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VESSEL CO-OPTION IN GLIOBLASTOMA: SPY IT, FIND THE TARGET AND SHOOT

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Gliomas comprise heterogeneous malignant glial and stromal cells. While blood vessel co-option is a potential mechanism to escape anti-angiogenic therapy, the relevance of glial phenotype in this process is unclear. We show that Olig2+ oligodendrocyte precursor-like glioma cells invade by single-cell vessel co-option and preserve the blood-brain-barrier (BBB). Conversely, Olig2-negative glioma cells form dense perivascular collections, promote angiogenesis and BBB breakdown leading to innate immune cell activation. Experimentally, Olig2 promotes Wnt7b expression, a finding that correlates in human glioma profiling. Targeted Wnt7a/7b deletion or pharmacologic Wnt inhibition blocks Olig2+ glioma single-cell vessel co-option and enhances responses to temozolomide. Finally, Olig2 and Wnt7 become upregulated after anti-VEGF treatment in preclinical models and patients. Thus, glial-encoded pathways regulate distinct glioma vascular-microenvironmental interactions.

Biography

Giorgio Seano is currently the Head of the Tumor Microenvironment Lab in Institute Curie Research Center, Orsay-Paris (France). He received his PhD in Complex Systems in Life Science in 2010 from University of Turin, Italy. During his PhD training and a Postdoctoral period in Italy, he investigated tumor angiogenesis and integrins and provided the first evidence of a new sub-cellular structure, the endothelial podosome rosette that controls blood vessel branching during sprouting angiogenesis. In 2012, he joined the Laboratory of Dr Rakesh K Jain in Harvard Medical School (Boston) and focused his research on tumor microenvironment, brain tumors and intravital microscopy. Specifically, he intravitally imaged and targeted vessel co-option in glioblastoma. In 2017, he was selected as a Junior Group Leader in Institute Curie and he is now setting up his new laboratory.

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