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Integrated Systems Biology and Drug Discovery Approaches for Combatting Pathogens & Human Diseases

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Abstract

The functions of cells depend on the interactions among genes, metabolites, and proteins through biochemical reaction networks. The malfunctions of these components may change the cell functions and thus cause diseases. Systems biology connects the cell phenotypes with its genotypes and surrounding environments by reaction network analysis. It aims to identify biomarkers essential for regulating the phenotypes (e.g., the growth) of cells. The biomarkers involved in human diseases are potential targets for drug discovery. Since it is costly and time-consuming to test potential drug candidates, computational approaches are essential for accelerating the pace of drug discovery. My research program seeks to implement systems biology approaches to identify biomarkers for cell phenotype regulation and develop computational pipelines to screen small molecule inhibitors for selected drug targets. This talk will highlight the applications of the developed approaches to combat Listeria infection, Alzheimer's disease, and genetic disorders. Listeria infection is caused by Listeria monocytogenes with high-rate mortality. Unfortunately, Listeria monocytogenes has been reported to be resistant to commonly used antibiotics. The genes involved in antimicrobial resistance of Listeria monocytogenes were identified by my group from genomic data analysis. The protein encoded by the top gene Fosx was then used as the drug target, and two chemical compounds were identified and validated by experiments. Alzheimer's disease has become the most common cause of dementia. After decades of extensive studies, eight drugs have been approved by FDA to treat Alzheimer's disease. Only three of these drugs address the fundamental pathophysiology of the disease. A systems biology approach was designed by my group to identify top drug targets from existing clinical data for Alzheimer's disease. Chemical compounds and their common structures were then identified for the selected drug target, i.e., Apolipoprotein E4 (ApoE4). Gene therapy holds tremendous potential for treating various genetic disorders by correcting or replacing defective genes. However, the innate immune response remains a significant hurdle, as it often hinders the successful expression of therapeutic genes. Our research focuses on identifying small molecule inhibitors for a series of antiviral genes (AVGs) to enhance gene therapy efficacy. Specifically, compounds inhibiting AVG OAS1, which is known for its crucial role in activating the immune response that degrades transgenes, were found to enhance luciferase transgene expression in PC-3 and MCF7 cells.

Biography

Dr. Huang is an associate professor in chemical and biological engineering at Villanova University. After he received his B.S. and M.S. degrees from Tsinghua University, he conducted his Ph.D. research at Texas A&M University. Since he joined Villanova University in August 2011, he has been an active researcher in systems biology and drug discovery to combat pathogens and improve understanding of cellular processes involved in gene and cell therapy. His group has developed a computational pipeline to identify small molecule inhibitors for protein targets involved in antimicrobial resistance of pathogens, replication of COVID-19, progression of Alzheimer's diseases, and immune response to hinder gene therapy. He and his colleagues have optimized the growth conditions of T cells for cell therapy. Supported by various federal and industry fundings, his research results have been presented in two patents, 50+ journal papers and 20+ conference papers. Dr. Huang is enthusiastic in bringing his research into classrooms and applying innovative teaching methods to educate students with data modeling and analysis skills. He was awarded the prestigious 2016 ASEE Joseph J. Martin Award. He is the chair-elect of ASEE Middle Atlantic Section. As the director of the master program in Biochemical Engineering at Villanova University, Dr. Huang has the passion for outreach activities to build a strong bioengineering workforce.