



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

**PROgrammable, cancer TargEted and Cancer responsive  
therapeutics and Theranostics**

**1st Call for H.F.R.I. Research Projects to Support Faculty  
Members & Researchers and Procure High-Value  
Research Equipment**

**Title of the research project:**

PROgrammable, cancer TargEted and Cancer responsive therapeutics and Theranostics

**Principal Investigator:**

Tzakos Andreas

**Reader-friendly title:**

PROTECT

**Scientific Area:**

Life sciences (Medical and Health sciences)

**Institution and Country:**

ELIDEK, GREECE

**Host Institution:**

University of Ioannina, Greece

**Collaborating Institution(s):**

University of Florence, Department of Chemistry

STANFORD UNIVERSITY, DEPARTMENT OF CHEMISTRY

Imperial College London, Department of Medicine

**Project webpage:**

<http://bac.chem.uoi.gr/protect/index.html>



**Budget: 179,685 €**

**Duration: 36 Μήνες**

## Research Project Synopsis

***Cancer is the leading cause of death in the developed countries, affecting nearly one in two people and despite much investment, clinical attrition rates remain high. These suggest that both the chemical space used for drug development, as also currently selected oncotargets are incompatible to combat this disease. Scientific discoveries of the last decade unveiled that proteins containing extensive structure disorder, the intrinsically disordered proteins (IDPs) are extensively associated with cancer. Nonetheless, numerous examples in current literature exist, where intrinsic disorder in proteins is still overlooked. Setting IDPs as oncotargets in drug discovery platforms could be a viable approach to evolve the new generation of cancer therapeutics. However, IDPs have been considered undruggable, since the chemical space suitable to discover compounds for these targets and screening platforms remain uncharted. Thus, this unexplored field for drug discovery, that could hold great promise for cancer treatment, remains untapped. The project proposed herein is aimed to systematically decipher the chemical space in order to develop selective modulators for oncogenic IDPs, based on chemo-enzymatically functionalized natural products/drugs, and moreover to generate drug delivery vehicles for selective transport of these modulators inside cancer cells. We will consolidate an integral drug discovery pipeline customized for these oncotargets. Preclinical evaluation of the drug delivery vehicles, tailored for different oncotargets and different types of cancer will be conducted. The insights expected to be obtained throughout this project will expand our understanding on the principles of designing selective compounds for IDPs, thereby bridging the gap in our understanding of their role in biology and disease, enabling the development of specific cancer therapeutics tailored for each undruggable target.***

## Project originality

The originality of the project is based on the targeting of entities that are still considered inaccessible for the design and development of drug molecules (undruggable). Specifically, these are intrinsically disordered proteins (IDPs) which make up to 79% of the proteins found in cancer. Our goal is to study how bioactive molecules can interact with these proteins. Characterization of this chemical space will allow the creation of a pioneering toolbox for exploring this unexplored space.

The scientific innovation stames in the creation of basic knowledge about the chemical space required for the development of targeted molecules for IDPs and the creation of transport vectors for their selective delivery to cancer cells. Technological innovation will be the integration of this knowledge into new technologies that will allow: (i) the design of a new generation of drugs targeting IDPs, (ii) personalized drug delivery systems as well as (iii) diagnostic and therapeutic molecules, using fluorescent compounds in the area near-infrared (NIR), in the context of non-invasive imaging

## Expected results & Research Project Impact

The project will:

- 1) Provide a new way of thinking for the discovery of drugs that will target the untapped area of IDPs.
- 2) Enable the targeting of several different untrackable cancer targets.
- 3) Contribute to the development of individualized cancer treatment and diagnosis through the development of different combinations of cancer targeting molecules and anti-cancer drugs.
- 4) Lay the groundwork for the discovery of innovative diagnostic and therapeutic molecules.
- 5) Establish a drug discovery platform tailored for IDPs.
- 6) Development of individualized anti-cancer compounds that could improve the quality of life of patients.
- 7) Targeted, non-invasive and non-radioactive diagnostic methods, focusing on imaging in the NIR region, could lead to cheaper and safer approaches for early diagnosis.

## The importance of this funding

**There is an urgent need for innovation in oncology, starting with the reassessment of the current drug design philosophy. The main questions that exist are: do we use the right chemical space and / or the right therapeutic targets to fight cancer? Can dominant drug design based on existing structural features address the major cancer targets? Can cancer drug targets such as intrinsically disordered proteins (IDPs) that are considered undruggable be targeted? Can available drug transport vehicles meet this difficult drug target? These are some questions that we will try to give answers to enabled by the funding of this research EL.ID.EK..**



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