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Title: Interaction of a snake venom L-amino acid oxidase with different cell types membrane

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### ACCEPTED MANUSCRIPT

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1314 **Abstract** 

- Snake venom L-amino acid oxidases are multifunctional enzymes that exhibited a wide range of
- pharmacological activities. Although it has been established that these activities are primarily
- caused by the H<sub>2</sub>O<sub>2</sub> generated in the enzymatic reaction, the molecular mechanism, however, has
- not been fully investigated. In this work, LAAO interaction with cytoplasmic membranes using
- 19 different cell types and Langmuir interfacial monolayers was evaluated. The Cerastes cerastes
- venom LAAO (CC-LAAO) did not exhibit cytotoxic activities against erythrocytes and peripheral
- 21 blood mononuclear cells (PBMC). However, CC-LAAO caused cytotoxicity on several cancer cell
- 22 lines and induced platelet aggregation in dose-dependent manner. Furthermore, the enzyme
- 23 showed remarkable effect against Gram-positive and -negative bacteria. These activities were
- 24 inhibited on the addition of catalase or substrate analogs, suggesting that H<sub>2</sub>O<sub>2</sub> liberated is
- 25 required for these effects. Binding studies revealed that CC-LAAO binds to the cell surface and
- enables the production of highly localized concentration of H<sub>2</sub>O<sub>2</sub> in or near the binding interfaces.
- 27 On another hand, the interaction of CC-LAAO with a mimetic phospholipid film was evaluated,
- for the first time, using a monomolecular film technique. Results indicated that phospholipid/CC-
- 29 LAAO interactions are not involved in their binding to membrane and in their pharmacological
- 30 activities.
- 31 **Key words:** L-amino acid oxidase; phospholipid monolayers; immobilized enzyme; membrane
- 32 interaction.
- 33 Abbreviations:
- 34 DiC<sub>12</sub>PC: 1,2-dilauryl-sn-glycero-3-phosphocholine
- 35 DiC<sub>12</sub>PG: 1,2-dilauryl-sn-glycero-3- phosphatidylglycerol

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