance, to demonstrate that the interaction between tPA and Galectin-1 is direct and of high affinity, and RNA interference techniques, to reduce Galectin-1 levels. **According to Pilar Navarro**, director of the study: *"The results have shown that Galectin-1, which is present in large quantities in tumour cell cultures and in the pancreatic tumours themselves, has shown a great affinity for union with tPA. When the presence of Galectin-1 "in vitro" is reduced, the effects of tPA on the proliferative and invasive capacity of the tumour are cancelled out, demonstrating that Galectin-1 acts as a mediator in functions of tPA in pancreatic cancer".* Furthermore, the authors of this study, whose first signatories are **Oriol Roda and Elena Ortiz-Zapater**, add that *"this union does not only occur between the tPA and Galectin-1 of pancreatic tumour cells but also in another type of cell: fibroblasts, a cell population that grows abnormally in the pancreatic ductal carcinoma and seems to play a crucial role in the malignity of the tumour."* Thus, tPA through Galectin-1 would also be capable of inducing the growth and invasion of fibroblastic tumour cells.

The study concludes that **the identification of Galectin-1 as a tPA receptor is a new molecular mechanism through which tPA could send proliferative and invasive signals to both pancreatic tumour cells and the fibroblasts that surround them, contributing to tumour progression**. Therefore, could Galectin-1 be a new therapeutic target for such an aggressive tumour? For now, Pilar Navarro states that *"our studies only show that blocking Galectin-1 could prevent the harmful effects that tPA has on this cancer".* Regrettably, increased tPA secretion is just one of the many disturbances present in this tumour, which means that blocking the interaction between tPA and Galectin-1 would be a small speck within the large group of other causes that contribute to tumour malignity. Pancreatic cancer studies with animal models, which are currently being conducted by this group, will make it possible to gain more accurate knowledge on the relevance and possible therapeutic use of blocking Galectin-1 in the development and progression of pancreatic ductal adenocarcinoma *in vivo*.

Reference article:

Galectin1 Is a Novel Functional Receptor for Tissue Plasminogen Activator in Pancreatic Cancer. Oriol Roda, Elena Ortiz-Zapater, Neus Martínez-Bosch, Ricardo-Gutiérrez-Gallego Miquel Vila-Perelló, Coral Ampurdanés,Hans-Joachim Gabius, Sabine André, David Andreu, Francisco X Real and Pilar Navarro. Gastroenterology April 2009. 136(4):1379-1390

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