

## The identification and characterization of breast cancer CTCs competent for brain metastasis

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Brain metastatic breast cancer (BMBC) is uniformly fatal and increasing in frequency. Despite its devastating outcome, mechanisms causing BMBC remain largely unknown. The mechanisms that implicate circulating tumor cells (CTCs) in metastatic disease, notably in BMBC, remain elusive. Here we characterize CTCs isolated from peripheral blood mononuclear cells (PBMCs) of patients with breast cancer, and also develop CTC lines from three of these patients. We identified an epithelial cell adhesion molecule (EpCAM)-negative CTC signature for brain metastasis selected markers (BMSM) that is HER2+/EGFR+/HPSE+/Notch1+. These CTCs-which are not captured by the CellSearch platform because of their EpCAM negativity-were analyzed for cell invasiveness and metastatic competency *in vivo*. CTC lines expressing the BMSM signature were highly invasive and capable of generating brain and lung metastases when xenografted in nude mice. Notably, increased brain metastatic capabilities, frequency, and quantitation were detected in EpCAM- CTCs overexpressing the BMSM signature. The presence of proteins of the BMSM CTC signature was also detected in the metastatic lesions of animals. Collectively, we provide evidence of isolation, characterization, and long-term culture of human breast cancer CTCs, leading to the description of a BMSM protein signature that is suggestive of metastatic competency to the brain.

### Biography

Dario Marchetti, tumor and molecular biologist, graduated from the Department of Molecular Biology, the University of Pavia, Italy in 1979. He worked as postdoctoral fellow at the University of Illinois, Chicago (1980-1982) and at the University of Texas Medical Branch-Galveston (Texas) (1984-1986). He then became a research scientist at the University of Texas Health Science Center-Houston (1986-1991), Research Associate and later Instructor at UT MD Anderson Cancer Center-Houston (1992-1999), Assistant Professor at UT-Houston (1999-2001), and Associate Professor and later Professor (with tenure) at LSU-Baton Rouge, Louisiana (2002-2007). He now works at Baylor College of Medicine in Houston as Professor in the Department of Pathology & Immunology with a joint faculty appointment in the Department of Molecular & Cellular Biology. He is also directs the Circulating Tumor Cell (CTC) Core, having conceptualized, developed, and established this facility at Baylor College of Medicine. Dr. Marchetti's bibliography include 145 publications of which 85 are in peer-reviewed journals in the neurosciences and oncology fields. He has received numerous awards and possesses an un-interrupted record of grant funding since 1991 from federal, state and private Agencies. He is a Reviewer of the most relevant journals in cancer research and also serves on grant reviewing panels of the National Institutes of Health of USA and Italy, the Department of Defense of the United States, and acts as selected grant Reviewer for several other national and international Agencies devoted to oncology research.

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