

International Conference on Pediatrics & Gynecology

Can correcting the $\Delta F508$ -CFTR Proteostasis-Defect rescue CF lung disease?

Neeraj Vij

Department of Pediatrics, The Johns Hopkins University School of Medicine, USA

Protein homeostasis (proteostasis) generates and maintains individual proteins in their folded and functional-competent states. The components of the cellular proteostasis machinery also dictate the functional lifetime of a protein by constantly regulating its conformation, concentration and subcellular location. The autosomal recessive disease cystic fibrosis (CF) is caused by a proteostasis-defect in CF transmembrane conductance regulator (CFTR). The most common CF mutation leading to this proteostasis-defect is the deletion of a phenylalanine residue at position 508 ($\Delta F508$) of the CFTR protein. This $\Delta F508$ -CFTR protein is prone to aberrant folding, increased ER-associated degradation, atypical intracellular trafficking, and reduced stability at the apical membrane. Thus $\Delta F508$ -CF proteostasis-defect leads to an obstructive lung disease characterized by impaired ion transport in airway epithelial cells, mucus buildup in air space and chronic airway inflammation. We assess here if correcting the underlying defect in $\Delta F508$ -CFTR protein processing by therapeutic proteostasis regulator can treat chronic CF lung disease. As a proof of concept, recent studies support that the selective modulation of mutant CFTR proteostasis may offer promising therapies to reverse chronic CF lung disease. Although to quantify the efficacy of therapeutic strategies that not only correct the $\Delta F508$ -CF proteostasis-defect but also chronic lung disease, pulmonary function tests and state of the art molecular imaging technologies that evaluate the state of lung disease need to be utilized. This will lead to the identification of novel therapeutics that can correct $\Delta F508$ -CFTR's underlying proteostasis-defect to treat the obstructive lung disease.

Biography

Dr. Neeraj Vij is an Assistant Professor at Department of Pediatric Respiratory Sciences and Institute of NanoBiotechnology, The Johns Hopkins University. Dr. Vij obtained his PhD in Biotechnology from Indian Institute of Technology, India in 2001 followed by postdoctoral fellowships at Institute of Genetics, BRC, Hungary, University of Heidelberg, Germany and Johns Hopkins University, USA. He joined Johns Hopkins faculty in 2006 and his major research interests includes inflammatory and protein misfolding disorders. The research focus of his laboratory is identification of molecular pathways leading to chronic disease pathophysiology with an aim to identify novel therapeutic sites. At the translational front his laboratory focuses on identification of novel therapeutic strategies including design of small molecules and nano- drug delivery systems.