# BRAIN METASTASIS JUNIOR GROUP

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## OVERVIEW

Brain metastasis is the most common neurological complication of cancer. When metastatic cells reach the brain, prognosis is poor given that available 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-cranial but not in the brain. In this scenario, cancer cells present at this highly demanding secondary site have additional time to evolve and develop 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.

**"The Brain Metastasis Group is seeking to identify novel ways to target both cancer cells and the associated microenvironment in order to reduce metastatic burden in the brain."**





Graduate Students
Catia P. Domingues, Pedro García (since October), Lucia Zhu

Technicians
Laura E. Doglio (until August), Lourdes Osuna (since November), Natalia Yebra

Student in Practice
Wendy E. Bindeman (since September)

## RESEARCH HIGHLIGHTS

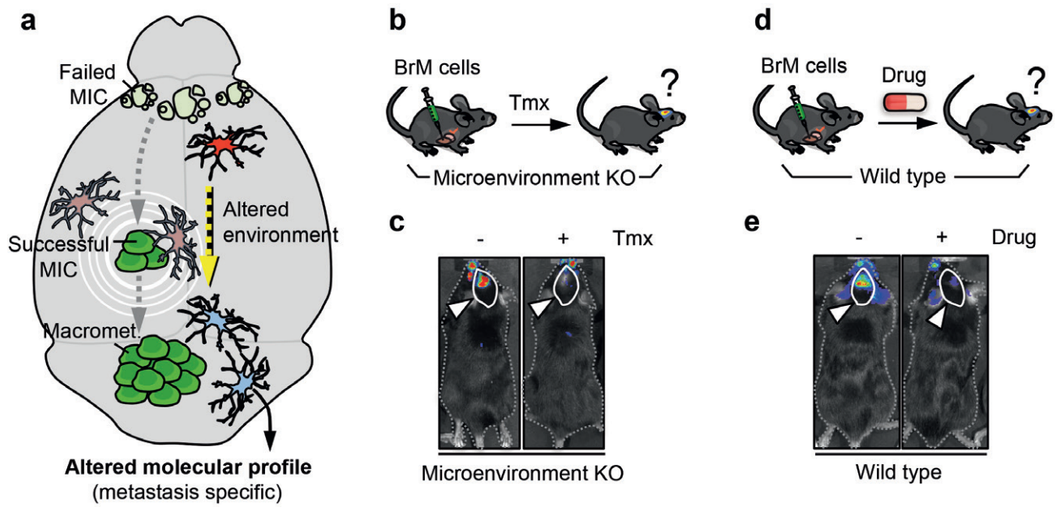


**Figure** (**a**) Metastasis initiating cells (MIC) not eliminated during the initial steps of colonisation grow in the brain and induce altered molecular profiles in the microenvironment. (**b-c**) Genetic and (**d-e**) pharmacologic approaches have validated important pro-metastatic components in the microenvironment.

We have identified a cell type-specific molecular marker that is present in the brain metastasis microenvironment and absent from the normal brain. This marker is present surrounding both experimental and human metastasis, independent of the source of the primary tumour.

By establishing a mouse model that is unable to activate this component of the microenvironment we have proven its pro-metastatic role, since the development of brain metastasis is significantly reduced.

We have translated this finding into a novel therapeutic approach by which we can target brain metastasis by blocking discrete pro-tumorigenic populations within the heterogeneous microenvironment of brain metastasis. ■

### PUBLICATIONS


- Bartolini G*, Sánchez-Alcañiz JA*, Osório C, Valiente M, García-Frigola C, Marín O (2017) Neuregulin 3 mediates cortical plate invasion and laminar allocation of GABAergic interneurons. *Cell Reports* 18, 1157-1170. (*) Shared authorship.
- Wasilewsky D, Priego N, Fustero-Torre C, Valiente M (2017). Reactive astrocytes in brain metastasis. *Frontiers in Oncology* 7, 298.


### PATENT

- Valiente Cortés M, Priego Bendeck N, Bosh Barrera J (2017). Methods for preventing and treating brain metastasis. *EP17382891.4*.

### AWARDS AND RECOGNITION

- Beug Foundation's Prize for Metastasis Research.
- Bristol-Myers Squibb-Melanoma Research Alliance (MRA) Young Investigator Award.
- Cátia Monteiro was awarded the *Best Poster Award*, CNIO Frontiers Meeting: 'Primary and Secondary Brain Tumours', Madrid, Spain.
- Wendy Bindeman was recipient of a Fulbright fellowship.
- Pedro García Gómez was awarded the La Caixa INPhINIT PhD Fellowship.