H.F.R.I.
Hellenic Foundation for Research & Innovation

ΙΣΝ/SNF ΙΔΡΥΜΑ ΣΤΑΥΡΟΣ ΝΙΑΡΧΟΣ
STAVROS NIARCHOS FOUNDATION

Description of the funded project

2nd Call “Science & Society”

“Always strive for excellence – Theodoros Papazoglou”

Title of the research project: **An atlas of circulating cancer-associated fibroblast for the prediction of response to immunotherapy in solid tumors: development of a "liquid biopsy".**

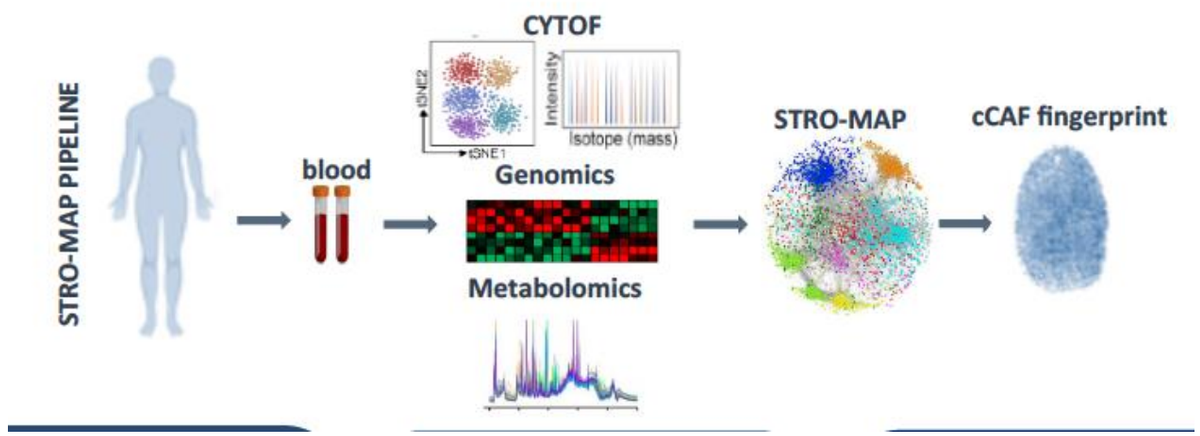
Principal Investigator: **Panayotis Verginis**

Reader-friendly title: **STROMAP**

Scientific Area: **SA3 Life Sciences**

Institution and Country: **IMBB, Greece**

Host Institution: **IMBB**



Budget: **250.000 euros**
Duration: **24 month**

Research Project Synopsis

The advent of checkpoint immunotherapy revolutionized cancer treatment, underscoring the pivotal role of immune system in cancer eradication. Despite the clinical success, cancer immunotherapy remains ineffective in a large proportion of patients, while responses are frequently accompanied by autoimmune manifestations. Understanding the mechanisms underlying the limited efficacy of immunotherapy and the ensuing autoimmunity is of urgent need in order to facilitate the discovery of predictive biomarkers and personalized therapy. Thus far efforts to achieve these needs were focused on immune cells while stromal cells were largely ignored. The most abundant stromal cells in tumor bed are cancer-associated fibroblasts (CAFs) and emerging literature suggests a prominent role in cancer recurrence and resistance to therapy due to their intrinsic survival advantage being resistant to chemotherapy/radiotherapy. Herein, we propose a paradigm shift in cancer immunotherapy and diagnosis through: a) development of a multi-parametric CAF atlas (STRO-MAP) based on single cell mass-cytometric, and transcriptomic analysis of cCAFs, towards a "liquid" biopsy for prediction of immunotherapy response; b) assessment of STRO-MAP fingerprints as potential therapeutic targets in humanized models carrying patient tumor xenografts. Comprehensive characterization of cCAFs in tumor patients and delineation of CAF-mediated mechanisms contributing in tumor development will empower the discovery of personalized biomarkers and targeted therapy.

Expected results & Project Impact

Despite major advances in the emerging success of cancer immunotherapy and our understanding of tumor tolerance mechanisms, cancer remains one of the leading causes of death globally. Fundamental discoveries made over the last decade have unequivocally shown that the immune system plays a vital role in tumor development with tumors exploiting sophisticated immune tolerance networks to avoid immune recognition and destruction. This knowledge led to the new era of cancer immunotherapy, which however promises durable and sustained responses only in a small proportion of cancer patients and also responses often accompanied by autoimmune diseases, which sometimes can be severe and life-threatening.

Deciphering new strategies to harness the anti-tumor immunity while keeping in check the autoimmune responses remains a daunting task and could ultimately lead to more effective management of cancer.

In this project we propose a paradigm shift in cancer immunotherapy and diagnosis by focusing on unexplored arms of tumor tolerance mechanisms within CAFs. Specifically we propose to:

a) Develop a multiscale atlas of cCAFs (STRO-MAP) for the generation of a cCAF-based "liquid" biopsy for predictive and diagnostic purposes

b) Elucidate novel therapeutic targets in humanized mouse models carrying patient tumors

Implementation of this proposal will contribute to the development of novel immunotherapeutic strategies and will pave the way for the identification of potential predictive and diagnostic biomarkers towards the design of personalized therapy.

The importance of this funding

The funding of this project by H.F.R.I and SNF will address fundamental questions in the field of Immunology and Oncology. The findings of this proposal will provide new knowledge on major unmet needs in cancer immunotherapy. It will also support the training of young investigators and importantly it will allow myself to obtain preliminary results to be competitive for major International funding. We expect that through different actions, these findings to be communicated to clinician oncologists, to patients as well as to researchers in the immuno0oncology fields in order to encourage their involvement in the effort of eradicating cancer. Finally, the findings of this proposal will be presented in International symposia which will enhance the recognition of our work and establish future collaborations

H.F.R.I.
Hellenic Foundation for Research & Innovation

ΙΣΝ/SNF ΙΔΡΥΜΑ ΣΤΑΥΡΟΣ ΝΙΑΡΧΟΣ
STAVROS NIARCHOS FOUNDATION

COMMUNICATION

185 Syggrou Ave. & 2 Sardeon St. 2
171 21, N. Smyrni, Greece
+30 210 64 12 410, 420
info@elidek.gr
www.elidek.gr