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Promising molecular mechanisms and therapeutic options for Chronic Obstructive Pulmonary Disease (COPD)

COPD is the third leading cause of mortality in the world and will be the second leading cause of death by 2020. However, the molecular mechanisms for this devastating disease remain largely unknown; currently, the clinical therapeutic options are neither specific and nor always effective. A major characteristic of COPD is expiratory airflow limitation, which can be attributed to airway hyperresponsiveness. A Very Important Player (VIP) in airway hyperresponsiveness is the increased contraction of Airway Smooth Muscle Cells (ASMCs). An increase in intracellular calcium ($[Ca^{2+}]i$) is a key factor in the increased contraction in AMCs. Consistent with this view, bronchodilators including muscarinic receptor antagonists, β-adrenergic receptor agonists and corticosteroids are used as the first-line drugs in the clinical treatment of COPD, and the functional role of all these forefront drugs are associated with their inhibition of the increased $[Ca^{2+}]i$ and contraction in ASMCs. Multiple ion channels such as inositol trisphosphate receptor (IP3R)/Ca^{2+} release channel, Ryanodine Receptor (RyR)/Ca^{2+} release channel and canonical Transient Receptor Potential-3 (TRPC3) channel, play a major role in initiation and maintenance of $[Ca^{2+}]i$. Recent studies suggest that these channels are essential for airway hyperresponsiveness in COPD and other pulmonary diseases. Equally interestingly, IP3R, RyR and TRPC3 channels are highly sensitive to Reactive Oxygen Species (ROS), and ROS are well known to mediate airway hyperresponsiveness and other unleashed cellular responses in COPD. ROS are primarily produced by mitochondria and NADPH oxidase (NOX). A number of antioxidants targeted at mitochondria and/or NOX are currently used in clinical trials and show potential effectiveness in the treatment of COPD. ROS may implement their role in COPD by causing of oxidation of IP3R, RyR and TRPC3 channels, leading to their hyperfunctions. Thus, it is reasonably believed that genetic and pharmacological inhibition of these channels, like antioxidants, may also be effective for therapies of COPD. In support, studies using animals have revealed their therapeutic for airway hyperresponsiveness and COPD.

Biography

Yong-Xiao Wang has been a Full Professor in Albany Medical College (USA) since 2006. Dr. Wang has had extensive research experience in basic, translational and drug research concerning pulmonary hypertension, asthma, chronic obstructive pulmonary disease, diabetes, and cardiac arrhythmia for over 30 years. As the Principal Investigator, he has/had numerous NIH R01 research awards, AHA Established Investigator Award, and various other grants, for which he often holds/held NIH R01 grants with other awards each year. As the corresponding author, first author and key contributor, he has had numerous publications in highly peer-reviewed journals including Antioxid Redox Signal (impact factor: 8.209), Proc Natl Acad Sci USA (9.432), Nature (34.480), Circ Res (9.214), etc. Dr. Wang has been the editor of academic books in the field including one entitled by "Redox Signaling in Health and Disease Pulmonary Vasculature" that was published by Springer (New York) last fall. Dr. Wang has also served as the editorial board member and/or section editor for the Clinical and Translational Medicine, Pulmonary Circulation and several other journals.

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