PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
promosso da: AIRC Fondazione CARIPLO | con il supporto di: SIBMM UNIVERSITÀ DEGLI STUDI DI MILANO

Principal Investigator	D'Incalci Maurizio
Hosting institution	Humanitas Mirasole S.p.A.
Proposal title	Analysis of DNA from cervical swabs for early detection of ovarian and p53-abnormal endometrial cancers
Keywords	Gene alteration/gain or loss; Diagnosis; Gynecological tumors; Retrospective studies
PhD project description	This project aims to validate and expand the EVA test, a novel molecular assay for early detection of ovarian cancer (OC) and p53-abnormal endometrial cancer (p53abn EC) through DNA analysis of cervical swabs. The test is based on the hypothesis that tumor DNA from ovarian surface, Fallopian tube, or endometrial tissues sheds into the cervical canal during early tumor progression, and could be detectable before blood biomarkers. Tumor DNA is identified by measuring genome-wide Copy Number Alterations (CNAs), indicative of chromosomal instability, using low-coverage whole genome sequencing. In a previous study (doi: 10.1126/scitranslmed.adi2556), we showed that Copy number Profile Abnormality (CPA) score, providing a quantitative determination of CNAs, can distinguish OC cases from controls with 75% sensitivity and 96% specificity, detecting tumor DNA up to 9 years before diagnosis. This project will validate the test's accuracy in high-grade serous OC and extend its evaluation to other OC histotypes and p53abn EC by examining archival cervical swabs from a large multicenter cohort, including age-matched healthy controls. It aims to optimize test cut-offs, explore clinical factors influencing accuracy, and assess test performance over time. Having already secured ethical approval and support from 23 Italian clinical centers, as well as a patient association, arranged for external management of the clinical study, and established a centralized database, the study now plans to select at least 320 OC cases, 200 p53abn EC cases, and 400 controls. This validation seeks to establish the EVA test as a sensitive, non-invasive screening tool for early diagnosis of gynecological cancers. The PhD Student will be based at Humanitas San Pio X Hospital, collaborating with the clinical team of the Gynaecological Oncology Unit for patient selection and sample collection, while performing molecular biology analyses in our laboratory. The Student will also contribute to data analysis, interpretation, reporting, and scientific publication.
Main topics of the lab	Translational genomics and molecular pharmacology
Short description of the lab activity	The Laboratory of Cancer Pharmacology, led by Maurizio D'Incalci, was established at Humanitas Research Hospital in 2021. The Laboratory is deeply committed to translational research, focusing on applying pharmacological and biological insights to advance the diagnosis and treatment of human malignancies. While the team has longstanding

	expertise in preclinical and clinical pharmacology, recent years have seen a growing emphasis on the molecular characterization of tumors. This shift began with the goal of identifying novel pharmacological targets during early tumor development and has since expanded to include the search for biomarkers useful for predicting and monitoring therapeutic responses. This work also supports the development of innovative diagnostic tools. Key research projects include: - Development of a non-invasive test for early detection of gynaecological cancers. - Development of agnostic liquid biopsy techniques to monitor therapeutic responses in solid tumors. - Identification of tumors exhibiting homologous recombination deficiency, a critical factor for targeted therapies. - Investigating the mechanism of action of alternating electric fields (TTFields) in mesothelioma treatment to optimize therapeutic efficacy. - Studying the tissue distribution of novel oncological drugs under development through advanced clinical pharmacology approaches. The research approach integrates genomics and transcriptomics analyses powered by sophisticated bioinformatics tools within the Unit of Molecular Pharmacology. Complementary in vitro pharmacological assays are performed by the Unit of Cellular Pharmacology. These efforts are supported by precise analytical techniques for measuring drug concentrations in biological samples within the Unit of Clinical Pharmacology. These studies are conducted in close collaboration with oncologists, radiation therapists, pathologists, and surgeons. In the Unit of Molecular Pharmacology, where the PhD student will be based, the primary experimental techniques include: Whole Genome Sequencing (WGS), targeted gene sequencing, RNA sequencing (RNA-seq), single-cell transcriptomics (scRNA-seq), microRNA analysis, and DNA methylation pattern analysis.
Main research area	Genomic Medicine
Group composition	Total lab members: 19 researchers Role distribution: - 1 Head of the Laboratory - 3 Heads of Units - 4 Experienced researchers: 2 biologists and 2 bioinformaticians - 1 Scientific coordinator - 2 Postdoctoral researchers: 1 biologist and 1 bioinformatician - 2 PhD students: 1 biologist and 1 bioinformatician - 4 Early-stage researchers: 4 biologists - 2 internship students
Institutional page link	https://www.humanitas-research.com/
Lab website link	https://www.humanitas-research.com/groups/maurizio-dincalci-group/
Social media link	https://www.linkedin.com/company/humanitas-research
Lab bibliography	Detection of TP53 Clonal Variants in Papanicolaou Test Samples Collected up to 6 Years Prior to High-Grade Serous Epithelial Ovarian Cancer Diagnosis. Paracchini L, Pesenti C, Delle Marchette M, Beltrame L, Bianchi T, Grassi T, Buda A, Landoni F, Ceppi L, Bosetti C, Paderno M, Adorni M, Vicini D, Perego P, Leone BE, D'Incalci M, Marchini S, Fruscio R JAMA NETW OPEN 2020 Jul; 3: e207566