

Principal Investigator	OTTINI LAURA
Institute of Affiliation	Università degli Studi di Roma "La Sapienza"
Title of the proposed project:	Dissecting Male Breast Cancer: Inherited Risk, Tumor Biology and Multi-Omics Integration for Clinical Translation
Short description of the project	<p>Male breast cancer is a rare, biologically and clinically under-characterized disease. Despite its rarity, it represents an important unmet clinical need as outcomes are often poorer than in female breast cancer, and clinical management is still largely extrapolated from female disease, highlighting the need for more appropriate male-specific strategies. This PhD project will use integrative multi-omics approaches to identify inherited risk factors and tumor molecular features associated with susceptibility, heterogeneity and clinical outcome. The project builds on the first Italian multicenter study on male breast cancer, coordinated by our group, providing a unique national framework and well-characterized clinical-biological resources for the proposed analyses. The candidate will combine germline genetic analyses with tumor profiling, including genomic, transcriptomic, epigenomic/methylomic and spatial omics data, integrated with clinical-pathological and epidemiological information. Particular focus will be on BRCA1/2 and other cancer-predisposition genes, sex-related differences in cancer risk, and the relationship between inherited predisposition and tumor biology. The PhD student will contribute to sample and data collection, molecular analyses, bioinformatic processing, statistical modeling, multi-omics integration and validation of candidate biomarkers. The project is innovative, competitive and feasible within four years, offering training in both wet-lab and dry-lab approaches. By focusing on a rare cancer with unmet biological and clinical questions, the project aims to generate new knowledge and support the development of sex-specific strategies for risk prediction, prevention, early diagnosis, precision oncology and tailored clinical management in breast cancer. Research activities will be carried out at the Department of Molecular Medicine, Sapienza University of Rome. The Department, recognized as a "Dipartimento Universitario di Eccellenza 2023-2027", provides all the necessary training resources and expertise in both experimental and computational aspects of translational cancer research. Clinical and translational research-related activities, where applicable and subject to appropriate agreement, may be carried out at Sapienza-associated clinical facilities.</p>
Main research area for the project	Genomic Medicine
5 keywords for the project	Breast ca. – BRCA – Biomarkers - Next generation sequencing - Patient risk stratification

LAB INFO	
Main topic/s of the lab	Cancer genetics and molecular epidemiology of solid tumors, with a focus on sex-related differences in cancer risk and multi-omics profiling of male breast cancer and BRCA-associated cancers.
Short description of the lab activity	<p>The Molecular Epidemiology of Cancer (MEC) Laboratory, LabOTTINI, at the Department of Molecular Medicine, Sapienza University of Rome, investigates inherited genetic variation and tumor molecular mechanisms that contribute to susceptibility, development and clinical heterogeneity of solid tumors. The laboratory combines molecular epidemiology, cancer genetics and genomics, and advanced omics technologies to improve cancer risk assessment, identify and validate clinically relevant biomarkers, and inform personalized prevention, surveillance and treatment strategies. Research focuses on breast, ovarian, prostate, pancreatic and other solid tumors, with a strong emphasis on male breast cancer and sex-related differences in cancer risk. A core activity is the genomic screening of cancer patients using next-generation sequencing (NGS), including targeted gene panels, whole-exome sequencing and whole-genome sequencing, to identify pathogenic alterations, including single nucleotide variants (SNVs) and copy number variants (CNVs) in established and candidate cancer susceptibility genes. The laboratory also investigates the contribution of common genetic variants to cancer risk through genome-wide association studies (GWAS), conducted within large collaborative consortia and studies such as BCAC, CIMBA, ENIGMA, MERGE and CONFLUENCE. These data are used to develop and validate polygenic risk score (PRS) models designed to improve risk stratification, particularly when integrated with family history, epidemiological exposures and clinical-pathological information. In addition, the laboratory characterizes the cancer spectrum and estimates gene-specific risks associated with major susceptibility genes, including BRCA1, BRCA2 and PALB2. This work aims to provide evidence for tailored genetic counseling and for more appropriate prevention and surveillance strategies in high-risk individuals and families. In parallel, the group performs tumor profiling to discover biomarkers with clinical relevance and to define genetic, transcriptomic and epigenetic signatures through genomic, methylation, miRNA and bulk RNA-seq analyses. These approaches are complemented by single-cell RNA-seq, spatial omics and integrated bioinformatic workflows to explore tumor heterogeneity, somatic alterations, inherited predisposition and features of the tumor microenvironment, with a particular focus on immune phenotypes. Current projects address the genetics, biology and clinical behavior of male breast cancer, BRCA2-associated tumors and cancer risk prediction in the Italian population. By integrating population-</p>

	<p>based resources, well-annotated clinical-pathological datasets and complementary wet-lab and dry-lab expertise, LabOTTINI aims to generate actionable biological and clinical knowledge that can support precision prevention, sex-specific risk assessment and precision oncology.</p>
Recent bibliography	<p>A case-only study to identify genetic modifiers of breast cancer risk for BRCA1/BRCA2 mutation carriers. NAT COMMUN 2021 Feb; 12: 1078</p> <p>Breast and Prostate Cancer Risks for Male BRCA1 and BRCA2 Pathogenic Variant Carriers Using Polygenic Risk Scores. JNCI-J NATL CANCER I 2022 Jan; 114: 109</p> <p>Cancer Risks Associated With BRCA1 and BRCA2 Pathogenic Variants. J CLIN ONCOL 2022 May; 40: 1529</p> <p>Male breast cancer risk associated with pathogenic variants in genes other than BRCA1/2: an Italian case-control study. EUR J CANCER 2023 Jul; 188: 183</p> <p>Transcriptomic deconvolution reveals prognostic immune signatures and immunotherapy-responsive subtypes in male breast cancer. BREAST CANCER RES 2026 Apr; 28:</p>
Group composition	<p>The group includes 14 members: one Full Professor and Head of the laboratory, one Associate Professor, two postdoctoral fellows, three PhD students, two research fellows, and five students (four Master's students and one Bachelor's student). The team is organized across integrated wet-lab and dry-lab activities.</p>
Institutional page link	<p>https://research.uniroma1.it/molecular-epidemiology-cancer-mec</p>
Lab website link	<p>https://sites.google.com/uniroma1.it/labottini</p>
Social media link	<p>https://it.linkedin.com/in/laura-ottini-b741b2b3</p>