Press release

Researchers identify the cell of origin of Ewing Sarcoma

- ***This discovery, carried out by a multidisciplinary team led by researchers from the Hospital del Mar Research Institute and the Sant Joan de Déu Research Institute, opens the door to understanding the mechanisms that trigger tumour proliferation and to exploring potential therapeutic targets.***
- ***Researchers suspect that the genetic alteration that activates the mechanisms behind this type of cancer occurs during embryonic development.***
- ***Ewing sarcoma is a highly aggressive tumour that can affect bones and soft tissues, and is the most frequent bone tumour in childhood.***

Barcelona, 20 November 2025. – One of the great mysteries of Ewing Sarcoma, a highly aggressive paediatric tumour, is where it originates. This information is essential to develop more effective ways to treat it. This question now seems to be resolved, thanks to the work of a multicentre team led by the Hospital del Mar Research Institute and the Sant Joan de Déu Research Institute, published in the journal *Nature Communications*. The study opens the door to identifying the factors that trigger tumour progression and its possible vulnerabilities.

Although the cure rate ranges between 60% and 70% of cases, the toxicity of current chemotherapy treatments results in side effects in children. Knowing where the disease originates—the cell that is the starting point—may enable more targeted and accurate therapeutic approaches, as explained by Dr. Inmaculada Hernández-Muñoz, researcher in the Inflammatory and Neoplastic Dermatological Diseases Research Group at the HMRIB. "***Now that we have identified the cell that originates the tumour, the next step is to determine which factors make a cell that, in principle, has no growth advantage, acquire this characteristic,***" she adds.

Early presence during fetal development

One of the main characteristics of Ewing Sarcoma is that, unlike most tumours, it is caused by a single oncogene. Two genes combine to generate a new one, **acquiring new functions that allow it to develop the disease when expressed in embryonic mesenchymal stem cells,** as the new study has demonstrated. These are the cells that form the mesenchyme, the embryonic tissue from which, among others, muscle and connective tissue, as well as blood and lymphatic vessels, are derived.

The study now published has succeeded, for the first time, in reproducing this mechanism. In collaboration with the laboratory led by **Dr. Àngel Raya** at the Center for Regenerative Medicine in Barcelona, human embryonic mesenchymal cells were generated and purified, into which the oncogene that causes Ewing Sarcoma was introduced. Although these cells do not show tumour characteristics *in vitro*, when inoculated into mice they generate tumours similar to human Ewing Sarcoma, maintaining the cellular and transcriptional patterns typical of the disease.

In this regard, Dr. Hernández-Muñoz noted that "***we are talking about a mesenchymal cell that, at a very early point in embryonic development, acquires the oncogene that may later give rise to Ewing Sarcoma." In other words, "the cell of origin of Ewing Sarcoma is already in the fetus during its intrauterine development, and our hypothesis is that when puberty arrives, hormonal factors cause this oncogene-bearing cell to develop into a tumour***."

With these results, Dr. Hernández-Muñoz states that "***we now have an experimental model that allows us to understand what this cell is like and study the changes it undergoes until it becomes tumoural.***" In this way, its strengths and weaknesses can be analysed, as well as the factors that trigger tumour proliferation and dissemination, to develop future treatments specifically aimed at preventing them.

In this sense, Dr. Jaume Mora, Scientific Director of the Pediatric Cancer Center Barcelona (PCCB) at Hospital Sant Joan de Déu and head of the Sarcomas and Neuroblastoma research group at the Sant Joan de Déu Research Institute, points out that "***this discovery represents a fundamental advance in understanding Ewing Sarcoma. Identifying the cell of origin allows us to better understand how and when the tumour process begins, which opens new avenues for developing more targeted and less toxic therapies for paediatric patients. Our goal is for this knowledge to translate into more effective treatments with fewer side effects for the children and adolescents affected by this disease.***"

Reference article

Hernández-Muñoz I, Cuervas I, Prada E, Pulecio J, Gimeno R, Andrades E, Gómez-González S, Berenguer-Molins P, Acedo-Terrades A, Perera-Bel J, Bódalo-Torruella M, Nonell L, Pérez E, Grases D, Mata C, Yélamos J, Richaud-Patin Y, Vidal E, Cuartero Y, Le Dily F, Suñol M, Manzanares A, Raya A, Mora J. *EWS::FLI1 expression in human embryonic mesenchymal stem cells leads to transcriptional reprograming, defective DNA damage repair and Ewing sarcoma*. Nat Commun. 2025 Oct 24;16(1):9427. doi: 10.1038/s41467-025-64475-y. PMID: 41136396; PMCID: PMC12552549.

More information

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About the Hospital del Mar Research Institute

The Hospital del Mar Research Institute in Barcelona is a scientific research center in the field of biomedicine and health sciences, organized into five major research programmes: Cancer, Epidemiology and Public Health, Biomedical Informatics, Neurosciences, and Translational Clinical Research. With around 700 professionals, it ranks among the ten Spanish institutions with the greatest scientific impact in the health area. It is a CERCA center of the Generalitat de Catalunya and is accredited as a Health Research Institute by the Carlos III Health Institute.

About the Sant Joan de Déu Research Institute (IRSJD)

The Sant Joan de Déu Research Institute (IRSJD) is a center dedicated to research and innovation in maternal-fetal, child and adolescent health, as well as mental health. Created in 2015, the IRSJD aims to improve health, well-being and quality of life through a collaboration agreement between Hospital Sant Joan de Déu Barcelona, the University of Barcelona, the Universitat Politècnica de Catalunya, the Parc Sanitari Sant Joan de Déu and the Sant Joan de Déu Research Foundation. In 2020, the IRSJD was recognized as a CERCA center by the Generalitat de Catalunya, consolidating its role as a reference in biomedical and translational research. More information: https://www.irsjd.org/en/

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