PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
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2026 Physician Scientist Call

AVAILABLE POSITIONS

| Principal Investigator | DEMICHELIS FRANCESCA |
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| **Institute of Affiliation** | Università degli Studi di Trento |
| **Title of the proposed project:** | Functional and Liquid Biopsy Genomics to Characterize PARP Inhibitor Responses in Prostate Cancer |
| **Short description of the project** | Poly (ADP-ribose) polymerase inhibitors (PARPi) have received regulatory approval for the treatment of several malignancies, including prostate cancer (PCa), a leading cause of cancer-related death among men. Although PARPi demonstrated remarkable therapeutic potential for PCa, important limitations have emerged -including a response rate of about 50% in patients with BRCA1/2 alterations and a heterogenous sensitivity to PARPi among patients with defects in DNA Damage Response and Repair genes (DDR)- underscoring the need for a better understanding of the molecular features of PARPi-responders and non-responders and for refined patient selection strategies. Building on yet unexplored dependencies nominated by in house CRISPR/Cas9 screens, which recently identified LIG1 as potential biomarker for PARPi response (Fracassi et al 2025), the project will investigate novel genetic dependencies that modulate PARPi treatment efficacy. In parallel, plasma samples from PARPi-treated PCa patients collected within the COROS observational multi-institutional trial (NCT06783127; access through the IG29370 to F.D.) will be analyzed to delineate the molecular underpinnings of treatment response and resistance. Through an iterative framework, candidate genes from functional genomic screens will be investigated in patient-derived molecular data and clinically informed findings will be integrated with screening results and validated and characterized in vitro. The activities related to the project include engineering of PCa cell lines using CRISPR/Cas and RNA interference, assessment of cell viability and cell death with metabolic assays and flow cytometry, isolation and sequencing of cell free DNA, interrogation of extracellular vesicle cargo (RNA and selected proteins), and integration of molecular findings with clinical variables. |
| **Main research area for the project** | Genomic medicine |
| **5 key words for the project** | Prostate ca., BRCA, Response and/or resistance to therapy, Liquid biopsy |

| LAB INFO | |
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| **Main topic/s of the lab** | The Computational and Functional Oncology laboratory at the University of Trento focuses on identifying biomarkers of tumor progression and the molecular characterization of lethal subtypes of genitourinary cancers. |
| **Short description of the lab activity** | Building over years of interdisciplinary work at the intersection of medicine, biology, and quantitative sciences, the laboratory integrates computational and experimental expertise in translational research projects, laser-focused on open clinical questions. The translational research focuses on three main |

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| | areas, which share analytical challenges and opportunities: • The exploitation of synthetic lethality (SL) for cancer treatment and SL biomarker identification, to be nominated through combined approaches such as allele-specific mining of multi-layer human data, drug/CRISPR screening, and/or rational combinations. • The role of cancer patient intra- and inter-tumor heterogeneity in treatment response, which we pursue by deeply characterizing - through dedicated computational approaches - patients' tissue and liquid biopsies to inform on tumor dynamics under treatment pressure; • The role of inherited (genetic)-somatic interactions in carcinogenesis. Relevant to this program, long-standing collaborations exist with international and national clinical scientists, including Prof. Himisha Beltran at the Dana Farber Cancer Institute/Harvard University in Boston, Prof. Gert Attard at University College London in the UK, Dr. Umberto Basso at IOV in Padova, Dr. Nicole Brighi at IRST in Meldola (Forlì), Dr. Consuelo Buttigliero at San Luigi Hospital in Orbassano (Torino), Prof. Orazio Caffo at Trento Hospital, Prof. Alfredo Berruti at Brescia Hospital, and Prof. Vincenza Conteduca at Foggia Hospital. |
| **Recent bibliography** | - Germline-somatic liaison dictates cancer subtype via de novo steroid biosynthesis. CANCER DISCOV 2025 Oct; 15: 2166<br>- Liquid Biopsy Identifies Taxane Resistance and Clonal Selection in Castration-Resistant Prostate Cancer. Clin Cancer Res 2025 Dec; 31: 4985<br>- CRISPR/Cas9 screens identify LIG1 as a sensitizer of PARP inhibitors in castration-resistant prostate cancer. J Clin Invest 2024 Dec; 135:<br>- Combined ctDNA and serum PSA for dynamic monitoring of metastatic prostate cancer starting first-line treatment: a prospective national cohort study. Nature Cancer 2026 Jun; 7: 915<br>- Noninvasive Detection of Neuroendocrine Prostate Cancer through Targeted Cell-free DNA Methylation. Cancer Discov 2024 Mar; 14: 424 |
| **Group composition** | The size of the laboratory varies between 14-16 members, including biologists, biotechnologists, computer scientists, and physicists. Currently, the team includes 14 members, 10 of which funded through competitive grants. Six are involved in experimental work (1 instructor, 2 post-docs, 2 PhD students, 1 technician), seven are involved in computational work (1 instructor, 3 post-docs, 1 PhD students, 2 Master students), and one member, with background in molecular biology and biobanking, acts as senior project manager while overseeing the liquid biopsy workflow and ethics protocols. |
| **Institutional page link** | https://www.cibio.unitn.it/83/laboratory-of-computational-and-functional-oncology |