PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
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Principal Investigator	Tamagnone Luca
Hosting institution	Università Cattolica del Sacro Cuore
Proposal title	Novel molecular mechanisms controlling metastatic ovarian cancer cells
Keywords	Cell signaling; Ovarian ca.; Metastasis; Spheroids/3D cultures; Liquid biopsy
PhD project description	High-Grade Serous Ovarian Carcinoma (HGSOC) is the most lethal malignancy in women. Current therapeutic options are limited, due to lack of specific molecular targets. Moreover, biomarkers predicting drug response are missing or unsatisfactory. There is a need for primary HGSOC models, enabling more reliable and significant studies on the mechanisms sustaining cancer cell renewal, invasiveness and metastatic dissemination, as well as drug-responsiveness. Liquid biopsies of the ascitic fluid of HGSOC patients could provide valuable information by enabling genomic and transcriptomic analyses of patient-derived disseminated cancer cells, tumor-associated inflammatory cells and extracellular vesicles. Furthermore, the host lab has established a protocol for isolating and propagating in culture self-renewing patient-derived HGSOC cells that can provide new significant experimental models to study molecular mechanisms controlling cancer cell behavior, therapeutic response, peritoneal nesting/invasion, and metastatic dissemination in murine preclinical models. A Physician Scientist aiming to accomplish her/his PhD in our labs at the Università Cattolica/Policlinico Gemelli-IRCCS in Rome will be deeply involved in this project at the crossroads between patients and molecular research. We are currently applying Next Generation Sequencing (NGS) to study the genomic and transcriptomic profile of cancer cells, as well as extracellular vesicles, retrieved from a growing collection of (over 100) ascitic fluid biopsies from advanced HGSOC patients with annotated clinical follow-up. We will furthermore perform single-cell analysis of a subset of these samples, to investigate cellular heterogeneity and potentially identify molecular subtypes of HGSOC cells (or peculiar inflammatory cell profiles). The prospective PhD candidate will be involved in these analyses, and in the functional validation of promising novel candidate therapeutic targets and biomarkers predicting drug responsiveness. To this end, the new lab member will be allowed to exploit patient-derived HGSOC 3D-models in culture and avatar xenografts in vivo.
Main topics of the lab	Molecular mechanisms controlling cancer progression and metastasis
Short description of the lab activity	Our lab studies novel molecular mechanisms controlling tumor progression. In previous years, the lab has discovered several novel signaling cascades active in the tumor microenvironment and

	controlling cancer cell behavior, angiogenesis, tumor inflammation, drug responsiveness and metastasis. In particular, the lab is at the forefront of research in semaphorin/plexin field at the international level. By exploiting experimental models in culture and in vivo, we previously shown that semaphorin signals regulate multiple steps of tumor progression, validating their relevance as targets for molecular therapy. Luca Tamagnone currently holds an H-index of 60, and his publications in peer-reviewed journals have so far gained over 16,000 citations (Google Scholar). In these years, he has supervised 16 PhD students and 19 Post-doctoral fellows in cancer biology field; at least six of these former trainees have become independent scientists in foreign institutions (in USA, UK, France, Belgium, Sweden, Spain). The Tamagnone lab is an international context, including foreign students and post-docs, and English is the official language for scientific reports and meetings. The laboratories and study rooms have been completely refurbished. The lab has access to state-of-the-art facilities at the Gemelli Science and Technology Park (https://gstep.policlinicogemelli.it/#/VetrinaFacilities). Notably, the presence of other groups, active in neuroscience and aging research, in the same university division led by Luca Tamagnone, ensures methodological cross-fertilization and scientific exchange in molecular medicine investigation. He is currently also the director of the Liquid Biopsy Facility on the campus. In recent years, the lab has been leading four collaborative studies concerning the role of PlexinB2 in metastatic cancers of unknown primary (Brundu et al., 2023), a Sema6C-dependent pathway controlling cancer cell viability (Fard et al., 2023), the role of PlexinB1 in the regulation of immune response in breast cancer microenvironment (Franzolin et al, 2024), and Neuropilin1-dependent control of the cargo of exosomes released by cancer cells (Palazzo et al, 2025). In the last two years the lab has been focusing on ovarian cancer, in collaboration with the gynecological oncology department at the Policlinico Gemelli Research Hospital. A large collection of patient-derived HGSOC models were derived from ascitic fluid liquid biopsies, through an ongoing clinical trial.
Main research area	Cancer biology
Group composition	3 Postdocs 2 PhD students 2 undergraduate students 2 Technicians
Institutional page link	https://docenti.unicatt.it/ppd2/it/docenti/59412/luca-tamagnone/profilo
Lab website link	nan
Social media link	nan
Lab bibliography	Mutated axon guidance gene PLXNB2 sustains growth and invasiveness of stem cells isolated from cancers of unknown primary. Brundu S, Napolitano V, Franzolin G, Lo Cascio E, Mastrantonio R, Sardo G, Cascardi E, Verginelli F, Sarnataro S, Gambardella G, Pisacane A, Arcovito A, Boccaccio C, Comoglio PM, Giraudo E, Tamagnone L EMBO MOL MED 2023 Mar; 15: e16104