Biomedical Technologies and Innovation Doctoral Programme (BIOTIN)

Title of the PhD Project	**Structure-based detection of critical mutations in redesigning protein-protein interfaces**
Acronym	**PROT-ON**
Research Fields of the Project	Computational Structural Biology
Keywords	Mutation, modeling, structural biology, simulation
Host Institution, Department and Campus Location	Izmir Biomedicine and Genome Center, Dokuz Eylul University Health Campus, Balcova, İzmir
PhD Awarding Institution and Graduate Programme	Dokuz Eylul University, Izmir International Biomedicine and Genome Institute, PhD in Biomedicine and Health Technologies
Name and Affiliation of Main Supervisor	Asst. Prof. Ezgi Karaca (IBG)
Name and Affiliation of Co-supervisors	Assoc. Prof. Gökhan Karakulah (IBG) Asst. Prof. Işıl Öz (IZTECH)
Research Environment and Infrastructure	IBG (Izmir Biomedicine and Genome Center) is the first independent and international life sciences research institution of Turkey. It is established with the aim of being a prominent health sciences hub in the MENA and South European regions. It has 28 independent basic and translational research groups working in diverse areas, such as genomics, epigenetics, bioinformatics, cancer biology, and bioengineering. Karaca Lab situation in IBG offers spacious office space and the necessary high performance computing facility required to carry out the proposed project. Karaca Lab also works in close collaboration with the bioinformatics and several experimental departments of IBG (https://www.ibg.edu.tr/research-programs/groups/karaca-lab/).
Scientific Context of the Project	Uncovering the principles of protein-protein interactions is essential for dissecting their biomolecular function. Computational methods developed based on this idea have recently been able to redesign the available biomolecular interactions. It has been shown that a handful of such methodologies could gain some proteins a new function. Considering the time course of the evolution, being able to re-model protein interactions in the computer environment is an unprecedented development. Therefore, day by day, the protein interaction re-design field has been gaining popularity. Though, the fact that the existing methods;

	(i) have a complicated algorithm, (ii) are not flexible enough to adapt themselves toward different binding types, (iii) are unable to make predictions of opposite characteristics, such as mutations that both enhance or abolish binding, (iv) do not have a scoring function that can eliminate noisy solutions via a statistics-based function, (v) do require big computational resources, which are unreachable for many institutions, creates an avenue for methodological improvement.
Brief Workplan	Year 1: Benchmarking the available methods for predicting the impact of mutations Year 2: Development of a new design algorithm that takes the best of the available methodologies Year 3: Testing the outcome of the algorithm through experimental collaborations Year 4: Establish a web service for the approach
Innovative Aspects of the Project	Taking the above-described problems into account, we will design the PROT-ON method, which aims at determining critical mutations that can strengthen or weaken protein-protein interactions based on the available protein complexes. PROT-ON targets to realize this objective in a reliable, flexible, and accessible manner.
Training Opportunities of the Project	The PhD candidate will have the opportunity to work in a leading interdisciplinary research institution, while working in a collaborative lab environment.
Interdisciplinary Aspects	The project combines different aspects of biophysics, computational structural biology, biochemistry, and protein design.
Intersectoral Mobility **☒ Short Visit** **☐ Secondment**	*Host: Solaris Genomic Health* *Context of Mobility: New skills and techniques for research in genomic, metagenomics, functional genomics and bioinformatics*
Intersectoral Mobility **☒ Short Visit** **☐ Secondment**	*Host: Istanbul Health Industry Cluster (ISEK)* *Context of Mobility: Entrepreneurship Training, Thematic Pre-incubation Program*

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International Academic Secondment	*Host Supervisor: Marisa Gil* *Host Institution: Polytechnic University of Catalonia* *Host Department: Computer Architecture Department* *Duration: 6 months* *Estimated Time of Mobility: 3rd year of the PhD*
Main Supervisor	
Brief CV	**Asst. Prof. Ezgi Karaca** **E-mail:** ezgi.karaca@ibg.edu.tr **ACADEMIC DEGREES** Ph.D. Computational Structural Biology Utrecht University, Netherlands 2013 M.Sc. Chemical Engineering Boğaziçi University, Turkey 2008 B.Sc. Chemical Engineering Boğaziçi University, Turkey 2006 Google Scholar: https://scholar.google.com/citations?hl=en&user=5mt6w7MAAAAJ https://orcid.org/0000-0002-4926-7991
Co-supervisors:	
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Brief CV	**Assoc. Prof. Gökhan Karakulah** **E-mail:** gokhan.karakulah@ibg.edu.tr **ACADEMIC DEGREES** Ph.D. Bioengineering Dokuz Eylül University, Turkey 2014 M.Sc. Medical Informatics Dokuz Eylül University, Turkey 2009 B.Sc. Biology Ege University, Turkey 2005 Google Scholar: https://scholar.google.com/citations?hl=tr&user=ac2JQN8AAAAJ https://orcid.org/0000-0001-6706-1375