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Chemical Signals in Immunology

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ABSTRACT

Kianic acid, glutamate, radiation and plant extracts are substances that produce a chemical signal in cell systems. These substances have the ability to upregulate caspase-3 expression, as well as a result in the migration of cellular components, viz. mast cells and macrophases, at the site of inflammation. This communication discusses chemical signal in immunology and their importance in regulating cellular responses.

KEYWORDS: Cytokines, Oxygen Radicals, Bax-Bcl Ratio, Null Mutation, Cellular Response, Ca^{2+}/calmodulin, thrombus, Injury, Caspase-3

Immunology is a branch of science, which encompasses biology and a variety of cellular components. Some of these cellular components are the immunoglobulins, viz. IgA, IgE, IgG, etc. These immunoglobulins each have a definite role in the cell, particularly during infection. For example, IgE has been found to be pivotal during skin inflammation reactions, since it has been found in rat experiments that the concentrations of IgE increases in response to skin injury. This skin is usually observed as being skin rupture and is often treated with diclofenic acid. Upon treatment, the levels of IgG cytokine increases at the site of infection, and this causes the migration of mast cells to the ruptured site where cellular responses begins. Therefore, IgE provides a chemical signal for tissue response in mammals (Singh, 2020). Another example where chemical signals are important are in artificial cell death studies. From an immunology perspective, these chemical signals are important in order to maintain homeostasis of a strong immune system (Singh and Reddy, 2012b). This means that artificial cell death studies, also known as programmed cell death, can be studied using cytokine signals to maintain the function of healthy cells, while eliminating harmful cells. For example, it is obvious that free oxygen radicals are harmful to cellular components and may cause the elimination of healthy cells, or the proliferation of harmful cells (Singh and Reddy, 2012a). Studies using extracts of *Bulbine frutescens* has been found to stimulate cell growth in cancer of the larynx, while the apoptotic inhibitors were able to inhibit the proliferation on of the same cancer. This has been ascribed to the release of calcium from endoplasmic reticulum (Hengartner, 2000), which has the ability to repair damaged membrane tissues (Singh and Reddy, 2012a). In addition, the inhibition of apoptosis, as well as the extracts of *Bulbine natalensis* and *Bulbine frutescens*, have been found to exhibit varying response in Hep-2 and HeLa cancer cells. This mixture in chemical signals mean that there could be a possibility that antioxidants have a repair function in these cell systems i.e. the antioxidants present in the extracts (Singh and Reddy, 2012a).

Although chemical signals can be of varying degrees in cells, ultimately the transducing the amplifying degree of the signal depends on the age of the cells. It has been found that ageing in poly-morphonuclear neutrophils (PMN) have a profound effect in apoptosis (Weinmann *et al.,* 1999). In this cell line, the decrease in expression of Bcl-X1 protein has been found to enhance the susceptibility

of PMN to programmed cell death. In addition, spontaneous apoptosis may also be present, depending on the rate of Bax-γ / Bcl-X1 ratio cellular components present (Weinmann, 1999).

During apoptosis, the cellular signals are transduced by many kinds of proteins, but, perhaps, the most important proteins are the anchoring, adaptor and scaffolding proteins (Open University, 2020). These proteins mediate the chemical signals into the cell. The immunological responses caused by these signals are either morphological or biochemical, and their effect depends on the threshold of the signal transduced (Jia *et al*., 2009). Although programmed cell death is driven by bax, bcl-2 and caspase-3 proteins, chemical messengers such as TNF- α, or tumour necrosis factor, amongst other, viz. interleukin-1 and interferon gamma (IFN-γ) produced by inflammatory cells also affect cellular responses (Mallat and Tedgui, 2000). Some immunological outcomes during inflammation in cells are the recruitment of macrophases to the site of infection. This is known to induce apoptosis by receptor-ligand mechanism, particularly in smooth muscle cells, where apoptosis is medicated by DAP proteins, which is autophosphorylated (Cohen *et al*., 1997). This enzyme is stimulated by the ratio of Ca^{2+} / calmodulin in the cell, and is also present in carotid endarterectomy specimens and mammary arteries (Martinet *et al*., 2002). When Bax proteins associate with DAP-kinase, atherosclerotic plagues in the smooth muscle cells increase, causing cell rupture. The immunological response is that a thrombus forms at the site of injury, causing the formation of a blood clot (Mallat and Tedgui, 2001). However, prior to clot formation, rupture occurs due to TNF-α and the release of the mentioned cytokines. Interleukin -1, TNF- α and IFN-γ causes Bax and p53 proteins to increase, while concurrently causing Bcl-2 proteins to remain substantially low (Martinet *et al*., 2002).

When cells are damaged due to DNA fragmentation or ageing, the p53 protein mediates cell cycle arrest. This immunological response has been exhibited by cultured cortical, hippocampal and sympathetic neurons, when they were exposed to isclaemia or kianic acid (Slack *et al.,* 1996). In mice that have a p53 null mutation, brain damage by the mentioned chemicals appeared to be less compared to p53-deficient mice (Crumrine *et al*., 1994). Kianic acids, in addition to glutamate are the main chemical signals for neuron cell arrest (Hengartner, 2000). However, p53-mediated cell deaths in neurons are able to occur without Bax protein upregulation, because the mentioned chemical substances affect the potassium concentration of cells (Singh, 2020). In cerebellar granule neurons, it has been stated that Bax upregulation plays a pivotal role n caspase-3 expression, and, thus, Bax deformity may result in the production of cells, thereby highlighting the protective function of Bax, as well as the activation of caspase-3 (Singh and Reddy, 2012a). The immunological response of cell systems are triggered by many compounds, *viz.* plant extracts, natural products, chemical stimuli and radiation. Even though chemical signals may enhance or diminish an immunological response in a cell, immunoglobulins will always play a pivotal role at sites of injury or inflammation. However, the chemical signals may cause cellular damage in the tissue or system of an organism due to the cleavage of DNA into interchromosomal fragments, nuclear breakdown, cell shrinkage, mitochondrion membrane and the release of apoptotic bodies, induced by a chemical substance (Singh, 2020).

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Rishan Singh is a biologist based in the province of KwaZulu-Natal in Durban, South Africa. He has published widely in the plant sciences. During the early phases of his career, his research focussed on the physiology of plants. He has had several career transitions as a biologist. At the University of KwaZulu-Natal and the Durban University of Technology, he has had some teaching responsibility in addition to laboratory exposure with students. He has enjoyed scholarships from the South African National Research Foundation and a private institution in South Africa. His science contributions have varied over the years, and have encompassed many disciplines. He has also published English literature.