

Principal Investigator	TIBERI LUCA
Institute of Affiliation	Università degli Studi di Trento
Title of the proposed project:	CAR-T Therapy for Glioblastoma
Short description of the project	<p>Background & Hypothesis Glioblastoma (GBM) is a highly aggressive adult brain cancer with a median survival of just 15 months. Current treatments offer limited efficacy. While CAR-T cell therapy shows promise, traditional preclinical mouse models fail to accurately replicate human tumor heterogeneity and immunosuppression. Patient-derived organoids (PDOs) serve as faithful 3D human tissue models. We hypothesize that implementing CAR-T therapy in GBM PDOs will significantly accelerate the development of effective clinical treatments. Core Aims Test Efficacy & Identify Antigens: Evaluate CAR-T cell therapy on deeply characterized GBM organoids to discover novel tumor antigens. Analyze the Microenvironment: Use a co-culture system and spatial transcriptomics to track CAR-T and tumor interactions over multiple timepoints, uncovering why certain immune cells become inactivated or "switched off." Bridge the Translational Gap: Create a more effective immunotherapeutic framework to successfully transition preclinical success into clinical applications for adult glioblastoma. Impact on Cancer With a 5-year survival rate under 5%, GBM urgently requires innovative intervention. Combining immunotherapy with PDOs allows researchers to address complex inter- and intra-tumoral heterogeneity in a human-recapitulating asset. Ultimately, this project is a pivotal step toward advancing personalized cancer medicine.</p>
Main research area for the project	Cancer Biology
5 keywords for the project	Drug screening - Mouse models - Medulloblastoma - Oncogenes - Organoids

LAB INFO	
Main topic/s of the lab	Brain Cancer
Short description of the lab activity	<p>Defeating childhood and adult brain cancers remains one of the greatest medical challenges of our time. Despite differences in biological mechanisms and sites of onset, these cancers share a common trait: genetic alterations that disrupt cell cycle regulation, leading to an imbalance between proliferation, differentiation, and cell death. The urgency of this challenge, combined with limited treatment options and poor patient prognosis, drives the research of our team. By integrating in vivo models with well-established brain organoid cultures, we accurately replicate both physiological brain development and the pathological mechanisms of tumor formation. Additionally,</p>

	cutting-edge bioengineering techniques and next-generation organoid models allow us to better mimic patient-specific disease conditions, increasing the precision and clinical relevance of our studies. Our ultimate goal is to uncover the biological mechanisms underlying brain cancers and develop novel therapeutic strategies that improve survival and outcomes for both pediatric and adult patients.
Recent bibliography	Notch1 switches progenitor competence in inducing medulloblastoma. SCI ADV 2021 Jun; 7: A slow-cycling/quiescent cells subpopulation is involved in glioma invasiveness. NAT COMMUN 2022 Aug; 13: 4767 Patient- and xenograft-derived organoids recapitulate pediatric brain tumor features and patient treatments. EMBO MOL MED 2023 Dec; 15: e18199 Medulloblastoma and high-grade glioma organoids for drug screening, lineage tracing, co-culture and in vivo assay. Nat Protoc 2023 Jul; 18: 2143 Modeling pediatric low-grade glioma heterogeneity using human forebrain organoids. MOL CANCER 2026 Apr; 25:
Group composition	Luca Tiberi, PI Matteo Giancesello, postdoctoral fellow Valerio Mignucci, postdoctoral fellow Cosimo Sabino, PhD Student Gloria Leva, PhD Student Lucrezia Ciccone, PhD Student Federica Ressa, PhD Student
Institutional page link	https://www.cibio.unitn.it/495/armenise-harvard-laboratory-of-brain-disorders-and-cancer
Lab website link	https://armeniseharvard.org/scientists/luca-tiberi/
Social media link	https://x.com/LucaTiberi_lab