Experimental Pharmacology

Team composition

Team Leader: Amalia Azzariti, PhD- Researcher – Laboratorio di Farmacologia Sperimentale- IRCCS Bari

Team members IRCCS "Giovanni Paolo II": Letizia Porcelli, PhD - Researcher – Laboratorio di Farmacologia Sperimentale; Simona Serratì, PhD - Researcher – Laboratorio di Farmacologia Sperimentale; Roberta Di Fonte, MS - Researcher – Laboratorio di Farmacologia Sperimentale; Rossella Fasano, MS - Fellow – Laboratorio di Farmacologia Sperimentale; Tania Rafaschieri, MS - Fellow – Laboratorio di Farmacologia Sperimentale

Background

The Experimental Pharmacology team will develop projects related to three macro-areas that specifically concern i) the search for new biomarkers for diagnosis, prognosis and prediction, ii) the experimentation of innovative pharmacological treatments and drug discovery and iii) drug delivery.

In the first macro-area, the studies are aimed at identifying biomarkers (extracellular vesicles-EVs, immunity cells, cytokines, ncRNA) present in biological fluids (blood, saliva, urine, pleural fluid, ascites, peritoneal washing fluid, etc.) which may have a role in early diagnosis or which are indicative of tumor progression (prognostics) or which allow to predict the response or resistance to anticancer drugs. In recent years, we have focused on determining the predictive role of response to immunotherapy, with anti-PD1, of some subpopulations of EVs that have also been shown to be directly involved in determining resistance to this therapeutic approach] and on the possible diagnostic/prognostic/predictive role of some lncRNAs present in the urine of patients with prostate cancer.

In the second macro-area, innovative combinations of drugs are developed aimed at optimizing treatments and overcoming drug resistance through either the experimentation of new or pre-existing active compounds as anticancer drugs (drug discovery and drug repurposing) and the combination of different categories of drugs available for the disease (chemotherapy, molecularly targeted drugs, immunotherapy and radiotherapy). This type of study involves the generation of cell models representative of various tumor pathologies, such as primary cell lines, short term-culture or patient-derived organoids (PDOs). In recent years, clinical and preclinical pharmacology studies have focused on the development of ex-vivo models of cancer in which it is possible to test the response to pharmacological treatment and to investigate the role of the tumor microenvironment in the response to drugs, with the aim to quickly predict which drugs or drug combinations can give an effective response (Personalized Medicine). Three-dimensional (3D) cell cultures are an alternative and/or parallel approach to 2D; they are therefore the link between traditional cell culture and in vivo models. The tumor PDOs represent a personal and dynamic model that allows to conduct investigations that were previously impossible to carry out at the individual patient level such as a) the characterization of specific molecular traits, b) the analysis of the response to chemotherapeutic agents, targeted drugs and newly synthesised compounds, c) the identification of biological therapies against specific tumor targets and the characterization of the mechanism of action, d) the identification of new therapeutic targets, e) the identification of biomarkers which allow to develop new targeted drugs and to follow the progression of the disease and the response to therapies, and f) to build an information database that will associate gene expression profiles with drug response.

The third macro-area includes the studies with the highest technological impact such as the generation of new nanosystems for drug deliveryand omic approaches for tumor neoantigens discovery.

Team networks:

VU University Medical Center, Amsterdam, Netherlands: dr. Elisa Giovannetti, University of Calgary, Calgary, Canada: dr. Afshin Derakhshani, IRCCS Istituto Nazionale Tumori, Milan, Italy: dr. Paola Perego, University of Florence, Florence, Italy: dr. Anna Laurenzana, University of Bari, Bari, Italy: dr. Rosa M. Iacobazzi, Prof. Nunzio Denora, Prof. Gabriella Guida, dr. Ciro L. Pierri, dr. Mariateresa Volpicella, University of Messina, Messina, Italy: Prof. Nicola Silvestris, CNR Nanotec, Lecce, Italy: dr. Loretta Del Mercato, dr. Francesca Gervasio, dr. Alessandro Polini, dr. Serena Chiriacò

Funded Projects

- RC 2022: Identificazione di fattori circolanti per la diagnosi, prognosi e/o predizione della risposta alle terapie in patologie tumorali solide. (PI: dott.ssa A. Azzariti)
- RC 2022: Messa a punto di modelli cellulari 3D di patologie tumorali solide (patient-derived organoids-PDOs, short term culture) e loro validazione per lo studio della predizione della risposta ai farmaci e per lo screening di nuovi principi attivi o combinazione di farmaci (PI: dott.ssa A. Azzariti)
- RC 2022: Ottimizzazione di trattamenti farmacologici mediante creazione di nanodelivery system per il rilascio selettivo di farmaci nei siti tumorali e analisi di metaboliti cellulari (metabolomica) e di farmaci e loro metaboliti nei fluidi biologici (PI: dott.ssa A. Azzariti)
- RC 2022: Studio delle caratteristiche cliniche, patologiche e bio-immunologiche di pazienti affetti da carcinoma cutaneo a cellule squamose e ricerca dei fattori predittivi di risposta all'anti-PD1 Cemiplimab (PI: dott.ssa L. Porcelli)
- RC 2022: Studio dei meccanismi di risposta e resistenza ad immunoterapia e terapia target nel melanoma (PI: dott. M. Guida)
- RC 2022: Biomarcatori predittivi di risposta all'immunoterapia nel microcitoma polmonare (PI: dott. V. Longo)
- RC 2022: Trascrittomica a singola cellula e patomica nel carcinoma del colon (PI: dott.ssa S. De Summa)
- Progetto Regionale: TecnoMed – Tecnopolo per la Medicina di Precisione -WP2.2. Sviluppo di modelli ex-vivo di tumore predittivi della risposta a farmaci(Del. 914 del 31/10/2019)(PI: dott.ssa A. Azzariti)
- Progetto ACC di Rete: Medicina personalizzata: Allestimento di biobanche e di modelli colturali organotipici da pazienti con melanoma per l'identificazione di nuovi marcatori prognostici e la realizzazione di saggi predittivi della risposta del paziente alla terapia – Ricerca Corrente Reti (RCR).(Responsabile per l'Istituto: dott.ssa A. Azzariti)
- Progetto ACC-Rete AMORe: Task 3.6 Identification of molecular targets expressed in the tumour microenvironment of Melanoma and DLBCL (PI: M. Mazza (IRCCS-IRST)
- Progetto ERC: Sensing dell'eterogeneità delle interazioni tra cellule nei modelli tumorali 3D: verso la medicina di precisione — INTERCELLMED" (PI: dott.ssa Loretta Del Mercato – CNR Nanotec – Lecce)
- MFAG 2019: Nano patterned metastatic melanoma for quantifying metabolic changes in mediated drug resistance (PI: dott.ssa Loretta Del Mercato – CNR Nanotec – Lecce)
- MIUR: Validazione di nuovi marker del tumore sieroso ovarico: studio di espressione del profilo di espressione genica e oncometabolico (PREGO) PI: Prof. A. Scillimati – Università di Bari
- AIRC: RLF and PVT1 transcripts as novel biomarkers in Small Cell Lung Cancer with amplifications of the MYC family genes. PI:dott.ssa C. Storlazzi

Papers 2021-2022

- Porcelli L, Di Fonte R, Pierri CL, Fucci L, Saponaro C, Armenio A, Serratì S, Strippoli S, Fasano R, Volpicella M, Daprile R, Tommasi S, Ressa CM, Guida M, Azzariti A. BRAFV600E;K601Q metastatic

melanoma patient-derived organoids and docking analysis to predict the response to targeted therapy.Pharmacol Res. 2022 Aug;182:106323. doi: 10.1016/j.phrs.2022.106323.

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