European School of Molecular Medicine

RESEARCH ACTIVITY SHEET

2025 PhD selections

YOUR DETAILS

* Name & Surname: Ugo Cavallaro

* Affiliation IEO

PHD PROJECT DETAILS

* Title of the proposed project

Crosstalk between tumor vasculature and ovarian cancer stem cells: the new role of L1CAM

* Short description of the project (up to 300 words)

Ovarian cancer stem cells (OCSC) account for dissemination, recurrence and therapy resistance in OC patient, thus emerging as main players in the high lethality rate of this neoplasm. Yet, very limited knowledge is available on the molecular and functional traits of this cell subpopulation. In particular, no or very little information is available on the regulation of OCSC pathophysiology by the tumor microenvironment (TME), especially the vascular compartment. We have previously reported a novel, soluble isoform of the L1 cell adhesion molecule (L1CAM), termed L1-DTM, which is specifically expressed and released by OC-associated vasculature (Angiolini et al, 2019). More recent data revealed that vessel-derived L1-DTM acts as an angiocrine factor on OCSC promoting their stem-like phenotype and inducing massive changes in their transcriptional activity. Such changes entail the induction of a pro-inflammatory phenotype, suggesting a role for L1-DTM in OCSC-driven regulation o tumor immunity.

The PhD project will aim at investigating the molecular and cellular mechanisms that underlie the stemness-inducing function of vascular L1-DTM. In particular, the student will apply a wide range of in vitro and in vivo technologies to dissect the role of L1-DTM in OCSC. These will include mass spectrometry-based interactomics coupled to subcellular fractionation (to define L1-DTM partners in different cell compartments), high-resolution imaging (to monitor L-DTM trafficking), biochemical assays to dissect intracellular signaling, OCSC-driven tumorigenesis in mice, etc. A parallel set of in vitro and in vivo methodologies will help to elucidate the impact of L1-DTM on the OC-associated immune response. Finally, based on preliminary observations, the possibility that L1-DTM modulates tumor response to specific treatments will also be assessed.

In vitro, ex vivo and in vivo models will support this research, including co-cultures in microfluidic chips, patient-derived tumor explants and mouse models of ovarian cancer, thus increasing the chance to gain relevant insights and define new vulnerabilities for such a devastating disease.

* Indicate the main research area for the project described above Cancer Biology

If needed indicate a second research area for the project described above Molecular & Cellular Biology

* Provide up to 3 key words for project:

Ovarian cancer; cancer stem cells; tumor microenvironment

YOUR LABORATORY ACTIVITIES DETAILS

* 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 (up to 500 words)

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.

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.

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.

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 (max 5 references)

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.
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.
3. Lupia M., Melocchi V., Bizzaro F., Lo Riso P., Dama E., Baronio M., Ranghiero A., Barberis M., Bernard L., Bertalot 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.
4. Giordano M., Decio A., Battistini C., Baronio M., Bianchi F., Villa A., Bertalot G., Freddi S., Lupia M., Jodice M.G., Ubezio P., Colombo N., Giavazzi R., and **Cavallaro U**. (2021) L1CAM promotes ovarian cancer stemness and tumor initiation via FGFR1/SRC/STAT3 signaling. *J Exp Clin Cancer Res* 40(1):319. doi: 10.1186/s13046-021-02117-z.
5. Angiolini F., Belloni E., Giordano M., Campioni M., Forneris F., Paronetto M.P., Lupia M., Brandas C., Pradella D., Di Matteo A., Giampietro C., Jodice, G., Luise C., Bertalot G., Freddi S., Malinverno M., Irimia M., Moulton J., Summerton J., Chiapparino A., Ghilardi C., Giavazzi R., Nyqvist D., Gabellini D., Dejana E., **Cavallaro U.***, and Ghigna C.* (2019) A Novel L1CAM Isoform with Angiogenic Activity Generated by NOVA2-mediated Alternative Splicing. *eLife*, 8. pii: e44305. *co-senior authorship

* Group composition: total members, and roles distribution (PhD, postdoc, technician, etc.)

Total members: 11 (4 postdocs; 1 PhD student; 3 junior fellows; 1 bioinformatician; 2 research technicians)

Institutional page link

https://www.research.ieo.it/research-and-technology/principal-investigators/unit-of-gynecological-oncology-research/

Lab website link, if any

N.A.

Social media links, if any

https://www.linkedin.com/in/ugo-cavallaro-87454524/

If you prepare a video to promote your lab/project, please include the link below

N.A.