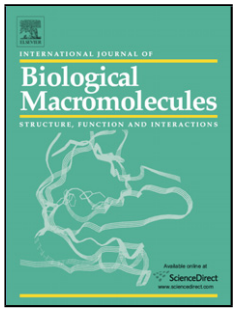

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PII: S0141-8130(17)34595-6
DOI: https://doi.org/10.1016/j.ijbiomac.2017.12.101
Reference: BIOMAC 8763

To appear in: *International Journal of Biological Macromolecules*

Received date: 20-11-2017
Revised date: 15-12-2017
Accepted date: 19-12-2017

Please cite this article as: Sandra M.Burin, Danilo L.Menaldo, Suely V.Sampaio, Fabiani G.Frantz, Fabíola A.Castro, An overview of the immune modulating effects of enzymatic toxins from snake venoms, International Journal of Biological Macromolecules https://doi.org/10.1016/j.ijbiomac.2017.12.101

An overview of the immune modulating effects of enzymatic toxins from snake venoms

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Abstract: Snake venoms are complex mixtures of organic and inorganic compounds, including proteins belonging to the protease (serine and metalloproteinases), oxidase (L-amino acid oxidases), and phospholipase (especially phospholipases A_2) enzyme classes. These toxins account for the serious deleterious effects of snake envenomations, such as tissue necrosis, neurotoxicity, and hemorrhage. In addition to their toxic effects, snake venom toxins have served as important tools for investigating the mechanisms underlying envenomation and discovering new pharmacologically active compounds with immunotherapeutic potential. In this sense, the present review discusses the new findings and therapeutic perspectives in the immune modulating potential of enzymatic toxins from snake venoms belonging to the classes metalloproteinase, serine protease, L-amino acid oxidase, and phospholipase A_2.

Keywords: Snake venoms; enzymatic toxins; immune system.

1. Introduction

The immune system is composed of cells (leukocytes and platelets) and soluble factors (or components of the humoral immune response, like complement system proteins, antibodies, acute-phase proteins, and arachidonic acid-derived lipid mediators) that work together to keep the host homeostasis by killing pathogenic microorganisms, clearing antigens, and maintaining the self-tolerance. As immune system imbalances can result in inflammatory and autoimmune diseases, hypersensitivity, cancer, and immunodeficiency, this system must be tightly regulated [1]. Modulation of the immune system may help to control exacerbation of the immune response in autoimmune and inflammatory diseases, as well as to activate the immune system components in antitumor responses and immunodeficiencies.

Recently, several medical and scientific studies have been searching for new treatment strategies, known as immunotherapy, which consists in the use of substances able to activate immune cells to battle the progression of different disorders, such as cancer and autoimmune diseases [2]. Considering the biodiversity of snake venoms, which are complex mixtures of organic and inorganic compounds, including enzymatic and non-enzymatic proteins, peptides, and non-protein molecules [3], one would expect that they could be potential sources of new immune modulating agents. Thus, the comprehension of the mechanisms underlying the immune modulating action of snake venom toxins may help to design new synthetic compounds or to engineer novel nanoconjugated molecules to pharmacologically manipulate the immune response. An example is the use of nanotechnology to build nano-engineered drug carrier systems with advantages in targeted delivery and controlled release [4, 5]. Some recent studies have shown the therapeutic potential of the nanoparticle-sustained delivery of snake venom toxins in cancer treatments by using silica or gold nanoparticle conjugates as a strategy to enhance the cytotoxicity of venom components on targeted tumor cells and reduce their toxicity towards normal cells [5-10].