Inhibition of a protein opens the door to treatment of pancreatic cancer

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Researchers from IMIM (Hospital del Mar Medical Research Institute) have identified a new protein, galectin-1, as a possible therapeutic target for pancreatic cancer. For the first time they have demonstrated the effects of the inhibition of this protein in mice suffering this type of cancer and the results showed an increase in survival of 20%. The work further suggests that it could be a therapeutic target with no adverse effects.

Until now, the strategies for treating this tumour were aimed at attacking the tumour cells and had little success. The latest studies indicate that trying to destroy what surrounds the tumour is possibly a better strategy. "Our contribution is directed toward this, as the reduction of galectin-1 mainly affects the immune system and the cells and structure that surrounds the tumour cells, which is called the stroma. Therefore, galectin-1 as a therapeutic target has great potential", explains Dr. Pilar Navarro, co-ordinator of the research group on molecular mechanisms of tumorigenesis of IMIM and director of the research.

It was known that galectin-1 was not found in the normal pancreas despite being strongly expressed in pancreatic tumours. Furthermore, some clear functions were known which demonstrate the relationship between galectin-1 and tumour progression in other contexts. In fact, some preclinical studies for other diseases use inhibitor molecules and antibodies against this protein. "We are aiming at its possible use in pancreatic cancer" states Dr. Neus Martínez, researcher of the group on molecular mechanisms and tumorigenesis of IMIM and first author of

this article. "We have also observed that the elimination of galectin-1 in mice has no harmful consequences, indicating that it could be a safe therapeutic target with no adverse effects", she adds.

In collaboration with the Hospital del Mar Anatomical Pathology Service, which has analysed some samples, pancreatic tumours were studied in mice with high levels of galectin-1 and after its depletion. They observed that tumours without this protein showed less proliferation, fewer blood vessels, less inflammation and an increase in the immune response. All these changes are associated with less aggressive tumours.

Pancreatic cancer is one of the tumours with the worst prognosis, with a survival rate of less than 2%, 5 years after diagnosis. Although it is not a very common tumour, it is the fourth cause of cancer-related death in developed countries. This is due, on one hand, to the fact that it is often diagnosed too late, when the tumour has already metastasised and, on the other hand, to the inefficacy of current treatments. In Spain 4000 cases are diagnosed each year. Although it is a tumour that is well known at molecular level, its diagnosis and treatment are still one step behind. In fact it is one of the tumours with the least therapeutic advancements in recent years.

The results are very encouraging but we must be prudent as there are many factors to take into account. The researchers now want to move the results obtained to preclinical studies, where they will treat mice with pancreatic cancer with chemical inhibitors or antibodies against galectin-1 (the same treatment that would be used for a cancer patient) in order to verify the therapeutic utility of this target. In the event that they obtain positive results and manage to halt the tumour, the next step would be to propose its use on patients. Obviously we are talking about long-term objectives, as the transfer of studies on animals to humans is usually a slow process.

More information: Galectin-1 drives pancreatic carcinogenesis through stroma remodeling and Hedgehog signaling activation. Neus Martinez-Bosch, Maite G Fernandez-Barrena, Mireia Moreno, Elena Ortiz-Zapater, Jessica Munné-Collado, Mar Iglesias, Sabine André, Hans-Joachim Gabius, Rosa F. Hwang, Françoise Poirier, Carolina Navas, Carmen Guerra, Martin E. Fernández-Zapico, and Pilar Navarro. *Cancer Res*. DOI: 10.1158/0008-5472.CAN-13-3013