University of Cyprus

University of Cyprus
Electromagnetics and Novel Applications Lab

Plasma Transport of Reactive Species on Tumors

PLASMA-TReatS-TUMORS

RESEARCH & INNOVATION FOUNDATION

2016-2020 RESTART SEARCH
ΠΡΟΓΡΑΜΜΑΤΑ ΕΡΕΥΝΑΣ, ΤΕΧΝΟΛΟΓΙΚΗΣ ΑΝΑΠΤΥΞΗΣ ΚΑΙ ΚΑΙΝΟΤΟΜΙΑΣ

Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο Περιφερειακής Ανάπτυξης

Κυπριακή Δημοκρατία

Διαρθρωτικά Ταμεία της Ευρωπαϊκής Ένωσης στην Κύπρο

Project Summary

The aim of Plasma Transport of Reactive Species on Tumors (PLASMA-TReatS-TUMORS) is to shine a light in key open questions of cancer medicine field such as how cold plasmas can be incorporated in novel anticancer strategies and through which mechanisms plasma-mediated anticancer effects are obtained. This intersectoral project benefits significantly from knowledge transfer between expert researchers in physical, electrical, and mechanical engineering, and pharmaceutical sciences. A fully customized plasma source will be used to produce a cold atmospheric pressure plasma jet (APPJ) in controlled gaseous atmospheres (dry and/or humid). The APPJ and its interaction with a solid tumor will be modelled using a technologically advanced multidimensional plasma numerical model. This model will be then combined with a novel multiscale, multiphysics, in-silico modelling framework (FEB3 Platform) that encompasses dynamic tumor growth, a feat that has not yet been attempted. As so, the interactions of APPJs with solid tumors will be modelled and simulated to interrogate how plasma components (such as electric fields and chemically reactive species) propagate though solid tissue and, hence, explore optimum APPJ-conditions for tumor regression. What is more, the numerical tool will be verified and validated against experimental data of APPJ effects on 3D melanoma cancer cells (good models of solid tumors). Therefore, the plasma model will be able to predict the suitable dosage of plasma components produced with the APPJ, which is needed for cancer elimination and which will be validated with the experiments.

The project started on 1/1/2021 and has a total duration of 24 months and is funded by the Research and Innovation Foundation (RIF) with 150.000 € (RESTART 2016-2020 Programme for Research, Technological Development and Innovation, Horizon 2020 – 2nd Opportunity Programme, Proposal Number: OPPORTUNITY/0916/MSCA/0023).

Project Objectives

PLASMA-TReatS-TUMORS proposes to develop a technologically advanced numerical tool which combines a **plasma fluid model (PFM)** and a **novel solid tumor model (STM)** (Figure 1). The numerical results will be verified and validated against experimental data of the APPJ alone and its interaction with melanoma cancer cells (Figure 2, PhD Thesis of Dr. Dimitrios Athanasopoulos, supervised by Prof. Panagiotis Svarnas, University of Patras/2020) and/or solid tumors. Therefore, a cutting edge numerical and experimental investigation is proposed in PLASMA-TReatS-TUMORS to combine and validate the PFM and STM models, investigate the APPJ parameter space that induces regression of tumors and apoptosis of cancer cells, and identify the role of different plasma components.

The project has four (4) research objectives:

1. Develop realistic numerical models for the APPJ alone and its interaction with solid tumors to study the influence on the generated plasma constituents of the tumor presence.
2. Use of a novel multiscale, multiphysics, in-silico modelling framework to inject plasma constituents (obtained from 1) in tumor models and define adequate APPJ operating conditions for tumor regression.
3. Characterize and adjust the APPJ source to operate on the parameter space defined from 1 and 2. The plasma source will be then used for experiments.
4. Experimentally verify the concept of the proposal by applying plasma energy on melanoma cancer cells, which are used in this project as a model of solid tumors. Results from 1, 2 and 3 will be needed for this research objective.

Graphic representations of the project's concept are shown in Figures 1 and 2.

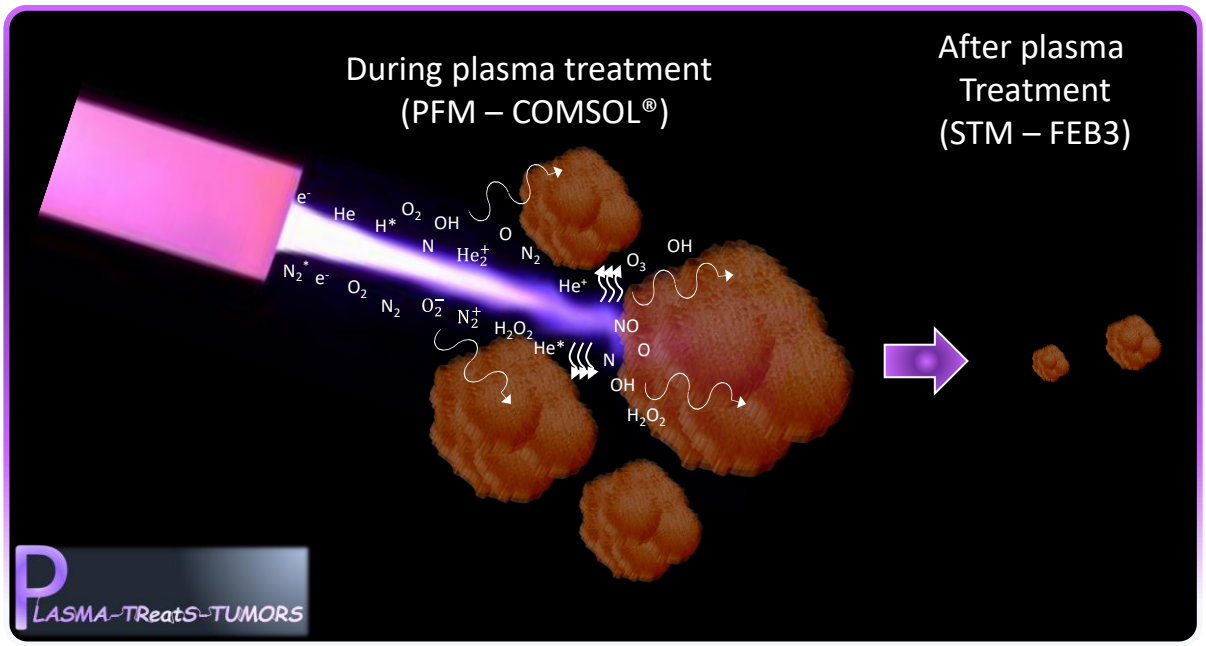

Figure 1. PLASMA-TReatS-TUMORS main concept. The interaction of the APPJ with solid tumors and the diffusion of plasma components (radicals, ions, electrons, reactive oxygen and nitrogen species, metastables, electric field, (V)UV radiation, heat) to the tumors are modeled, and optimum conditions leading to the regression of tumor growth are obtained.

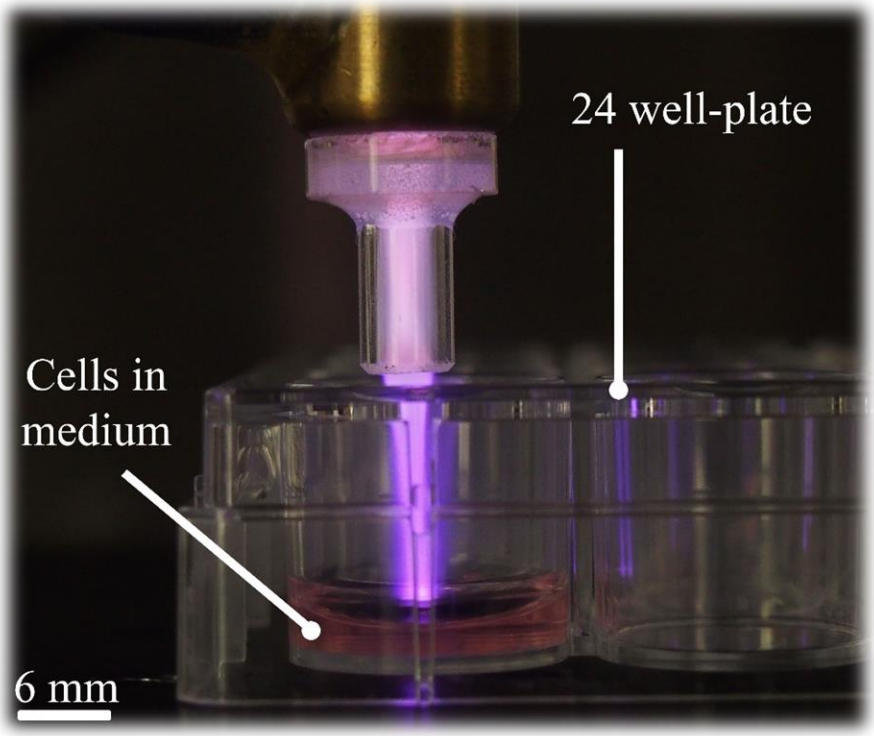

Figure 2. The physical APPJ device that will be investigated in PLASMA-TReatS-TUMORS in interaction with solid tumors and cancer cells. This APPJ will be considered in the models (Figure 1) in order to be optimized in terms of reactive species production, electric fields, etc. Those optimum conditions will be used in the experiments to achieve apoptosis of melanoma 3D cancer cells and/or solid tumors. The figure shows the APPJ interaction with 2D cancer cells placed in a culture medium maintained in a 24 well-plate. Figure is taken from the PhD thesis of Dr. Dimitrios Athanasopoulos (supervisor: Prof. Panagiotis Svarnas, Department of Electrical and Computer Engineering, University of Patras). For more details see https://upatrasece.wixsite.com/hvlab.

Structure and Methodology of the Project

The main part of the work proposed in PLASMA-TReatS-TUMORS (PFM and STM models) will be realized by Dr. K. Gazeli (experienced researcher – ER, photo on the left) at the Electromagnetics and Novel Applications Lab (ENAL) in collaboration with the Department of Mechanical and Manufacturing Engineering (MME) both located at University of Cyprus. The project coordinator will be Prof. G. E. Georghiou (ENAL) and the ER will be also trained by Assist. Prof. V. Vavourakis (MME). Furthermore, a secondment is foreseen for the experimental part, which will be done at the University of Patras (UoP) in collaboration with Prof. P. Svarnas and Prof. S. G. Antimisiaris. The detailed work plan is divided into **four** (**4) Work Packages (WPs**), which are described below:

- **WP1. Project Management (ENAL)**: This WP lasts for the duration of the project. Its main objective is to achieve the appropriate management of the proposed project and to ensure its successive realization by the project partners. It also ensures that new career opportunities will be opened for the experienced researcher (ER) after the project is completed. Finally, it ensures that all the necessary equipment for the project will be acquired on time. It has 5 deliverables.
- **WP2. Dissemination of the Results (ENAL – MME – UoP):** This WP aims to achieve an appropriate dissemination of the project results and to ensure their wide communication to public and scientific audiences through personal and professional social media pages, scientific article publication, international conference attendance, etc. It has 7 deliverables.
- **WP3. Numerical Models (ENAL – MME – UoP):** WP3 refers to the adequate training of the ER on the mastering of the plasma fluid model for the simulation of the interaction of plasma with solid tumors. Also, to the validation of the fluid model against experimental data, the injection of model outputs to a solid tumor model for studying their effects on tumor regression, and the use of the physical APPJ source for the treatment of melanoma cancer cells. It has 5 deliverables.
- **WP4. APPJ experimental characterisation and interaction with melanoma cancer cells (UoP):** WP4 refers to the experimental part of the proposal. First the experimental investigation of the physical plasma source will be realized by means of advanced electrical and optical methods for the conditions provided by the fluid model. Then, the effect of the plasma on melanoma cancer cells will be investigated under optimum conditions for the production of chemically reactive species, electric fields, etc. It has 2 deliverables.

Anticipated Project Outcomes

The principal anticipated outcomes of the present project are the following:

- Model the interaction of an APPJ with solid tumors (STs) and determine optimal plasma conditions for enhanced production of chemically reactive species, electric fields, electric charges, temperature, etc., which will be injected to STs.
- Take advantage of a novel multiscale, multiphysics, in-silico modelling framework to investigate and better understand the diffusion of plasma components in solid tumors and, hence, explore optimum APPJ-conditions for tumor regression.
- Validate the numerical models by studying experimentally the APPJ and analyzing its interaction with melanoma cancer cells.
- Identify the role of different plasma components on tumor growth regression and cancer cells apoptosis.

- Stimulate the transfer of knowledge between expert researchers in physical, electrical, and mechanical engineering, and pharmaceutical sciences in National and International level. Use of this knowledge to predict the suitable dosage of plasma components in new plasma-based cancer therapies.

Project Updates and links

The detailed project log and the main project updates can be found in the project's personal page in ResearchGate:

https://www.researchgate.net/project/PLASMA-TReatS-TUMORS

Major projects achievements will be also published to the ER's personal LinkedIn page:

https://www.linkedin.com/in/kristaq-gazeli-christakis-gazelis-2b85806b/

Project Contacts

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