

Reactive Oxygen Species in Inflammation

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ABSTRACT

One of the key signaling molecules that play a major role in inflammation is ROS. Polymorphonuclear neutrophils enhance and activate the generation of ROS at the site of the endothelial dysfunction and tissue injury. The migration of inflammatory cells from blood to tissue is facilitated by the vascular endothelium. Followed by the inflammation there is opening of indo-endothelial junction through which migration of inflammatory cells takes place. The migration of inflammatory cells across the endothelial barrier not only clears the way to pathogens and foreign particles but also causes serious tissue injury. This review highlights the oxidative stress mediated signaling mechanisms involved in inflammation leading to serious illnesses like diabetes.

Inflammation is highlighted as a defective immune response that is conferred by the host against the foreign pathogens. The body's own inbuilt immune system response which is triggered under the encountering of the pathogenesis is referred as innate immunity. This elicits many acute inflammatory responses accompanied by systemic vasodilation, vascular leakage and leukocyte immigration. According to the roman physician Celsius, the four cardinal signs of localized acute inflammation are calor, heat, rubor, redness, tumor swelling and dolor pain leading to impairment of function.

The recognizing of the wide range of pathogens by the innate immune system is due to the presence of germ-line encoded receptor known as Pattern-Recognition Receptors (PPRS). TLRs (Toll like Receptors) C type lectin receptors and NLR (Cytoplasmic Nod like Receptors) came under the category of PPRS. Those receptors recognize the pathogen associated molecular patterns as well as the danger associated molecular patterns released by the mechanism of dsDNA and uric acid crystals. The PPRS are expressed as a variety of immune cells includes macrophages, neutrophils, monocytes and DCs (dendritic cells) helping in the early detection of the pathogens.

Followed by the activation of the immune response, the activation of acute immune response takes place resulting in the secretion of cytokines and chemokines. The first cells that act is neutrophils, which by adhering to the endothelial wall and later migrating to vascular wall at the site of infection, engulf the invading pathogens. It also secretes vasoactive as well as pro-inflammatory mediators. The early vascular change at the site of infection is due to the pro inflammatory mediators. The mediators include histamine, PAFS (platelet activating factor, bradykinins and thrombins. These increase the vascular permeability followed by fluid accumulation (edema) and leukocyte extravasation. If innate immune system exceeds its capacity or if its defensive capacity is limited, the adaptive immune system is engaged acting specific T and B cells for pathogen clearance. If this process also gets

inefficient it progresses to chronic state of inflammation. This is associated with many diseases such as diabetes and many heart diseases. The center of progression of many inflammatory disease is the production of ROS. The PMNS (polymorphonuclear neutrophils) are the ones which produce ROS. This promotes the oxidation of cellular signaling proteins such as tyrosine phosphatases promoting endothelial dysfunction. The two roles played by ROS in inflammation are as a signaling molecule and a mediator. Superoxides like ROS can easily diffuse with NO and can form RNS (reactive nitrogen species). This induces nitrosative stress which adds to the proinflammatory burden of ROS. The focus of this review is the ROS dependent mechanism of inflammation leading to diseases like diabetes.

Intricate relationship between oxidative stress and inflammation has been described by various intensive researches in to mechanisms of inflammation. The principle objective of inflammation is the clearance of pathogen from the body. In this process the fundamental role is played by the ROS produced by the phagocytic cells. For maintaining homeostasis ambient level of ROS is needed whereas for killing pathogens excessive ROS is needed, uncontrolled generation of ROS leads to tissue injury. So the generation of ROS plays a crucial role in inflammation. It is also important to the pathogenesis of tissue injury. Even though the role of ROS in chronic inflammatory diseases such as diabetes, heart diseases is known, the how they contribute to the mechanism is still under study.

Keywords: Inflammation; Neutrophil; Immune System; Cytokines.