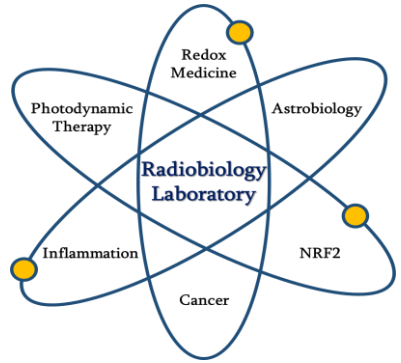
PN 23.16.02.01 project
Objective 1



Stress genes as therapeutic targets in radiotherapy and photodynamic therapy for the treatment of colon cancer

Project coordinator
CSI Dr. Gina Manda
Radiobiology Laboratory

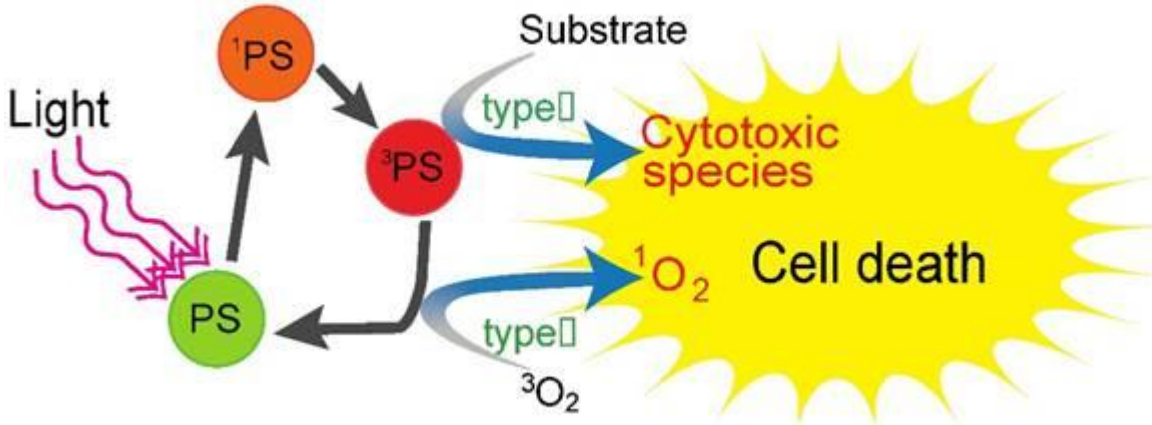
Medical issue

Intrinsic radioresistance of colon tumor cells

Lordick F, Gockel I. Chances, risks and limitations of neoadjuvant therapy in surgical oncology. Innov Surg Sci. 2016 Aug 9;1(1):3-11.

Alternative to radiotherapy -

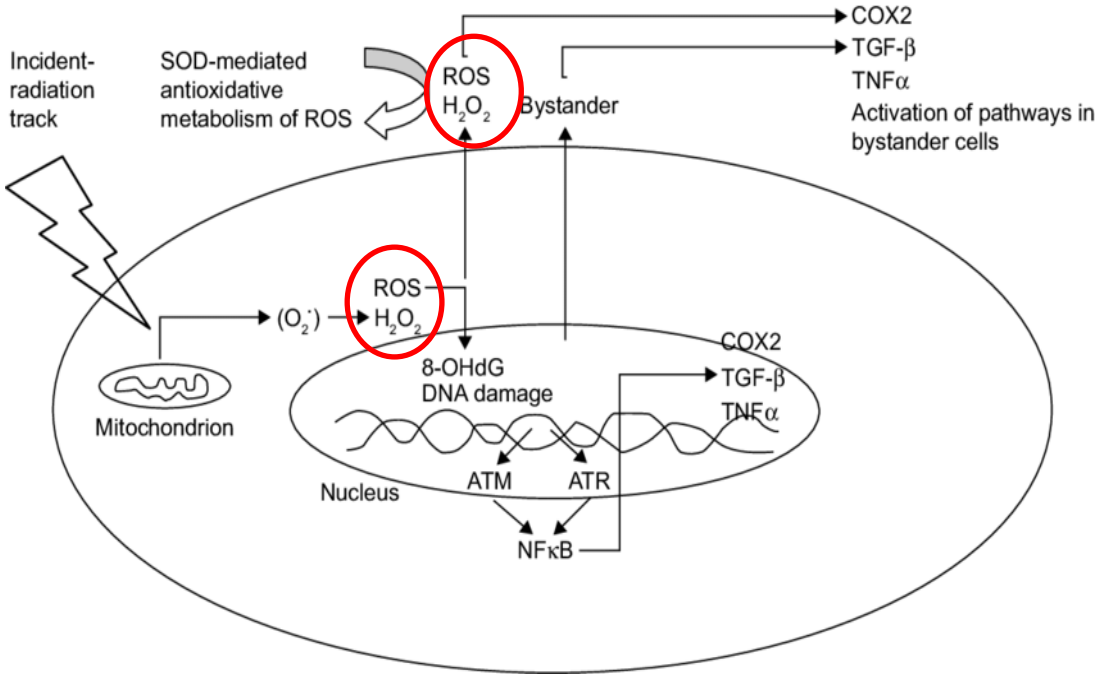
the photodynamic therapy (PDT)



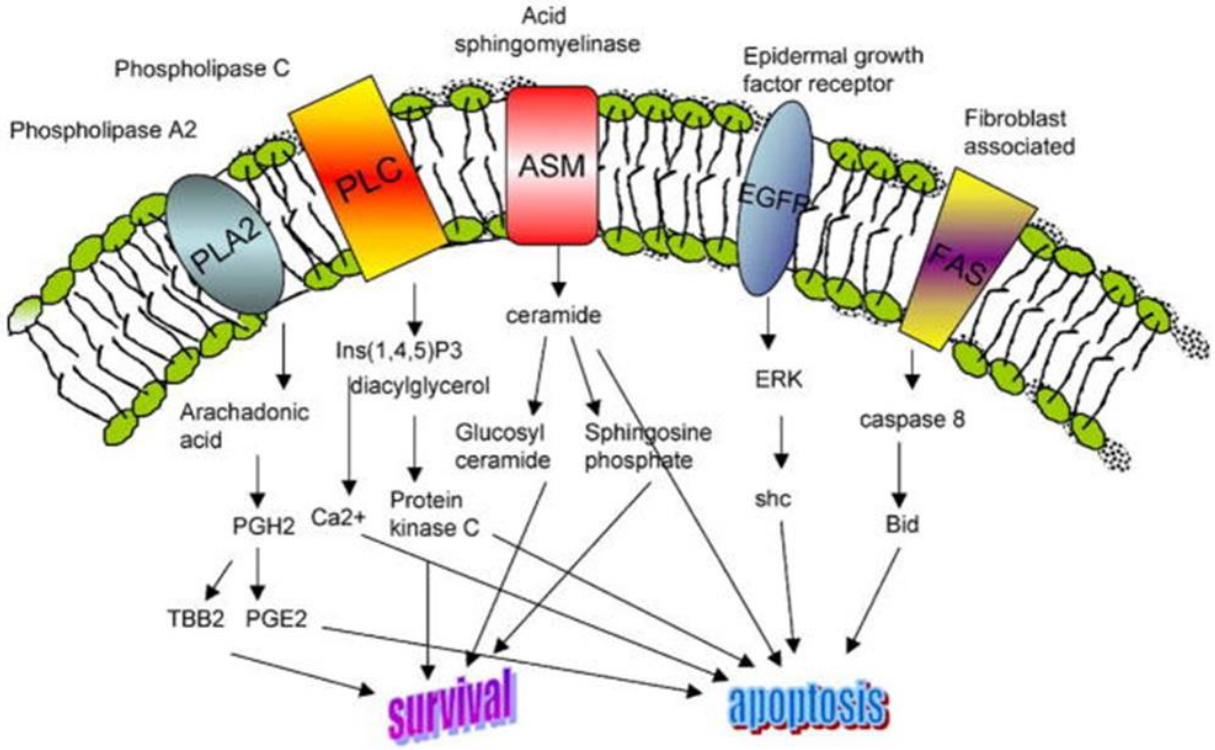
RT → **Reactive oxygen species in cancer therapy** ← PDT

Proposed solution for increasing the efficacy of RT și PDT

To therapeutically target stress genes that protect tumor cells against the cytotoxic effect of RT or PDT



RT

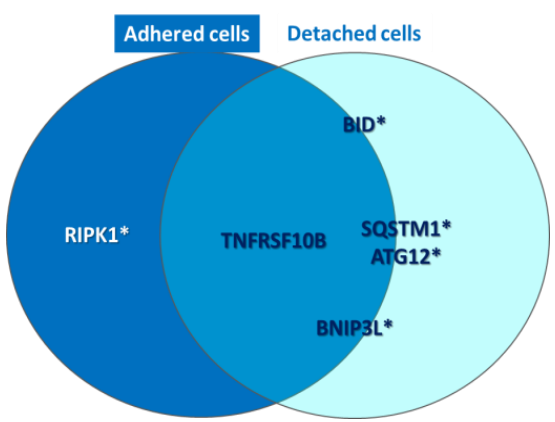


PDT

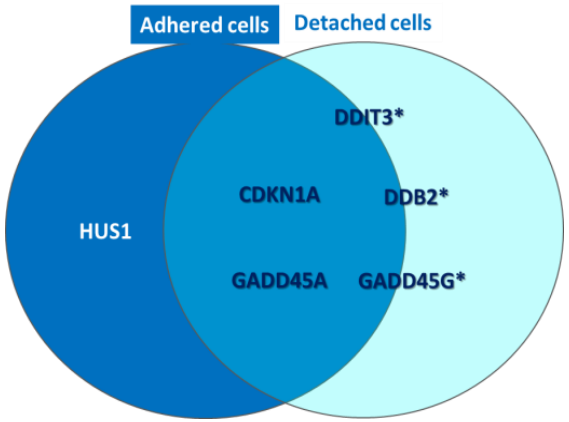
Preliminary results

- A network of stress genes with modified expression was evidenced in human colon carcinoma cells exposed to γ radiation (8 Gy, 25 Gy, 50 Gy/h).

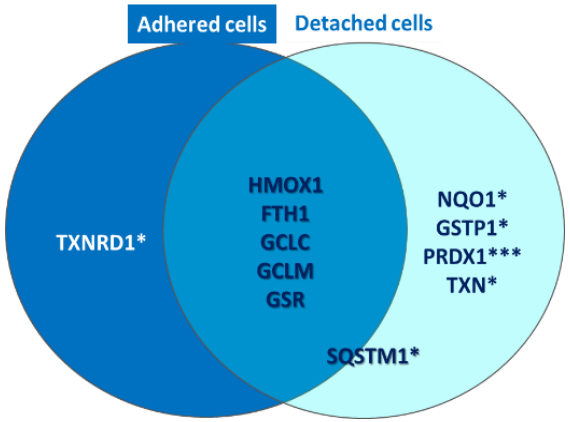
- Overexpressed stress genes in human colon carcinoma cells exposed *in vitro* to PDT.



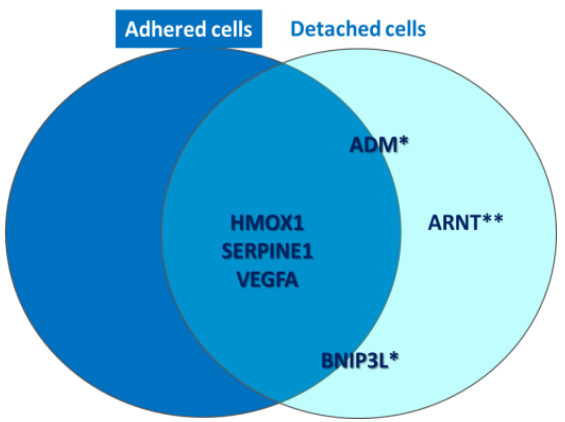
Cell death



DNA damage & repair



Antioxidant response



Response to hypoxia

Dobre M, Boscencu R, Neagoe IV, Surcel M, Milanesi E, Manda G. Insight into the Web of Stress Responses Triggered at Gene Expression Level by Porphyrin-PDT in HT29 Human Colon Carcinoma Cells. Pharmaceutics. 2021 J13(7):1032.

The search continues…

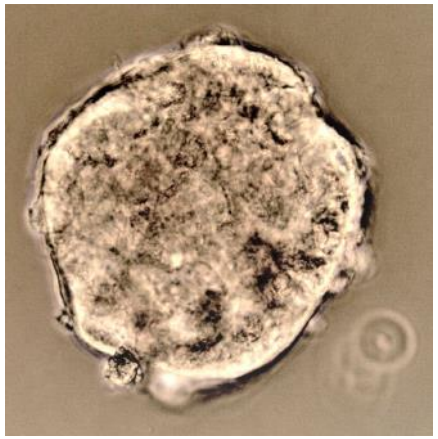
Scientific objectives of the project

1. To identify and validate several stress genes involved in the repair mechanisms developed by tumor cells exposed to RT or PDT, using 2D / 3D cellular models, and to demonstrate their role in resistance to therapy;

2. Therapeutic targeting of repair mechanisms in 2D/3D models and in tumor-bearing animals using modulators of stress genes, aimed at decreasing the resistance to therapy (RT or PDT) or at protecting normal cells;

3. Improvement of the *in vitro* investigation methods addressing cells in the rifle of RT or PDT by using 3D cellular models of organoids and tumorspheres;

4. *In silico* studies on the characteristics of 3D cellular models, that are relevant for “real” human tumors.



Will we be able to avoid animal studies by using 3D cultures?

Objectives for institutional development

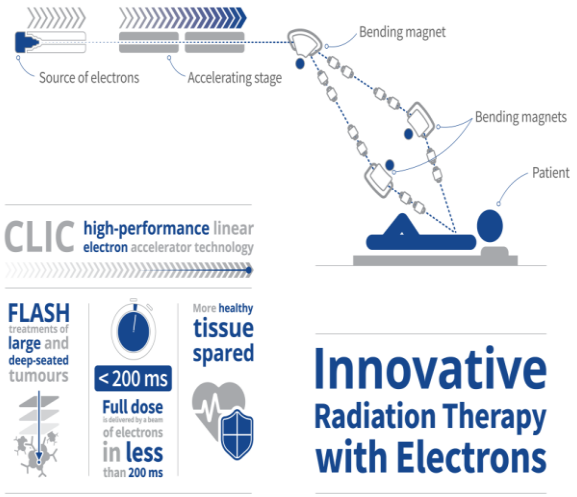
1. New conceptual and methodological approaches implemented in the Institute for investigating at preclinical level antitumor therapies primarily relying on oxidative damages;
2. Training of young researchers in the field of radiobiology;
3. Increase of the international visibility of the Radiobiology Laboratory by publications and communications in the field of RT, PDT and radiotoxicology;
4. Preparation of future experiments at ELI-NP in the frame of the European ELI Call for Users;
5. To obtain relevant experimental results for our participation to international projects in the field of radioprotection, cancer therapy and astrobiology;
6. To strengthen the existent collaborations in the field of radiobiology and to develop new international partnerships.

    - Autonomous University of Madrid și Acțiunea COST CA20121 – Prof Antonio Cuadrado, antonio.cuadrado@uam.es,
    - BIOSPHERE consortium – Dr. Faton Krasniqi, Physikalisch-Technische Bundesanstalt, Germania, faton.krasniqi@ptb.de,
    - National Technical University of Athens, Grecia – Dr. Alexandros Georgakilas, Alexg@mail.ntua.gr,
    - Institut für Radiobiologie der Bundeswehr & Universität Ulm – Christina Beinke, christinabeinke@bundeswehr.org.

Ongoing projects in the field of Rdiobiology

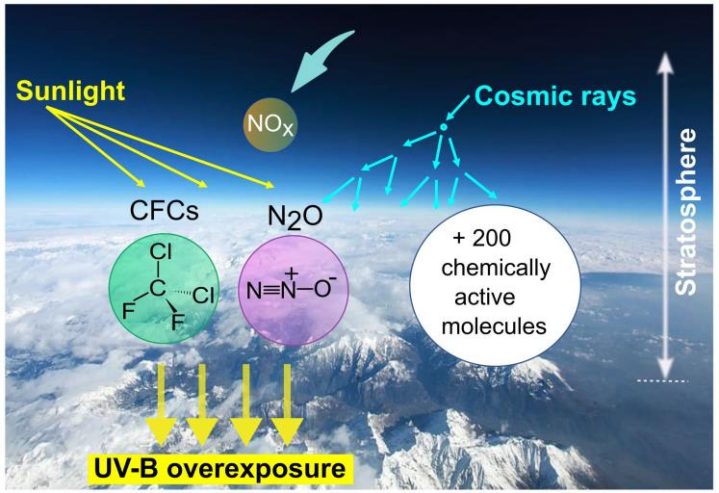
CELLI

Preparation of the radiobiology platform for investigating FLASH-RT @ ELI-NP



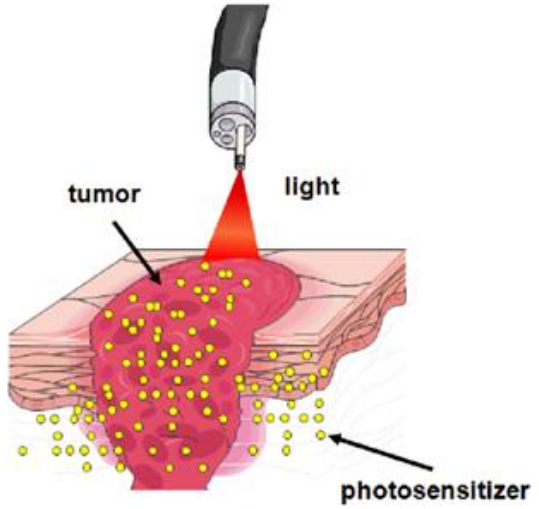
BIOSPHERE

(22 European partners)
The behavior of normal cells exposed to secondary cosmic rays and UV radiation



PORPHYDERM

New photosensitizing systems for the treatment of actinic keratosis by PDT



NUCLEU project

Estimated results

- Project proposal in the field of radiobiology and redox medicine, in collaboration with European partners;
- 8 studies (2 studies / year) and at least 9 operational procedures;
- Project-dedicated biobank;
- At least 4 publications: 1 review and 3 original papers;
- At least 7 communications at national and international conferences;
- A patent request regarding a new method for validating repair mechanisms in tumor cells exposed to RT/PDT;
- Knowledge transfer towards a SME involved in drug development;
- A demonstrative workshop at the end of the project;
- Participation to an international course organized by the COST Action CA20121;
- The project-dedicated webpage;
- Adhesion to an international consortium (BIOSPHERE, COST),
- 2 PhD thesis defended.

Team

Gina Manda	Elena Milanesi
Ionela Victoria Neagoe	Elena Mihaela Dragnea
Andrei Constantinescu	Maria Dobre
Mihnea-Ioan Nicolescu	Maria Olinca și Andrei Niculae
Valeriu Cișmașiu and Mihaela Surcel	Laurentiu-Iliuță Anghelache and Gheorghița Isvoranu
Emanuel Fertig and Victor Peteu	

Budget

Personal costs	**3.558.300**
Reagents and consumables	**344.124**
Equipment	**87.000**
Publication	**80.000**
Irradiation services	**75.000**
Animals	**68.850**
Travel	**58.900**
IT equipment and software	**35.800**
Other small objects	**10.000**
Indirect costs	**3.267.976**


COLLABORATION
TOGETHER
TERM
WORKING
SMALL
PERSONAL
USED
COMMUNITY
ADDING
SKILLS
INDIVIDUAL
IMPORTANT
CHALLENGED
COMMUNICATION
INDUSTRY
CONSTRUCTION
ESTABLISHED
WELL
COLLECTIVE
INCLUDING
INFORMATION
BEST
ECONOMIC
TRUST
SUCCESS
KNOWLEDGE
LEARNING
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SET
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COMPLEX
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CORPORATION
BLOGS
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POLITICAL
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HIGH
EDUCATION
ORGANIZATION