

Drug screening

Zhu et al. reported a medium-throughput drug-screening platform (METPlatform) based on organotypic cultures that allow evaluating inhibitors against [metastases](#) growing in situ. By applying this approach to the unmet clinical need of [brain metastases](#), they identified several vulnerabilities. Among them, a [blood-brain barrier](#) permeable [HSP90](#) inhibitor showed high potency against mouse and human brain metastases at clinically relevant stages of the disease, including a novel model of local relapse after neurosurgery. Furthermore, in situ proteomic analysis applied to metastases treated with the chaperone inhibitor uncovered a novel molecular program in brain metastasis, which includes biomarkers of poor prognosis and actionable mechanisms of resistance. The work validates METPlatform as a potent resource for metastasis research integrating [drug screening](#) and unbiased omic approaches that are compatible with human samples. Thus, this clinically relevant strategy is aimed to personalize the management of metastatic disease in the brain and elsewhere ¹⁾.

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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, Varešlija D, Cosgrove N, Couch FJ, Cussó L, Desco M, Mouron S, Quintela-Fandino M, Weller M, Pastor J, Valiente M. A clinically compatible drug-screening platform based on organotypic cultures identifies vulnerabilities to prevent and treat brain metastasis. *EMBO Mol Med*. 2022 Feb 17:e14552. doi: 10.15252/emmm.202114552. Epub ahead of print. PMID: 35174975.

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