Krisna Prak[1], Christin Luft[2], Janos Kriston-Vizi[2], Vania M. M. Braga[1]

[1] *National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, UK*

[2]*Laboratory for Molecular Cell Biology, University College London, London, UK*

Insight into structure-function of Bothrops atrox snake venom LAAO and its mechanism of action on cell apoptosis

ABSTRACT

Snakebite is a major health issue worldwide with long-lasting impairment of patient income and the quality of life. There is currently a poor understanding of the cellular mechanisms triggered by snake toxins underpinning the devastating symptoms during envenomation. LAAO is a highly toxic enzyme that oxidises L-amino acids and participates in tissue necrosis. Kinetic analyses and mechanistic studies using recombinant LAAO reveal key catalytic residues and striking cellular defects preceding cell death. LAAO wild-type increases oxidative stress levels and inhibits autophagic flux, reducing lysosome number and size. Higher mitochondrial fission indicates that LAAO impairs mitochondria dynamics and function, leading to mitophagy. However, mitochondrial clearance is prevented by the lysosomal defects. These phenotypes are accompanied by a shutdown of cell respiration and energy production. Thus, LAAO cytotoxicity targets co-ordinately the function of essential organelles and compromises cell metabolism and fitness prior to cell death. Our work highlights potential steps to reverse LAAO toxicity and facilitate adaptive cellular responses to restore homeostasis.

doi.org/10.51219/URForum.2026.salahaldeen-m-a-aljafreh | ISBN: 978-1-917892-52-0