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Transient Receptor Potential Vanilloid 1 - A Doubtful Ambitious Modality for Manipulation

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Sir,

Transient Receptor Potential Vanilloid 1 (TRPV1) is the most widely studied member of the TRPV family. They act as a non-selective cationic ligand-gated channel on neuronal and non-neuronal cell membrane and highly permeable to calcium. TRPV1 is distributed widely in the peripheral nervous system, autonomic nervous system and different parts of the brain and essential organs such as the pancreas, liver, lung, kidney and heart. TRPV1 acts as a multisensory receptor for receiving potential injury signals, they can be activated by many exogenous and endogenous mediators that involve in physiological reactions, initiate inflammation and transmit pain signal.[1] TRPV1 mediates secretion of proinflammatory factors such as tachykinin and calcitonin gene-related peptide (CGRP) in nerve endings that causes "neurogenic inflammation" which includes bronchoconstriction, tracheal mucosal edema, inflammatory cell chemo taxis and increased protein secretion. Exogenous and endogenous pro-inflammatory mediators such as capsaicin, resiniferatoxin, PGE2, citric acid and low pH lead to inflammation and chronic cough by increasing TRPV1 expression. TRPV1 can impair immune system by the action of a suppressor of interferon-gamma released by CGRP which is a critical cytokine for innate and adaptive immunity, activation of macrophages, stimulation of natural killer cells down-regulation and neutrophils to prevent virus replication and anti-inflammatory action by promoting some interleukins (IL-10). TRPV1 is a chemosensor in sympathetic neurons and promoter of airway inflammation in the non-neural system. All these evidences indicated that capsaicin, a TRPV1 agonist induces the release of IL-8, as a chemokine that triggers cytokine storm in infections while capsazepine, an antagonist of TRPV1 blocks the pro-inflammatory process.[1-4]

TRPV1 has dual action in the respiratory system. TRPV1 blocking acts as an anti-inflammatory factor and used as a novel anti-diabetic drug while TRPV1 activation halt diabetic complications by the effects of vasodilation and anti-atherosclerosis properties.[1,5] There are many factors affecting TRPV1. Aging is a factor that changes the action of TRPV1 from anti-inflammatory function in the young to a pro-inflammatory properties in the elderly population.[6] TRPV1 polymorphism variant is another factor which play role in our response to noxious stimuli that has been studied in type 2 diabetes and cough sensitivity following irritants.[7,8]

In pathologic conditions, both TRPV1 expression rate and their distribution patterns change. They increase in large myelinated A-fiber of dorsal root ganglion neurons and decrease in small unmyelinated C-fiber neurons in diabetes with vascular complications.[1,9,10] All these revealed that expression pattern of TRPV1 channels in immune and inflammatory cells can mediate different, sometimes opposite reactions that currently make it difficult to assign specific, coordinated processes to find the novel effective drugs.[1]

Infections can increase TRP channels. They are up-regulated very early from 2–4 h up to 12 hr in neural and non-neural cells without virus replication following respiratory infection, after then virus-induced soluble factors can increase cytokines such as IL-6 and IL-8 in infected cells and reactive antibodies that downregulate TRP expression rate.[11,12] Such TRPV1 expression rate following infection can be a predictable risk of mortality in Middle East respiratory syndrome (MERS) and severe pneumonia in smokers and in chronic lung diseases.[1,13] TRPV1 ablation improve neutrophil bactericidal functions and decreases pain and severity in some infections.[14] During a respiratory insult, hypoxia can upregulate TRPV1 receptors while capsazepine (a TRPV1 antagonist) alleviate cough following infection and decreases respiratory system airway resistance, tissue damping, area of collapsed lung parenchyma. Resiniferatoxin (RTX), an ultra-potent agonist (chemical ablation) of TRPV1 receptors placed in pulmonary sensory neurons, improves survival against Methicillin-resistant *Staphylococcus aureus* (MRSA) cytokine storm in lethal pneumonia and inhibits CGRP release.[11,12,15] Inspite of all benefits, TRPV1 blocker administration is not safe. It has been shown that RTX prescription cause permanent neurolysis and apoptosis.[15,16]

TRPV1 characteristics predict our response to physiological and pathological conditions. Many studies about TRPV1 focused on managing chronic pain without considering TRPV1 effects on vital organs. Various TRPV1 functions and distribution throughout the body, mechanisms of their activation or control and unpredictable reactions or adverse

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reactions following their use are main obstacles for TRPV1 which interferes as therapeutic target.[1]

CONFLICT OF INTEREST

The Author declares no Conflict of interest.

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