VASOACTIVE AGENTS

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Inflammation is a physiological response to a infections and tissue injury. It could lead to acute phase or to a chronic inflammation, which often has pathologic consequences.[1]

Inflammation process starts with a increase in vascular diameter and vascular permeability followed by chemotaxis and clotting.[2,3]

Inflammation combat the infection by delivering effector molecules, clotting and repairing.[3]

Biotechnology has been taken advantage of vasoactive agents characteristics, to obtain treatments for diseases as we can see it this five important articles:

In the first report [4] they created transgenic mice (l2-IL5) to study Eosinophilic oesophagitis (EoE) which is a is a chronic inflammatory condition of the oesophagus ,with limited treatment option, and they treated it with corticosteroids that significantly reduced eosinophilia and epithelial inflammation.

This kind of studies will lead to a greater understanding of the pathophysiological role of eosinophils in barrier dysfunction and remodelling in EoE.

The second article [5]addresses the issue of vasoactive intestinal peptide (VIP) which is a basic acid peptide that binds to a member of the class II family of G protein-coupled receptors (GPCRs). It is widely expressed throughout the body adn it's expression and signaling is altered in numerous neurological disorders.

They describe the pathology of several major neurological disorders and discuss the potential pharmacotherapeutic role of VIP;

→ In AD and PD; VIP has shown to be a major neuroprotective factor against this inflammatory response by inhibiting microglia-derived proinflammatory factors.

→ADS; this peptide is worthy of future pharmacotherapeutic exploration and design, as several studies have indicated a strong link between this peptide and ASD

Third article explains Septic shock which is characterized by vasoplegia, resulting in inadequate of effective circulatory volume. Some vasopressors are potentially beneficial to counteract inappropriate vasodilation during septic shock and they explain some of them:

Dopamine has equivalent effect on heart and vasculature, which can result in increases in cardiac output, mean arterial pressure and heart rate.

Dobutamine is considered as inodilator because it has potent effect on cardiac systole and vasculature.

Levosimendan calcium. it is shown to be potentially beneficial in reducing mortality risk, but its high cost has limited its use in low-income and middle-income countries.[6]

Fourth article,[7] deals with nitroimidazoles since they have been shown to be potent sensitisers of certain clinically active chemotherapeutic agents. This process of chemopotentiation has been shown to be hypoxia-mediated. The present studies evaluated whether increasing the level of hypoxia in the tumour tissue, by treatment with the vasoactive agent hydralazine, could modify the chemosensitising ability of nitroheterocyclics.

The results imply that the addition of hydralazine to the chemotherapy, or chemotherapy-sensitiser protocol, led to a therapeutic advantage.

In the fifth [8]article explains that tight regulation of vascular permeability is necessary for normal development and deregulated vascular barrier function contributes to the pathogenesis of various diseases, including acute respiratory distress syndrome, cancer and inflammation. The angiopoietin (Ang)-Tie2 pathway is known to control vascular permeability. However, the mechanism by which the expression of Tie2 is regulated to control vascular permeability has not been fully elucidated. Here we show that transcription factor Twist1 modulates pulmonary vascular leakage by altering the expression of Tie2 in a context-dependent way. Twist1 knockdown in cultured human lung microvascular endothelial cells decreases Tie2 expression and phosphorylation and increases RhoA activity, which disrupts cell-cell junctional integrity and increases vascular permeability *in vitro*. In physiological conditions, where Ang1 is dominant, pulmonary vascular permeability is elevated in the Tie2-specific Twist1 knockout mice. However, depletion of Twist1 and resultant suppression of Tie2 expression prevent increase in vascular permeability in an endotoxin-induced lung injury model, where the balance of Angs shifts toward Ang2. These results suggest that Twist1-Tie2-Angs signaling is important for controlling vascular permeability and modulation of this mechanism may lead to the development of new therapeutic approaches for pulmonary edema and other diseases caused by abnormal vascular permeability

As a conclusion we can say that the need for a continue studying of vasoactive agents is evident in order to apply biotechnology in an efficiently way , obtaining therapies against diseases as common as cancer [9].

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