European School of Molecular Medicine

2026 spring call PhD selections

AVAILABLE POSITIONS

| Principal Investigator | UGO CAVALLARO |
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| **Institute of Affiliation** | IEO |

| PROJECT INFO | |
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| Title of the proposed project: | A systems-level approach to unravel the crosstalk between tumor microenvironment and ovarian cancer stem cells |
| Short description of the project | Ovarian carcinoma (OC) remains an unmet need in clinical oncology due to the high frequency of tumor recurrence and the poor response to treatment. The subpopulation of ovarian cancer stem cells (OCSC) is thought to play a pivotal role in tumor relapse after surgery and chemotherapy as well as in the establishment of chemoresistance. Yet, the molecular and functional traits of OCSC remain largely elusive, and even less knowledge is available on the crosstalk of these cells with the peritoneal microenvironment, which is the main site of OC dissemination.<br>The student will leverage a platform of patient-derived organotypic co-culture systems to explore the influence that the peritoneal tumor microenvironment (TME) exerts on different biological aspects of OCSC. In particular, the project aims at 1) defining the mechanisms of TME-induced quiescence of OCSC; 2) assessing quiescence inhibition as a strategy to overcome chemoresistance; 3) profiling the effect of TME on OCSC at single-cell resolution.<br>The PhD project will entail a wide spectrum of technologies, including patient-derived organotypic modeling, single-cell sequencing associated to bioinformatics, flow cytometry, pharmacological intervention, etc.<br>Overall, the project is expected to provide novel insights into the role of the TME in the pathophysiological role of OCSC in tumor progression and drug resistance, with a potential impact on the design of innovative therapeutic approaches for such a devastating disease. |
| Main research area for the project | Cancer Biology |
| Second research area for the project | Molecular and Cellular Biology |
| 3 key words for the project | Ovarian cancer, tumor microenvironment, cancer stem cells |

| LAB INFO | |
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| Main topic/s of the lab | Molecular oncology of ovarian cancer; Pathophysiology of ovarian cancer stem cells; Tumor/microenvironment crosstalk. |
| Short description of the lab activity | The Cavallaro lab has a long-standing interest in ovarian cancer (OC), with the ultimate objectives of unraveling the biological mechanisms that drive the aggressiveness of the disease and identifying vulnerabilities that could open new treatment approaches. The lab is pursuing such objectives through two main research lines. |

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| | 1) Ovarian cancer stem cells (OCSC). OCSC have emerged as causal factors in OC progression, fueling tumor initiation, dissemination, relapse and therapy resistance. The lab is applying multi-omics strategies to investigate the molecular makeup of OCSC and a broad spectrum of molecular/cell biology methods to dissect their functional features.<br>2) Tumor/microenvironment crosstalk. The tumor microenvironment (TME) of OC modulates most aspects of neoplastic behavior, while at the same time cancer cells "educate" the TME towards a pro-tumoral niche. Yet, the molecular players and pathways that drive or are modulated by this interplay remain largely uncharacterized, and this is particularly true for the crosstalk of TME with OCSC. We have set up in vitro and in vivo models to mimic this crosstalk, and are currently applying them to investigate the interaction of OCSC with the peritoneal TME as well as with the vascular compartment. In this regard both systems-level (omics) and high-resolution studies are being carried out to identify and validate the determinants of the OCSC/TME interplay.<br>For the implementation of these studies, the Cavallaro lab capitalizes on a wide array of experimental settings, ranging from cell lines to patient-derived models (primary cells, organotypic co-cultures, mouse xenografts). The latter are routinely established thanks to the long-standing collaboration with the clinical staff of the Program of Gynecology at IEO (which includes the lab itself). This enables the group to address outstanding scientific and clinical questions in disease-relevant settings, thus increasing the translational value and the applicability of the results. |
| Recent bibliography | 1. Franciosa G, Nieddu V, Battistini C, Caffarini M, Lupia M, Colombo N, Fusco N, Olsen JV, and **Cavallaro U.** (2025) Quantitative proteomics and phosphoproteomics analysis of patient-derived ovarian cancer stem cells. *Mol Cell Proteomics*, 24(5):100965. doi: 10.1016/j.mcpro.2025.100965.<br>2. Battistini C, Kenny HA, Nieddu V, Melocchi V, Decio A, Gatto A, Ghioni M, Porta FM, Giavazzi R, Colombo N, Bianchi F, Lengyel E, and **Cavallaro U.** (2024) Tumor microenvironment-induced FOXM1 regulates ovarian cancer stemness. *Cell Death Dis*, doi: 10.1038/s41419-024-06767-7.<br>3. Nieddu, V., Melocchi V., Battistini C., Franciosa G., Lupia M., Stellato C., Bertalot G., Olsen J.V., Colombo N., Bianchi F., and **Cavallaro U.** (2023) Matrix Gla Protein drives stemness and tumor initiation in ovarian cancer. *Cell Death Dis*, 14:220. doi: 10.1038/s41419-023-05760-w.<br>4. Battistini C. and **Cavallaro U.** (2023). Patient-Derived In Vitro Models of Ovarian Cancer: Powerful Tools to Explore the Biology of the Disease and Develop Personalized Treatments. *Cancers*, 15:368. doi: 10.3390/cancers15020368.<br>5. Lupia M., Melocchi V., Bizzaro F., Lo Riso P., Dama E., Baronio M., Ranghiero A., Barberis M., Bernard L., Bertalot |

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| | G., Giavazzi R., Testa G., Bianchi F., and **Cavallaro U** (2022). Integrated molecular profiling of patient-derived ovarian cancer models identifies clinically relevant signatures and tumor vulnerabilities. *Int J Cancer*, 151(2):240-254. doi: 10.1002/ijc.33983. |
| Group composition | 12 (1 PI; 1 staff scientist; 3 postdocs; 3 PhD students; 1 junior fellow; 1 junior bioinformatician; 2 research technicians) |
| Institutional page link | https://www.research.ieo.it/research-and-technology/principal-investigators/unit-of-gynecological-oncology-research/ |
| Social media links | https://www.linkedin.com/in/ugo-cavallaro-87454524/ |