Divergence in toxin antigenicity and venom enzymes in Tityus melici, a medically important scorpion, despite transcriptomic and phylogenetic affinities with problematic Brazilian species

Yan Kalapothakis, Kelton Miranda, Matheus Aragão, Débora Larangote, Gracielle Braga-Pereira, Marina Noetzold, Denis Molina, Rafael Langer, Izabela Mamede Conceição, Clara Guerra-Duarte, Carlos Chávez-Olórtegui, Evanguedes Kalapothakis, Adolfo Borges

Abstract

The Brazilian scorpion Tityus melici, native to Minas Gerais and Bahia, is morphologically related to Tityus serrulatus, the most medically significant species in Brazil. Despite inhabiting scorpion-envenomation endemic regions, T. melici venom remains unexplored. This work evaluates T. melici venom composition and function using transcriptomics, enzymatic activities, and in vivo and in vitro immunological analyses. Next-Generation Sequencing unveiled 86 components putatively involved in venom toxicity: 39 toxins, 28 metalloproteases, seven disulfide isomerases, six hyaluronidases, three phospholipases and three amidating enzymes. T. serrulatus showed the highest number of toxin matches with 80–100 % sequence similarity. T. melici is of medical importance as it has a venom LD_{50} of 0.85 mg/kg in mice. We demonstrated venom phospholipase A2 activity, and elevated hyaluronidase and metalloprotease activities compared to T. serrulatus, paralleling our transcriptomic findings. Comparison of transcriptional levels for T. serrulatus and T. melici venom metalloenzymes suggests species-specific expression patterns in Tityus. Despite close phylogenetic association with T. serrulatus inferred from COI sequences and toxin similarities, partial neutralization of T. melici venom toxicity was achieved when using the anti-T. serrulatus antivenom, implying antigenic divergence among their toxins. We suggest that the Brazilian therapeutic scorpion antivenom could be improved to effectively neutralize T. melici venom.