Biomedical Technologies and Innovation Doctoral Programme (BIOTIN)

Title of the PhD Project	**Ultrasound-assisted drug delivery for cancer research**
Acronym	**USaddCARE**
Research Fields of the Project	Drug delivery systems for cancer
Keywords	Ultrasound, microbubble, cancer, anticancer drug delivery
Host Institution, Department and Campus Location	Izmir Institute of Technology (IZTECH), Department of Chemical Engineering, Urla, İzmir
PhD Awarding Institution and Graduate Programme	Izmir Institute of Technology, Graduate School, PhD in Chemical Engineering
Name and Affiliation of Cosupervisor(s)	Assoc. Prof. Sevgi Kılıç Özdemir (IZTECH)
Name and Affiliation of Co-supervisors	Prof. Bunyamin AKGUL (IZTECH) Prof. Gunes OZHAN (IBG)
Research Environment and Infrastructure	The project will be implemented by a team gathered from academicians in the field of chemical engineering, molecular and cell biology, oncology and radiology. Besides the cosupervisors, Prof. Zekiye Altun at Basic Oncology and Assoc. Prof. Mustafa Barış at Department of Radiology in Dokuz Eylul University also will be involved in the project, with their expertise, laboratories and equipment. Main equipment in the laboratory include fluorescence microscopy, Beckman Multisizer 4 coulter counter, Zetasizer nanoZS, Microplate reader, Langmuir-Blodgett system equipped with KSV Optrel BAM 300 Brewster Angle Microscope, VisualSonics Vevo 2100 Ultrasound imaging system (ultrahigh frequency small animal ultrasound system), animal laboratory equipments (including metabolic cages, individually ventilated cages, animal activity monitoring system, etc).
Scientific Context of the Project	Cancer is a leading cause of death worldwide. Treatment usually includes surgery, radiotherapy, and/or systemic therapy such as chemotherapy. Unfortunately, the chemotherapy drugs used in the cancer treatment affect not only the cancer cells but also the healthy cells by distributing in the other regions of the body, causing as cardiotoxic, nephrotoxic, hematological side effects. Moreover, chemotherapy drugs are extremely susceptible to efflux pumps on the cell membrane pumping anticancer drugs out of cells, a process known as multidrug resistance and thus resulting in intracellular sub-lethal drug concentration and failure of chemotherapy treatment.

	Therefore, it is necessary to develop new strategies to enhance the effectiveness of chemotherapy. Drug efflux mediated by membranal P-glycoprotein (P-gp) is believed to be one major cause of multidrug resistance. It has been proven that nano-sized drug delivery systems can bypass P-gp mediated drug efflux. Ultrasound has been shown to have the ability to open transient pores in the cell membranes (sonoporation effect) and thus overcome multidrug resistance also in cancer cells, enhancing delivery of drugs through the cell membrane.
Brief Workplan	1st year - Preparation and characterization of targeted anticancer drug-loaded nano vesicles 2nd year- Preparation of microbubbles and their conjugation with drug loaded nano vesicles 3rd year - In vitro evaluation of drug delivery system 4th year - In vivo evaluation of drug delivery system
Innovative Aspects of the Project	In this project, targeted anticancer drug-loaded nano-sized vesicles will be prepared for a specific cancer model and injected into a tumor-bearing small animal under ultrasound. This study aims to design, preparation and evaluation of a targeted nano-sized drug delivery system which facilitates the drug to accumulate at the tumor site followed by their entry into cancer cells by sonoporation. This study aims further to improve ultrasound- mediated delivery by using microbubbles as ultrasound contrast agents developed in our laboratory and registered by Turkish Patent and Trademark Office.
Training Opportunities of the Project	Courses and trainings on in vivo molecular and diagnostic imaging will be provided by Fujifilm VisualSonics (the world leader in ultrahigh-frequency (UHF) ultrasound and photoacoustic imaging systems designed specifically for preclinical translational research) through intersectoral secondments and by University of Pittsburg Medical Center through international mobility.
Interdisciplinary Aspects	The project will be implemented by a strong team gathered from academicians in the field of chemical engineering, molecular and cell biology, oncology, radiology and cardiology.
Intersectoral Mobility **☒ Short Visit** **☐ Secondment**	*Host: Fujifilm VisualSonics* *Context of Mobility:* Courses and training on in vivo molecular and diagnostic imaging, exploitation of research results, and ethics **AND/OR** *Host: Siemens Healthineers (TR and GER)* *Context of Mobility: Research and Innovation Program*
Intersectoral Mobility	*Host: Istanbul Health Industry Cluster (ISEK)* *Context of Mobility: Entrepreneurship Training, Thematic Pre-incubation Program*

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☒ **Short Visit** ☐ **Secondment**	
International Academic Secondment	*Host Supervisor: Prof. Flordeliza Villanueva* *Host Institution: University of Pittsburgh, School of Medicine, Pittsburgh, USA* *Host Department: Department of Medicine* *Duration: 6 months* *Estimated Time of Mobility: 2nd or 3rd year*
Main Supervisor	
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Co-supervisors	
Brief CV	**Prof. Bünyamin Akgül** **E-mail:** bunyaminakgul@iyte.edu.tr **ACADEMIC DEGREES** Ph.D. Genetics — Pennsylvania State University, USA — 2001 M.Sc. Genetics — Pennsylvania State University, USA — 1995 B.Sc. Veterinary — Ankara University, Turkey — 1991 Google Scholar: https://scholar.google.com/citations?hl=tr&user=55y3LvkAAAAJ https://orcid.org/0000-0001-9877-9689
Brief CV	**Prof. Güneş Özhan** **E-mail:** gunes.ozhan@ibg.edu.tr **ACADEMIC DEGREES** Ph.D. Developmental Biology — Eberhard Kals Universitaet Tübingen, Germany — 2009 M.Sc. Molecular Biology — Georg-August-Universitaet Göttingen, Germany — 2005 B.Sc. Molecular Biology & Genetics — Middle East Technical University, Turkey — 2003 Google Scholar: https://scholar.google.com/citations?user=N8a9_1oAAAAJ&hl https://orcid.org/0000-0002-4806-5917