Indian Journal of Experimental Biology
Vol. 56, February 2018, pp. 101-111

Proteomic investigation of the molecular mechanism of king cobra venom L-amino acid oxidase induced apoptosis of human breast cancer (MCF-7) cell line

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Received 20 May 2015; revised 24 May 2017

Snake venom is known for its therapeutic applications since long. Researchers have earlier demonstrated antiarthritic, anticancer, anti-inflammatory, antinociceptive activities of snake venom toxins apart from their use in the treatment of alzheimer's disease, neural trauma, parkinson's disease, stroke, etc. King cobra [*Ophiophagus hannah* (Cantor)] venom L-amino acid oxidase (OH-LAAO), a LAAO that possesses unusual thermal stability, also exhibits potent and selective antiproliferative activity against human tumorigenic cell lines. In this study, we investigated molecular mechanism of the enzyme induced apoptosis by examining the differential protein expressions in MCF-7 cell after treatment with the enzyme, using 2DE for separation and MALDI-TOF/TOF for protein identification. Proteomic analysis revealed a total of 21 differentially expressed proteins that are involved in various biological processes, of which 8 were involved in LAAO-induced cell death, including stress response, oxido-reduction, protein ubiquitination, proteolysis, and apoptosis. Upregulation of NADPH-cytochrome P450 reductase, in particular, may trigger excessive production of cellular ROS and contribute further to cellular oxidative stress and potentiate the cytotoxic action of the enzyme. These alterations of protein expression that are involved in different pathways or cellular functions were presumably caused by the non-specific oxidative modification of transcriptional factors, which may further modulate the activity of the signalling proteins that eventually lead to apoptosis and cell death. The results are consistent with earlier observations from gene expression studies that also demonstrated the involvement of non-specific oxidative modifications of signalling molecules in the apoptosis induced by OH-LAAO.

Keywords: Anticancer, Antiproliferative activity, Breast adenocarcinoma, Cytotoxicity, MALDI-TOF/TOF, *Ophiophagus hannah*, Oxidative stress, 2D-PAGE, Protein expression, ROS, Snake vernom, Transcriptional factors modification