conferenceseries.com PULSUS WWW.PULSUS.COM

Ashim Malhotra, Chron Obstruct Pulmon Dis 2017, 2:2
DOI: 10.21767/2572-5548-C1-001

CO-ORGANIZED EVENT

International Conference on **Chronic Diseases**

&

6th International Conference on **Microbial Physiology and Genomics**

August 31-September 01, 2017 Brussels, Belgium

Ashim Malhotra

Pacific University Oregon, USA

Targeting the cardiolipin biosynthetic machinery in KRAS-mutant pancreatic cancer: A search for novel therapeutics

Pancreatic cancer (PCa) has only 6-8% five-year survival rate kills as many as 53,000 Americans each year, and active-duty military personnel and veterans are at a high risk for this fatal disease. Therapy is challenging due to substantial drug resistance and lack of knowledge about how the Kirsten Rous Sarcoma (KRAS) oncogene mutated in 90% cases, affects PCa cell biology. Our approach to address this knowledge gap is to identify synthetic lethal targets (SLTs). SLTs are non-KRAS pathway proteins which when targeted by drugs will initiate apoptosis in the mutant but not the wild type KRAS cells. We hypothesize that the enzymes that make and remodel the mitochondrial phospholipid cardiolipin (CL), cardiolipin synthase (CLS) and tafazzin respectively, are SLTs for PCa. Reason is that suppressing these enzymes specifically in PCa cells with KRAS mutations will compromise the mitochondria in these cells by depleting CL, which will induce apoptosis. We screened FDA-approved drugs for their ability to cause apoptosis and suppress tafazzin and CLS expression in mutant but not wild type KRAS PCa cells and identified the selective estrogen receptor modulator raloxifene as the prime candidate. Our objective is to use raloxifene as a small molecule probe to investigate the involvement of tafazzin and CLS in maintaining and renewing mitochondria in KRAS-mutant PCa cells. Aims of this study are to: Evaluate the effect of suppressing CLS and tafazzin on mitochondrial viability and production; investigate the effect of CLS and tafazzin suppression on mitochondrial function in KRAS-PCa and; determine the mechanism of raloxifene-mediated suppression of CLS and tafazzin. Our proposal delineates the regulation of mitochondrial viability, production and function by mutant KRAS gene, while establishing CLS and tafazzin as SLTs and raloxifene as a potential candidate drug for PCa therapy.

Biography

Ashim Malhotra serves as an Assistant Professor of Pharmacology at School of Pharmacy, Pacific University in Oregon. He is a Pharmacist and Expert in Mitochondrial Pharmacology. He has served as a grant Reviewer for National Science Foundation (NSF) and private biomedical foundations in the United States. He has also served as Chair of the national sub-committee on strategic planning for Biological Sciences Section of the American Association of Colleges of Pharmacy (AACP). During his career, he has been felicitated with awards for teaching, service and scholarship including the American Society of Pharmacology and Experimental Therapeutics Pharmacology Educators award in 2017, the 2016 Pacific University Junior Faculty Award, the 2016 AACP Teacher of the Year Award, and along with his colleagues, the 2014 AACP Innovations in Teaching Award. Prior to joining Pacific University, he worked at the New York University School of Medicine for five years and the New York Methodist Hospital for two years. He received his PhD in 2006 from St. John's University in New York, USA.

ashim.malhotra@pacificu.edu