Dipartimento di Farmacia
Dipartimento di Eccellenza
2018-2022 2023-2027
UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

PROPOSTA PROGETTUALE
DOTTORATO IN RNA THERAPEUTICS AND GENE THERAPY
(Mechanisms of diseases and Drug Target identification)
CICLO XLI

Tutor: Angelo Antonio Izzo - Co-tutor: Francesca Borrelli

PROJECT TITLE
Bile Acid-CoA:Amino Acid N-Acyltransferase as a Novel Target for RNA-Based Therapies in Colon Carcinoma

Project description (max 300 words**)**
Colorectal cancer (CRC) is the second leading cause of cancer-related deaths worldwide. Currently, the 5-year survival rate for patients in advanced stages remains only 14%[1]. This poor prognosis is largely attributed to the emergence of an immunosuppressive tumor microenvironment (TME), which can severely limit the efficacy of advanced immunotherapies, especially immune checkpoint inhibitors[2]. Preclinical in vitro and in vivo studies have shown that polyunsaturated fatty acids (PUFAs) are abundant in the TME and that their dysregulation contributes to cancer development and progression[3]. N-acyl taurines (NATs) are a new class of endogenous PUFAs, composed of long-chain fatty acids conjugated to the amino acid taurine. In humans, NATs are synthesized in peroxisomes by the enzyme bile acid-CoA:amino acid N-acyltransferase (BAAT)[4].
Based on these premises, this project aims to provide unprecedented insights into the role of the enzyme BAAT enzyme and NATs in CRC development and progression, with a particular focus on tumor-stroma interactions. To achieve this goal, a multidisciplinary approach will be employed, combining multi-omics analyses and functional assays across a range of experimental models: human colon biopsies, patient-derived organoids (PDOs), genetically modified mouse models of CRC with high endogenous NAT levels, and 3D co-culture systems (PDOs/immune cells) to better mimic the complexity of the TME.
The findings of this project are expected to deepen the understanding of a novel molecular pathway involved in CRC and may pave the way for the identification of new therapeutic targets or strategies aimed at modulating the tumor microenvironment.

REFERENCES
1. Siegel R, et al. *CA Cancer J Clin*. doi: 10.3322/caac.21871 (2025)
2. Tan E, et al. *Expert Review of Gastroenterology & Hepatology*. doi: 10.1080/17474124.2021.1886077 (2021)
3. Arul Prakash S, Kamlekar RK. *Chem Phys Lipids*. doi: 10.1016/j.chemphyslip.2020.104929 (2020)
4. Benatti P, et al. *J Am Coll Nutr*. doi: 10.1080/07315724.2004.10719371 (2024)

FUNDS
PRIN ,JAZZ PHARMACEUTICALS

Dipartimento di Farmacia
Via Domenico Montesano, 49 • 80131 Napoli, Italia
angelo.izzo@unina.it • + 39 081678658
www.farmacia.unina.it