YEDITEPE UNIVERSITY

Department of Biomedical Engineering

SEMINAR

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RNAi Based Functional Pharmacogenomics for Drug Target Identification in Cancer and Applications of QPCR

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Abstract

A classical technique for determining the function of a gene is to experimentally inhibit its expression in order to examine the resulting phenotype or effect on molecular endpoints and signaling pathways.

RNA interference (RNAi) is one of the most recent discoveries of a naturally occurring mechanism of gene regulation, which is triggered by the introduction of double stranded RNA into a cell. This phenomenon can be exploited to down-regulate expression of specific genes by transfecting mammalian cells with synthetic short interfering RNAs (siRNAs). siRNAs can be designed to silence the expression of specific genes bearing a particular target sequence and may potentially be presented as a therapeutic strategy for inhibiting transcriptional regulation of genes, which in such instances constitute a more attractive strategy than small molecule drugs. Low dose drug and siRNA combination studies are promising strategies for the purpose of identifying synergistic targets that facilitate reduction of cell proliferation. Commercially available RNAi libraries have made high-throughput genome-scale screening a feasible methodology for studying mammalian cell systems. However, it is crucial that any observed phenotypic change be confirmed at either the mRNA and/or protein level to determine the validity of the targeted genes. Quantitative real-time PCR (qPCR) is now widely used owing to its simplicity, wide dynamic range of quantification, sensitivity, and precision, for accurate evaluation and validation of gene expression.

We describe here a high-throughput screening of RNAi based gene silencing process and qPCR validation of specific transcript levels. In light of such advantageous applications, siRNA technology has become an ideal research tool for studying gene function and holds the promise that siRNA-based therapeutic agents will soon

be put to test in clinical trials.

Şükrü Tüzmen / Biography

Dr. Sukru Tuzmen is a molecular biologist, graduated from the Ph.D. program of the Department of Molecular Biology and Genetics, Bosphorus University, Istanbul in 1995. He has more than twenty-three years of multi-disciplinary research experience integrating studies of the molecular basis of human diseases, including cancer genetics. Dr. Tuzmen has a passion for advancing the molecular genetics of diseases by studying the associations between drugs, genes, pathways, and diseases. His mission is to discover and validate links between gene states and disease phenotypes, and further use these links to identify druggable targets to be utilized as biomarkers in the early diagnosis stages of genetic diseases such as cancer.

Dr. Tuzmen has focused his career to develop and apply cutting edge methods and technologies to ensure excellence in translation of his basic scientific research including cancer genetics, from bench to bedside. He has been involved with the development of new high-throughput biochip technologies. Specifically, screening of druggable compound libraries and siRNA libraries, and validation of gene expression levels via quantitative real-time PCR (qPCR) technology.

Previously, as a PhD scholar, Dr. Tuzmen was involved with nationwide screening and prenatal diagnosis of beta-thalassemia in the Turkish population using state-of-the-art molecular biology techniques and has participated in the development of a Nationwide Molecular Diagnostic Reference Laboratory at Bosphorus University. Dr. Tuzmen has received many National and International Scholarships/Awards including a six year NIH Fogarty Fellowship at the Laboratory of Chemical Biology, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD U.S.A. to work on globin gene regulation.

Dr. Tuzmen has been invited to deliver talks in many National and International settings, and he has served on many expert panels including The Research Grant Council, Hong Kong, China.