Hospital del Mar Research Institute Barcelona

Nota de premsa

Study published in PNAS

Key to the high aggressiveness of pancreatic cancer identified

- ***A study by researchers from the Hospital del Mar Research Institute, IIBB-CSIC-IDIBAPS, Mayo Clinic, IBYME (CONICET), and CaixaResearch Institute demonstrates the role of the Galectin-1 protein in the nucleus of the cells surrounding the tumor—fibroblasts—contributing to their activation.***
- ***Activated fibroblasts promote tumor growth and spread, while also conferring resistance to treatments. This may be one of the reasons behind the high aggressiveness of pancreatic cancer, which has a five-year survival rate of only 10%.***
- ***The study's findings open the door to new therapeutic strategies against this type of cancer, focusing on the possibility of inhibiting this protein within the cells that surround and protect the tumor.***

Barcelona, 15th April 2025. – Pancreatic cancer is one of the most aggressive cancers and has one of the lowest survival rates—only 10% after five years. One of the factors contributing to its aggressiveness is its tumor microenvironment, known as the **stroma**, which makes up the majority of the tumor mass and consists of a network of proteins and different non-tumor cells. Among these, fibroblasts play a key role, helping tumor cells to grow and increasing their resistance to drugs. Now, a study led by researchers from the Hospital del Mar Research Institute, IIBB-CSIC-IDIBAPS, Mayo Clinic, Instituto de Biología y Medicina Experimental (CONICET, Argentina) and CaixaResearch Institute, has identified a new key factor contributing to this feature of pancreatic cancer**: a previously unknown function of Galectin-1 protein inside the nuclei of fibroblasts**. This discovery, published in the journal PNAS, offers new insights into the role of these cells in the progression of pancreatic cancer.

"The stroma is considered a key component in the aggressive nature of pancreatic cancer, as it interacts with tumor cells, protects them, and hinders the action of drugs. Moreover, stromal cells, particularly fibroblasts, produce substances that support tumor growth and dissemination," explains Dr. Pilar Navarro, coordinator of the Cancer Molecular Targets Research Group at the Hospital del Mar Research Institute and IIBB-CSIC-IDIBAPS. Until now, fibroblasts were known to secrete Galectin-1, a protein with pro-tumoral properties. This study, however, shows that the molecule is also located inside fibroblasts—specifically in their nuclei—where it plays a key role in gene expression regulation.

The presence of this molecule activates fibroblasts, making them support tumor cell development. The researchers also discovered that "**Galectin-1 can regulate gene expression in these cells at a highly specific level without altering the DNA sequence, through epigenetic control. One of the genes it regulates is KRAS, which plays a critical role in pancreatic tumors**," explains Dr. Navarro. This gene is also present in tumor cells in 90% of patients, though in this case it is mutated. It is considered one of the main drivers of uncontrolled growth and tumor aggressiveness.

Designing new strategies

The team behind the study had previously identified the prominent role of Galectin-1 in pancreatic cancer. However, the newly discovered functions now pave the way for developing

new strategies to tackle this type of tumor. **"Until now, efforts have focused on inhibiting Galectin-1 secreted by the stroma surrounding the tumor. Now, we see that we also need to block the protein inside the fibroblast nuclei**," says Dr. Neus Martínez-Bosch, researcher at the Hospital del Mar Research Institute**."We need to find new inhibitors that work inside fibroblasts, not just on the protein they secrete**," she adds.

To carry out the study, researchers worked with tissue samples from pancreatic cancer patients, allowing them to analyze the presence and function of Galectin-1 in fibroblast nuclei. They also performed *in vitro* experiments with human fibroblast cell lines, investigating the effects of inhibiting both the protein and the KRAS gene, and observed **deactivation of these cells—effectively halting their cooperation with tumor cells.**

Dr. Judith Vinaixa, also a researcher at the Hospital del Mar Research Institute and first author of the study, highlights the importance of these results: **"We have confirmed the key role of Galectin-1 in the fibroblast cell nucleus, where it regulates the expression of multiple genes critical for cell behavior**.". Dr. Gabriel Rabinovich, researcher at IBYME (CONICET) and the CaixaResearch Institute, adds: "**The next steps will involve exploring therapeutic combinations that inhibit both extracellular and intracellular Galectin-1. This protein also participates in key processes such as blood vessel formation and resistance to immunotherapy. Therefore, this strategy becomes particularly relevant given the multiple antitumoral effects of Galectin-1 inhibition**."

The study also involved contributions from the Pathology Department at Hospital del Mar and researchers from the Cancer Area of CIBER (CIBERONC).

Reference article

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More information

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