

Biomedical Technologies and Innovation Doctoral Programme (BIOTIN)



Title of the PhD Project	<i>Development of patient derived cancer organoid on a chip platform for preclinical testing of CAR-mediated immunotherapy</i>
Acronym	oCARs (Organoid based CAR screening)
Research Fields of the Project	Molecular Cell Biology, Immunology, Cancer
Keywords	Patient derived cancer organoid, CAR-mediated immunotherapy
Host Institution, Department and Campus Location	Izmir Biomedicine and Genome Center, Dokuz Eylül University Health Campus, Balçova, İzmir
PhD Awarding Institution and Graduate Programme	Dokuz Eylül University, Izmir International Biomedicine and Genome Institute, PhD in Molecular Biology and Genetics
Name and Affiliation of Main Supervisor	Prof. Esra Erdal (IBG)
Name and Affiliation of Cosupervisors	Prof. Mayda Gürsel (IBG) Prof. Devrim Pesen Okvur (IZTECH)
Research Environment and Infrastructure	<p>Izmir Biomedicine and Genome Center (IBG) (https://www.ibg.edu.tr) has effectively started to operate in January 2018 as the first Center of Excellence of Türkiye. The mission of IBG is to develop innovative technologies and products for prevention, diagnosis and treatment of diseases using basic research in life sciences as a driving force. Located within the Dokuz Eylül University (DEU) health campus, IBG houses NEVCELL-Cell Therapy Unit with cGMP facility accredited by Ministry of Health of Türkiye, Drug Analysis and Control Lab. accredited by OECD, vivarium for rodent and zebrafish and Biobank for clinical samples governing by BBMRI as well as 32 research team under basic and translational research program, technological research program and industrial R&D program. The Center has core facilities including imaging, histopathology, bioinformatics, cell cultures,...,which are also open for the use of all public and private sector institutions in Türkiye. IBG is the largest and one of the well-equipped research infrastructures in Türkiye in the field of life sciences. IBG research teams are focused in the fields of cancer, rare diseases, genomics, epigenetics, stem cells and regeneration, immunology and infectious diseases, neuroscience and bioengineering. In addition to these, international conferences and symposiums are held every year, as well as comprehensive training activities such as courses, workshops, summer schools and seminars.</p> <p>Under partnership of IBG, Dokuz Eylül University Izmir International Biomedicine and Genome Institute provides the international graduate programs in 'Molecular Biology and Genetics' (MSc and Ph.D.) and students conduct their research in IBG labs under supervision of research group leader.</p>

<p>Scientific Context of the Project</p>	<p>Immunotherapy using chimeric antigen receptor (CAR)-engineered lymphocytes has shown impressive results in leukemia. However, for solid tumors such as colorectal cancer (CRC), new preclinical models are needed that allow to test CAR-mediated cytotoxicity in a tissue-like environment. Patient-derived cancer organoids (PDCOs) are derived with high success rate from cancer cells of individualized patients. Studies have also shown that PDCOs can recapitulate the biological characteristics of primary tumors including histological complexity and genetic heterogeneity of cancer. When combined with immune cells and fibroblasts, tumor organoids become models for the cancer microenvironment enabling immune-oncology applications. The project will focus to develop an innovative organ-on-a-chip platform combining micro vascularized microfluidic system with patient derived cancer organoid to visualize immune cell (T or NK)-tumor interactions as well as measurements of immune cell cytotoxicity against tumor (and normal-matched) organoids for cancer. So, the organoid based CAR screening platform, named oCARs will offer opportunities in preclinical development and validation of cancer immunotherapy as well as to predict individual patient response to immunotherapy. The project will be led by Izmir Biomedicine and Genome Center (İBG) and will be performed in collaboration with research group leaders from Faculty of Bioengineering and from Izmir Institute of Technology, Faculty of Science, Department of Molecular Biology and Genetics. Moreover, XNK Therapeutics, Sweden and Villanova's Center for Cellular Engineering, USA will be the international industry partner and secondment of the project.</p> <p>https://www.ibg.edu.tr/research-programs/groups/erdal-lab/</p>
<p>Brief Workplan</p>	<p>Phase 1- PhD Courses, Research Project Writing, Seminars & Journal Club</p> <p>Outcomes: Having Excellence Knowledge in Cell Biology, Immunology, Stem Cell Biology and Matlab, Project Application to National and International Calls (at least 2)</p> <p>Phase 2- PhD Courses & Qualification Exam, Research Project (Management, wet lab experiments), Seminars & Journal Club, Innovation Courses</p> <p>Outcomes: Having Excellence Knowledge in Cell Therapies and Bioengineering, Improved skills in research and design, creativity, problem-solving and innovation for entrepreneurs: from idea to marketplace.</p> <p>Phase 3- Developing PDCO on a chip Platform, Research Project (wet lab experiments), Visit to NovaCell-Center for Cellular Engineering in Villanova University (6 months), Attending International Congress</p> <p>Outcomes: oCARs Platform prototype, Oral and/or poster presentation</p> <p>Phase 4- Testing CAR-T on oCARs Platform, Research Project (Experiments, Data Analysisi & Scientific Paper writing), Visit to XNK Therapeutics, Attending International Congress</p> <p>Outcomes: Successful screening of CAR-T therapy candidates on oCARs Platform, At least one scientific paper and one patent application</p>
<p>Innovative Aspects of the Project</p>	<p>Patient derived cancer organoids (PDCOs) have many potential uses to predict personalized chemotherapy responses guiding therapy. Besides conventional chemotherapies, Chimeric antigen receptor (CAR) T-cell therapy is a way to get immune cells called <i>T cells</i> to fight cancer by changing them in the lab so they can find and destroy cancer cells. There have been several CAR T-cell agents approved by the FDA to treat hematologic malignancies. However, this type of therapy has not seen the light of victory in the fight against solid tumors because of various restricting caveats including heterogeneous tumor antigen</p>

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	<p>expression and the immunosuppressive tumor microenvironments (TME) that negatively affect the tumor-site accessibility, infiltration, stimulation, activation, and persistence of CAR-Ts.</p> <p>oCARs platform will have novelty with having microvascularized channels to mimic a physiologically relevant transport system to deliver candidate CAR-Ts as well as co-culture with other immune cells to recapitulate TME.</p>												
Training Opportunities of the Project	<p>PhD candidate will have several training opportunities during her/his education in Türkiye and in a broad. They will be trained in the area of patient derived organoid technology, CAR-mediated therapies, pre-clinical drug screening, organoid on a chip and bioengineering.</p> <p>Moreover, Co-FUND programme will cover the innovation courses in which candidate will have some certifications and IBG will serve her/his some trainings including lab biosafety, imaging, bioinformatic, cell engineering.</p>												
Interdisciplinary Aspects	<p>Developing organoid based CAR screening platform (oCARs) requires different disciplines on the cell biology, biochemistry, immunology and bioengineering as well. On this interdisciplinary approach, researchers will have deep knowledge and experience about patient derived cancer organoid technology, organoid on a chip technology, microfluidics, bioprocessing and micro bioreactor systems, developing CAR based therapies</p>												
Intersectoral Mobility <input type="checkbox"/> Short Visit <input checked="" type="checkbox"/> Secondment	<p>Host: XNK Therapeutics, biotechnology company located in Sweden</p> <p>Context of Mobility: Under collaboration, PhD candidate will test the efficacy of individualized natural killer (NK) or T cell-based cancer therapies on the oCARs platform.</p>												
Intersectoral Mobility <input checked="" type="checkbox"/> Short Visit <input type="checkbox"/> Secondment	<p>Host: Istanbul Health Industry Cluster (ISEK)</p> <p>Context of Mobility: Entrepreneurship Training, Thematic Pre-incubation Program</p>												
International Academic Secondment	<p>Host Supervisor: Prof. William J. Kelly</p> <p>Host Institution: Villanova University, Center for Cellular Engineering, Villanova, USA</p> <p>Host Department: Biochemical Engineering and BioProcessing Laboratory</p> <p>Duration: 6 months</p> <p>Estimated Time of Mobility: After 2nd year of PhD program</p>												
Main Supervisor													
Brief CV	<p>Prof. Esra Erdal</p> <p>E-mail: esra.erdal@ibg.edu.tr</p> <p>ACADEMIC DEGREES</p> <table border="0"> <tr> <td>Ph.D.</td> <td>Molecular Biology and Genetics</td> <td>Bilkent University, Türkiye</td> <td>2002</td> </tr> <tr> <td>M.Sc.</td> <td>Biotechnology</td> <td>Middle East Technical University, Turkey</td> <td>1994</td> </tr> <tr> <td>B.Sc.</td> <td>Biology</td> <td>Middle East Technical University, Turkey</td> <td>1991</td> </tr> </table>	Ph.D.	Molecular Biology and Genetics	Bilkent University, Türkiye	2002	M.Sc.	Biotechnology	Middle East Technical University, Turkey	1994	B.Sc.	Biology	Middle East Technical University, Turkey	1991
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