

## **Demonstration of the usefulness of a biomarker in the prognosis and possible treatment of glioma**

- ***The Molecular Mechanisms of Cancer and Stem Cell Research Group of the Hospital del Mar Research Institute is the only center in Spain to participate in an international study that validates the deficiency of a protein, IκBα, as a marker of poor prognosis in this type of tumor***
- ***The work, published in Cell Reports Medicine, has analyzed data from more than 2,000 patients. In addition, the researchers have identified one of the pathways on which this protein acts, which makes it a possible therapeutic target***
- ***The Hospital del Mar Research Institute group is already working on a model to search for possible treatments that modulate the function of this marker. It should be considered that at present there are very few therapeutic alternatives for glioma, which has a very high mortality rate***

**Barcelona, June 21, 2023.** – An international team, with the participation of the Research Group on Molecular Mechanisms of Cancer and Stem Cells of the Hospital del Mar Research Institute and the Cancer CIBER (CIBERONC), has determined that a specific type of protein, IκBα, is a **prognostic marker** in one of the types of cancer with the highest mortality, diffuse glioma. Specifically, in the case of patients with this type of tumor, which affects the brain, lower levels of this protein cause **survival to drop dramatically**. The work has been led by the *University of Alabama at Birmingham*, in the United States, and is published in the journal *Cell Reports Medicine*.

To reach this conclusion, data from more than 2,300 patients from different centers around the world and with different characteristics and stages of progress were analyzed. And in all of them, **low levels of this marker indicate a worse prognosis** and a much-reduced survival. ***"The IκBα protein regulates inflammatory processes and when there is a decrease in this protein in tumors, the life expectancy of patients is drastically reduced"***, notes Dr. Lluís Espinosa, second signatory of the paper and coordinator of the research group at the Hospital del Mar Research Center.

In addition to this finding, the researchers have also been able to verify that this protein interacts with chromatin, a structure composed of DNA, RNA and proteins that regulates genetic activity. This opens the door to using this interaction as a therapeutic target, an approach different from that proposed so far in these patients. ***"What we have seen is that the role of this protein is different from what had been attributed to it as regulator of inflammatory processes through the modulation of cytokines. Its interaction with chromatin encourages us to continue investigating this pathway, in what we consider promising research aimed at identifying a treatment for glioma"***, explains Dr. Espinosa.

The influence of this protein on patient prognosis is now being investigated in other tumor types.

### **Model for finding IκBα regulators**

The group coordinated by Dr. Espinosa at the Hospital del Mar Research Institute already has a patent for a model with molecules that can enable them to search for modulators for the different functions that the IκBα protein has. This will make it possible to test the effectiveness of different treatments that activate or deactivate the various cell signaling pathways on which they act. As

*Press release*

Dr. Espinosa details, ***"finding out what is increasing the malignancy of tumors when IκBα is lost is essential for treating patients, since if the wrong pathway is attacked, the desired therapeutic effect will not be achieved"***.

Diffuse gliomas are primary tumors of the central nervous system (CNS), accounting for approximately 5% of these tumors. They typically affect a young population, with an average age of 40 years. Conventional treatment is based on maximum resection, provided it remains safe, and in some cases, if they are low-risk tumors, on close follow-up. As Dr. María Martínez, head of the Neuro-oncology section of the Oncology Service of the Hospital del Mar and researcher at the Hospital del Mar Research Institute, explains, ***"these are neoplasms that will invariably progress. Until now they have been considered incurable tumors"***.

One of the characteristics of these tumors is the presence of mutations in the IDH1 and IDH2 genes, which have a good prognosis. In this field, ***"the results of a phase 3 study, the INDIGO study, which have recently been published, have demonstrated a significant impact on progression-free survival in patients with diffuse gliomas with mutations in these genes treated with vorasidenib"***, Dr. Martínez points out. Therefore, ***"identifying prognostic and predictive markers in diffuse gliomas, as the new Hospital del Mar Research Institute study does, is extremely relevant for designing future clinical approaches for these patients"***, says the oncologist and researcher.

**Reference article**

Markus Bredel, Lluís Espinosa, Hyunsoo Kim, Denise M. Scholtens, Joseph P. McElroy, Rajani Rajbhandari, Wei Meng, Thomas M. Kollmeyer, Tathiane M. Malta, Michael A. Quezada, Griffith R. Harsh, Teresa Lobo-Jarne, Laura Solé, Aran Merati, Surya Nagaraja, Sindhu Nair, Jaclyn J. White, Nanda K. Thudi, Jessica L. Fleming, Amy Webb, Atsushi Natsume, Seishi Ogawa, Ruthild G. Weber, Joan Bertran, S. Jaharul Haque, Bettina Hentschel, C. Ryan Miller, Frank B. Furnari, Timothy A. Chan, Anca-Ligia Grosu, Michael Weller, Jill S. Barnholtz-Sloan, Michelle Monje Houtan Noushmehr, Robert B. Jenkins, C. Leland Rogers, David R. MacDonald, Stephanie L. Pugh and Arnab Chakravarti. Haploinsufficiency of NFKBIA reshapes the epigenome antipodal to the IDH mutation and imparts disease fate in diffuse gliomas. *Cell Reports Medicine* 4, 101082 June 20, 2023. <https://doi.org/10.1016/j.xcrm.2023.101082>

**Further information**

Hospital del Mar Research Institute Communications Service: Marta Calsina (+34)933160680 [mcalsina@imim.es](mailto:mcalsina@imim.es), David Collantes (+34)600402785 [dcollantes@hmar.cat](mailto:dcollantes@hmar.cat)