

OncoProTools - A European Doctoral Network developing protease-guided tumor targeting tools to revolutionize cancer diagnosis and treatment



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www.oncoprotocols.eu



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What is OncoProTools

A Marie Skłodowska-Curie Actions (MSCA) doctoral network that brings together **7 beneficiaries, 11 associated partners, 1 hospital, and 1 patient organization, from across Europe**

Objectives

To drive breakthroughs in cancer diagnosis and therapy through **innovative protease-targeting technologies**. To achieve this, the consortium is organized into three focus areas:

1. Safer and more effective CAR T-cell therapies for cancer patients
2. Personalized protease targeting for minimally invasive, miniaturized diagnostics
3. Novel ligands for targeting proteases in the tumor microenvironment



An International, Interdisciplinary, and Intersectoral (3i) Team



1. Safer and more effective CAR T-cell therapies for cancer patients

SIMONA MATTIUSSI
Design of novel FAP target modules for simultaneous delivery of CAR T-cells and radiotherapy

THERANOSTIC PLATFORM

Design of novel small-molecule FAP Targeting Modules (TM)

UniCAR epitope, Linker, Small-molecule FAP Targeting Vector, Fibroblast Activation Proteases

TM, UniCAR T-cell, Tumor, DNA damage, Tumor cell death, Tumor apopt.

University of Copenhagen

HUGO BOUTIER
Innovative Target Modules for FAP-Targeting UniCAR T therapy

SWITCHABLE THERAPY
Immune attack with safety control

UniCAR T-cell, Anti-FAP Target Module (TM), ESRS

DIAGNOSTIC IMAGING
See the cancer, track the treatment

Detected cell, Killed cell

Advantages over conventional CAR T-cells:

- Flexibility (multiple targets)
- Controllability (ON/OFF)
- Overcoming antigen loss

Smart radiation with precision and safety
TARGETED RADIOTHERAPY

HZDR (Helmholtz-Zentrum Dresden-Rossendorf)

2. Personalized protease targeting for minimally invasive, miniaturized diagnostics

ALBERTO BIGOGNO
The role of p38 MAP kinase pathway in the tumor microenvironment: effect on protease expression

Ex-vivo analysis
CAC primary tumor, p38 Knock-Out, Lung metastasis, Intestinal & pulmonary fibrosis, CAF & MMP

In-vivo analysis
CAC primary tumor, p38 Knock-Out, Lung metastasis, Tumor Microenvironment

Tumor proteases analysis: FAP, CatB, CatL, CatD

Centro Nacional de Biotecnología, CSIC

HECTOR CABALLERO GONZALEZ
Microfluidics-based single-cell characterization of innovative cellular immunotherapies

UniCAR-T cell, Tumor cell, target module

Serial killers, Moderate killers, Mono killers

Single-cell analysis to capture functional heterogeneity

'Lab-in-a-box' microfluidic platform

Single-cell resolution: 19,200 miniaturized co-cultures

CELLPLY

ADRIANNA BILIŃSKA
Innovative in vitro and in vivo models for TME protease research

TARGETING FIBROBLAST ACTIVATION PROTEIN (FAP) WITH THERANOSTICS

⁶⁴Ga Diagnostic, ¹⁷⁷Lu Therapeutic

Linker, FAP receptor, FAP inhibitor

IN VITRO STUDIES
Tumor models to evaluate selected radiopharmaceuticals and to study the role of FAP in the TME biology

IN VIVO STUDIES
Tumor xenografts to study the therapeutic potential of selected radiopharmaceuticals and to understand the role of FAP in the TME

PET/SPECT/CT, Biodistribution, Autoradiography, Immunohistochemistry

INSELSPITAL, UNIVERSITÄT BERN

3. Novel ligands for targeting proteases in the tumor microenvironment

NIKITA SHIKUT
Design and discovery of novel Grn2B ligands and evaluation as diagnostics tools in CAR T-cell therapy assessment

Novel target - Granzyme B.

- Highly expressed in tumor-microenvironments and inflammatory areas.
- Highly potent protease inhibitors developed.
- Biotin and PET Granzyme B probes developed.

PART I
Structure optimization, Synthesis optimization, Biological assays, Lead optimization

PART II
Starting inhibitor, Synthesis optimization, Biological assays, Lead optimization

PART III
In vivo imaging, Injection of a probe, In vivo imaging, Labeling with a dye/biotin

Novel potent and selective Granzyme B* probe

Universität Antwerpen

MAGDA THANOPOULOU
Novel Granzyme B inhibitors for early cancer treatment response measurement via PET

***Granzyme B: a serine protease** secreted by T-cells and natural killer cells to kill cancer cells.

Cytotoxic T-cell, Cancer cell, Apoptosis

Compound library, Biological assessment, Optimal inhibitor selection, Radioligand introduction, In vivo studies

Novel potent and selective Granzyme B* probe

Perforin, Granzyme B, Granzyme B inhibitor with radiolabelled tag

Universität Antwerpen

THALES DO VALLE MOREIRA
Novel Cathepsin S ligands as PET and fluorescent probes for oncology

Tuned reactive Warhead, Linker, Reporter

Cathepsin S, TME core, TME frontier

PET, Fluorescence

Theranostics, TME study, Secondments & Collabs

CSIC, SCV, CellCats

Universität Antwerpen

OLIVIERO CINI
Novel probes for imaging of tumor-associated cathepsins via PET

CatB and CatL radio-ligands

Overexpression of CatB and CatL

Tumor detection and therapy monitoring

PET imaging probes

Synthesis of a library of CatB and CatL inhibitors, Biochemical assays, Radiolabeling, In vivo studies

Universität Antwerpen