

## Immune mediators produced by Ts2 and Ts6 isolated from *Tityus serrulatus* scorpion venom

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**Introduction:** Scorpion envenomation has become a public health problem in many regions of the world due to the increasing number of accidents. In Brazil, *Tityus* is the main genus responsible for scorpion envenomation. Scorpion venom mainly consists of neurotoxins that bind to specific sites on ion channels of cell membranes leading to an increase in their permeability. *Tityus serrulatus* venom (TsV) induces a systemic inflammatory response characterized by increased levels of cytokines and chemokines. The pulmonary edema is the main cause of children death. There are many studies regarding venom actions, however little is known about the interactions of the fractions IX (Ts2) or X (Ts6) with the immune system. **Objective:** Our aim was to characterize the local and systemic inflammatory response induced by intraperitoneal injection (i.p.) of Ts2 or Ts6 isolated from *T. serrulatus* venom. We analyzed influx of leukocytes into the peritoneal cavity and the profile of white blood cells. In addition, we investigated the production of cytokines and oxide nitric (NO) in the lavage peritoneal cavity. **Methods:** Ts2 or Ts6 (250µg/Kg) or PBS were injected in the peritoneal cavity of 129sv mice and after 4, 24 and 96 hours the lavage fluid was collected. Blood and peritoneal total cells were counted in Turk solution using Neubauer chambers. Differential peritoneal and blood leukocyte counts were obtained using Panoptic-stained (Laborclin, Paraná, Brazil) cytospin preparations. Cytokines were measured by ELISA and nitric oxide (NO) by Greiss method. **Results:** The kinetics of cell recruitment induced by either Ts2 or Ts6 revealed an increase in neutrophils in the blood and in the peritoneal cavity. In contrast, mononuclear cells were elevated mainly after 96 hours. Our results also demonstrated that Ts2 or Ts6 toxins were not able to stimulate NO, however they stimulated the release of inflammatory cytokines, such as IL-6, TNF- $\alpha$ , TGF- $\beta$ , IL-1 $\beta$  and IFN- $\gamma$  in different manner depending of the time-point analyzed. **Conclusion:** Our results showed that Ts2 and Ts6 induced an inflammatory response with recruitment of neutrophils and inflammatory cytokines in a time-dependent manner. We suggest that the physiopathological manifestations of *T. serrulatus* envenomation may be mediated by the release of inflammatory mediators. These finding could be important in the development of specific drugs for scorpion sting therapy.

**Keywords:** *T. serrulatus*; Ts2; Ts6; cytokines; oxide nitric.

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