**Title:**
Personalized Hybrid Nanocarriers for Targeted Glioblastoma Therapy

**Abstract:**
In the framework of the AIRC-funded CyberNano project, we developed an innovative, patient-personalized nanomedical platform for the treatment of glioblastoma (GBM). Leveraging patient-derived GBM cells, we established primary cultures and 3D organoids, enabling the generation of tailored cell membrane-coated magnetic nanovectors (CDMNVs) loaded with the chemotherapy drug regorafenib. These nanovectors demonstrated selective targeting *via* homotypic adhesion, effective blood-brain barrier (BBB) crossing, and magnetic hyperthermia-induced drug release. *In vitro* experiments showed significant uptake by GBM cells, reduced cell viability under magnetic stimulation, and apoptosis induction, confirmed by caspase-8 activation and lysosomal membrane permeabilization. Additionally, magnetic nanovectors were shown to modulate microglia toward a tumor-suppressive M1 phenotype, offering a novel immunotherapeutic strategy. *An ex ovo* quail embryo model validated CDMNV biodistribution and targeting efficiency, with internalization nearly doubling that of uncoated controls. CyberNano effectively demonstrated the feasibility of combining nanotechnology, magnetic control, and personalized medicine for non-invasive, targeted GBM therapy.

**Short bio:**

Gianni Ciofani is Senior Researcher Tenured at the *Istituto Italiano di Tecnologia* -Italian Institute of Technology, IIT- (Pontedera, Italy; since 2019), where he is Principal Investigator of the Smart Bio-Interfaces Research Unit (since 2017) and Coordinator of the Center for Materials Interfaces (since 2021). He has been Associate Professor at the Polytechnic University of Torino (Torino, Italy; 2015-2019) and Visiting Professor at Waseda University (Tokyo, Japan; 2021) and at the Pontifical Catholic University of Rio de Janeiro (Rio de Janeiro, Brazil; 2024). His main research interests concern smart nanomaterials for nanomedicine, microphysiological systems, and nanomedicine in altered gravity conditions. He is coordinator or unit leader of several projects (about 6.5 MEur granted): in particular, he was awarded a Starting Grant and three Proof-of-Concept Grants by the European Research Council (ERC). Thanks to grants from the Italian Space Agency and the European Space Agency, he had the opportunity to carry out four experimental campaigns onboard the International Space Station. In 2018, his real-scale model of the blood-brain barrier was highlighted in the Annual Report on the ERC Activities and Achievements.

He is co-founder (2022) and Scientific Advisor of “Kidaria Bioscience *SRL*”, an IIT spin-off company dedicated to the preparation and characterization of cosmetic and nutraceutical products based on natural-derived active ingredients. He is also co-founder (2021) and member of the executive committee of “ERC in Italy *APS*”, a non-profit association of ERC awardees born to promote fundamental and frontier research in Italy.

Gianni Ciofani is Knight of the Order of Merit of the Italian Republic, appointed by the President of the Italian Republic on December 27th, 2022.