We pioneered the first report proving the importance of gial heterogeneity associated with metastatic brain tumours. As previously shown in other diseases affecting the brain, understanding the contribution of specific gial subpopulations could provide novel therapeutic targets.

The use of genetic and pharmacological approaches has enabled us to discover the critical role of this disease-specific subpopulation of reactive astrocytes in brain metastasis, which is characterised by activation of the STAT3 pathway. Its presence, induced by metastatic cells, involves the establishment of an immunosuppressive local environment that favours tumour growth.

In collaboration with four different national and international clinical institutions we have proved the importance of this finding in patients with brain metastasis. Treatment of stage IV lung adenocarcinoma patients with the STAT3 inhibitor silibinin reduced brain metastasis in 75% of them, which led to an increased survival. This finding involves a proof-of-concept regarding the possibility of developing effective therapies against metastasis by targeting the microenvironment.

**RESEARCH HIGHLIGHTS**

**OVERVIEW**

Brain metastasis is the most common neurological complication of cancer. When metastatic cells reach the brain, prognosis is poor given that local therapies (i.e. surgery and radiation) have limited benefits for patients and the disease inevitably progresses. The rise in the number of patients with brain metastasis is partially due to the increasing number of systemic therapies that work extra-cranially but are unable to provide the same therapeutic benefit in the brain. Consequently, cancer cells present at this secondary site have additional time to evolve and to grow into clinically detectable lesions. In the laboratory, we study why and how cells from different cancer types (breast cancer, lung cancer and melanoma) are able to access the brain, survive and colonise this vital organ. We dissect the biology of these processes in vivo using experimental models in order to challenge the current status of this unmet clinical need.

“We have treated brain metastasis by targeting the microenvironment. We have used a novel therapy both in mice and in patients that reduces established metastasis in the brain and increases survival.”

**PUBLICATIONS**


**AWARDS AND RECOGNITION**

- Elected Member of the Scientific Committee of the European Association of Neuro-Oncology.
- Laura-Alier Espinosa was recipient of a MINECO Severo Ochoa PhD Fellowship.
- Neblía Priego received the CNIO Award for Excellence in Research by Postdoctoral-Staff Investigators, CNIO Lab-Day.
- Lucía Zhu received the “Best Poster” Award at the CNIO Lab-Day.
- STAT3 labels a subpopulation of reactive astrocytes required for brain metastasis, by Priego et al., was selected as paper of the month by the Spanish Society for Biochemistry and Molecular Biology.

**TECHNICIANS**

Lourdes Osuna, Natalia Yebra

**GRADUATE STUDENT**

Laura A. Álvaro (since July), Wendy E. Binderman (until May), Carla P. Domingues, Pedro García, Lucía Zhu

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