ENGINEERED ANTIBODY FRAGMENTS FOR RECOGNISE AND NEUTRALIZE THE DERMONECROTIC TOXINS OF LOXOSCELES INTERMEDIA

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Loxosceles spiders have a worldwide distribution and are considered one of the most important medical group of spiders. Envenomation (loxoscelism) can result in degenerative necrotic skin lesions, kidney failure, hematological disorders and, less commonly, in a systematic illness that can be fatal. In Brazil, loxoscelism is a serious public health threat and three prominent species (L. intermedia, L. gaucho and L. laeta) are responsible for more than 6000 cases of envenomation per year. There is a wide variance in envenomation profile of patients and diagnosis is difficult due to the number of diseases that mimic loxoscelism. In addition, no definite therapy has yet been established and serum therapy has been used clinically since several decades. In such a context, it is of interest to consider the design of standardized recombinant antibody fragments not only for diagnosis and specific detection of individual circulating toxins in biological fluids of envenomed patients but also for venom’s neutralization and treatment. We prepared a hybridoma that secretes an IgG (LiMab7) reacting with L. intermedia venom components of 32-35 kDa. This monoclonal antibody shows high neutralizing potency for the dermonecrotic activity of the venom. It has now been re-engineered into colorimetric bifunctional protein consisting in the corresponding single-chain antibody fragment (scFv) fused to alkaline phosphatase of E. coli. This recombinant fusion protein can be used for rapid, specific and sensitive immunodetection of L. intermedia toxins. In addition, antibody LiMab7 has been reformatted into diabody structure with high neutralizing potential. This work paves the way to the design of well-standardized reagents with high potential for diagnosis and treatment of envenomed patients. Key words Loxoscelism, recombinant antibody, diagnosis. Financials Support: CNPq, CAPES and Fundaçao Araucaria.