

BRAIN METASTASIS JUNIOR GROUP

Manuel Valiente
Junior Group Leader

Post-doctoral Fellows
Mariam Al-Masmudi, Lluís Cerdón (since May), Neibla Priego

Graduate Students
Laura Adriana Álvaro, Ana De Pablos Aragonés, Pedro García, Carolina Hernández, Lucía Zhu (until September)

Visiting Graduate Student
Lauritz Miarka (until September) (Boehringer Ingelheim Fonds MD Fellowship) (Christian-Albrechts-University Kiel, Kiel, Germany)

Technicians
Patricia Baena (since July), María Isabel García (until July), María Perea, Diana Patricia Retana, Oliva A. Sánchez (since November)

Visiting Master's Students
Irene Salgado (since November) (Universidad Autónoma de Madrid, Spain), Paniz Rahimi (until August) (Universidad Complutense de Madrid, Spain)



RESEARCH HIGHLIGHTS

We have applied single cell technology (scRNAseq) both within the cancer cell and the non-cancer cell (microenvironment) compartments of brain metastasis in our experimental models, identifying previously unknown subpopulations that we are currently evaluating functionally.

We have confirmed that our drug-screening platform (METPlatform) could be exploited clinically as a patient

“avatar”, being potentially transformative for the future design of clinical trials.

We have initiated a novel research line to evaluate the influence of metastases in neural circuits and brain function in order to elucidate the molecular mechanisms underlying neurocognitive deterioration in patients. ■

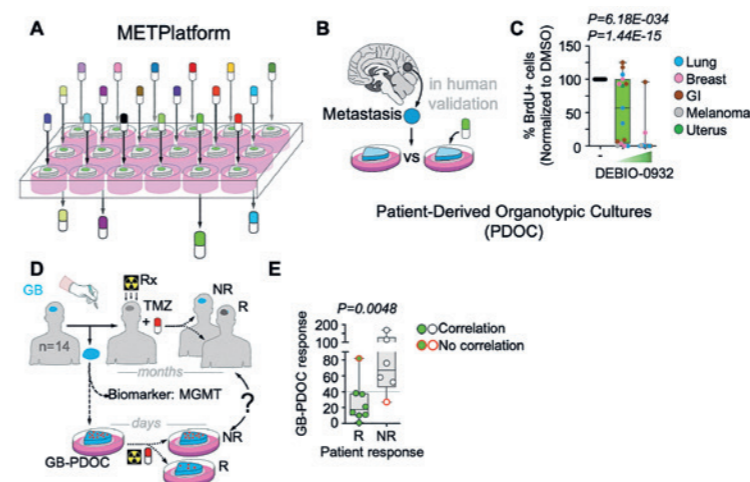


FIGURE (A) METPlatform is a novel drug-screening strategy using live organs with metastases. (B, C) Selected drugs can be translated to patient-derived organotypic cultures. (D, E) METPlatform has the potential to predict within days the response of a patient to a given therapy.

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 benefit 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 established a nation-wide network of hospitals (RENACER) to generate a large repository of brain metastases and patient-derived organotypic cultures, which we have used in our projects.”

► PUBLICATIONS

- Masmudi-Martín M*, Zhu L*, Sanchez-Navarro M, Priego N, Casanova-Acebes M, Ruiz-Rodado V, Giralt E, Valiente M** (2021). Brain metastasis models: what should we aim to achieve better treatments. *Adv Drug Deliv Rev* 169, 79-99. (*) Equal contribution. (**) Corresponding author.
- Zhu L, Retana D, García-Gómez P, Álvaro-Espinosa L, Priego N, Masmudi-Martín M, Yebra N, Miarka L, Hernández-Encinas E, Blanco-Aparicio C, Martínez S, Sobrino C, Ajenjo N, Artiga MJ, Ortega-Paino E, Torres-Ruiz R, Rodríguez-Perales S; RENACER, Soffietti R, Bertero L, Cassoni P, Weiss T, Muñoz J, Sepúlveda JM, González-León P, Jiménez-Roldán L, Moreno LM, Esteban O, Pérez-Núñez Á, Hernández-Lain A, Toldos O, Ruano Y, Alcázar L,

Blasco G, Fernández-Alén J, Caleiras E, Lafarga M, Megías D, Graña-Castro O, Nör C, Taylor MD, Young LS, Varešijija D, Cosgrove N, Couch FJ, Cussó L, Desco M, Mouron S, Quintela-Fandino M, Weller M, Pastor J, Valiente M* (2021). A clinically compatible drug-screening platform based on organotypic cultures identifies vulnerabilities to prevent and treat brain metastasis. *EMBO Mol Med*. PMID: 35174975. (*) Corresponding author.

Pisano F, Kashif MF, Balena A, Pisanello M, De Angelis F, de la Prida LM, Valiente M, D'Orazio A, De Vittorio M, Grande M, Pisanello F (2021). Plasmonics on a neural implant: engineering light-matter interactions on the nonplanar surface of tapered optical fibers. *Adv Opt Mater*. doi: 10.1002/adom.202101649.

Álvaro-Espinosa L, de Pablos-Aragoneses A, Valiente M, Priego N* (2021). Brain

microenvironment heterogeneity: potential value for brain tumors. *Front Oncol* 11, 714428. (*) Corresponding author, postdoc in the lab.

Jablonska PA, Bosch-Barrera J, Serrano D, Valiente M, Calvo A, Aristu J (2021). Challenges and novel opportunities of radiation therapy for brain metastases in non-small cell lung cancer. *Cancers (Basel)* 13, 2141.

Miarka L, Valiente M* (2021). Animal models of brain metastasis. *Neurooncol Adv* 3, 144-156. (*) Corresponding author.

► AWARDS AND RECOGNITION

Manuel Valiente:
- Co-founder of the National Network of Brain Metastasis (RENACER), Spain.
- Finalist, Dr Josef Steiner Cancer Research Award, Switzerland.

ASPIRE Award (Accelerating Scientific Platforms and Innovative Research), The Mark Foundation for Cancer Research, USA.

Lluís Cerdón was awarded a “CNIO Friends” Postdoctoral Contract.

Lucía Zhu: “Best Talk Award”, UAM PhD Research Symposium in Health Sciences and Biomedicine; selected oral presentations at the 16th EANO Meeting (European Association of Neuro-Oncology) and the 3rd Annual SNO Conference on Brain Metastases (Society for Neuro-Oncology).

Neibla Priego: Invited talk at the 19th National Congress of the Italian Society for Neuroscience.

Lauritz Miarka: Selected oral presentation at the 3rd Annual SNO Conference on Brain Metastases (Society for Neuro-Oncology).