Hospital del Mar Research Institute Barcelona

PRESS RELEASE

A new strategy against pancreatic cancer attacks tumour cells and activates the immune system

- ***A study in mice by the Hospital del Mar Research Institute and the IIBB-CSIC, published in Science Advances, identifies inhibition of the PARP2 protein as a therapeutic target for treating pancreatic cancer, the third leading cause of cancer death worldwide***
- ***The study analyses the role of this protein in tumour development and protection, and describes how its elimination leads to tumour cell death and activation of the immune System***
- ***Specifically blocking this protein may be a useful strategy for treating a large number of patients with pancreatic cancer and could even be applicable to other types of tumours***

Barcelona, June 18, 2026 – Pancreatic cancer is one of the tumours with the worst prognosis due to its often late diagnosis and the limited effectiveness of available treatments. It is also one of the so-called **cold tumours**, in which the immune system has only a limited presence. An international study led by researchers from the Hospital del Mar Research Institute (HMRIB) and the Barcelona Institute for Biomedical Research (IIBB-CSIC), a CSIC centre associated with the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), shows in animal models that inhibiting the **PARP2 protein** makes it possible to tackle pancreatic cancer in two ways: from within, by causing cancer cells to die by preventing them from repairing the DNA errors they accumulate as they divide; and from outside, by making it easier for the immune system to access and attack the tumour. The findings, published in Science Advances, identify this protein as a potential therapeutic target not only for pancreatic cancer but also open the door to its application in other tumours with limited immune system infiltration.

The principle behind the study is to exploit one of the weak points of tumour cells, known as **replicative stress**, that is, the pressure they undergo when they divide very rapidly. These cells multiply at high speed and, as they do so, can generate errors in their DNA that may trigger their death, a process known as apoptosis. This is where PARP2 plays a key role, as it is an essential protein for keeping DNA in good condition. Using two mouse models, the researchers have shown that specifically inhibiting this protein causes this protection system to fail and tumour cells ultimately die.

At the same time, they have observed how **this inhibition makes it easier for immune system cells to access the tumour and attack it.** Although the exact mechanism that enables this is still unknown, the researchers have shown that the absence of PARP2 increases the activity and effectiveness of immune cells in eliminating tumour cells. As Dr Pilar Navarro, coordinator of the New Molecular Targets in Cancer Research Group at the HMRIB and the IIBB-CSIC-IDIBAPS, explains, **'in this way we would be attacking the tumour through two routes: from within, by facilitating apoptosis or cell death, and from outside, by promoting the work of immune cells'**.

Search for PARP2 inhibitors

The results obtained with the mouse models have been **corroborated with data from a cohort of patients** with pancreatic cancer. Differential gene expression and cell signalling pathways were compared between patients with higher and lower PARP2 expression, confirming that the molecular mechanisms observed in mouse models are also conserved in humans and suggesting that this protein may be a therapeutic target for patients

According to Dr Navarro, the results point to the need to **develop specific PARP2 inhibitors**. At present, there are only drugs targeting the PARP protein family as a whole, which have not achieved the expected results and have side effects. **'The currently approved PARP inhibitors are administered to a small group of patients, between 5 and 10%, only those with mutations in genes involved in DNA repair. In contrast, the potential target, PARP2, is proposed for patients with pancreatic cancer in general, taking advantage of the fact that this is a tumour with high replicative stress'**. In this way, the potential treatment could be extended to most patients with pancreatic cancer.

Dr José Yélamos, coordinator of the Poly(ADP-ribose) Polymerases Research Group at the Hospital del Mar Research Institute, states that **'we have identified a therapeutic target that we can act on in pancreatic cancer'**. This opens the way to developing new treatments specifically targeting PARP2, since **'our work shows that the specific inhibition of PARP2, and not of other members of the family, is a more appropriate therapeutic strategy than the current one'**

In addition, as HMRIB researcher Dr Neus Martínez-Bosch explains, **'if we focus on controlling replicative stress, a specific function of PARP2, we may gain selectivity and move beyond some of the side effects of the PARP inhibitors currently available'**. At the same time, this **'opens the door to combining treatments against PARP2 with other existing and approved therapies, such as immunotherapy, thereby enhancing their effects**.'

The effectiveness of this strategy could be applied to other so-called cold tumours that show high replicative stress. In this regard, Dr Yélamos notes that **'PARP2 is possibly a good pathway for acting on cold tumours, those with limited infiltration by the immune system'**

Researchers from several national and international institutions also took part in this international collaborative project, including the National Cancer Research Centre (CNIO) in Madrid, IMIB-LAIB-Arrixaca and the University of Murcia, Pompeu Fabra University, the University of Barcelona, the Bellvitge Biomedical Research Institute (IDIBELL), the CaixaResearch Institute, as well as the National Scientific and Technical Research Council (CONICET) and the University of Buenos Aires, in Argentina.

Reference article

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More information

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