Human oligoclonal recombinant antivenom against the black mamba (Dendroaspis polylepis)

Laustsen, Andreas Hougaard; Karatt-Vellatt, Aneesh; Slavny, Peter; M. Luther, Alice; L. Olesen, Majken; W. Masters, Edward; Lomonte, Bruno; Gutiérrez, José María; McCafferty, John

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Citation (APA):
Human oligoclonal recombinant antivenom against the black mamba (*Dendroaspis polyplepis*)

Andreas H. Laustsen1,2, Aneesha Karatt-Vellatt3; Peter Slavny3; Alice M. Luther3, Majken L. Olesen3

Edward W. Masters4, Bruno Lomonte1; José Maria Gutiérrez4; John McCafferty3

1Department of Biotechnology and Biomedicine, Technical University of Denmark

2Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen

3ONTAS Ltd., Babraham Research Institute, Cambridge CB22 5AT, United Kingdom

4Instituto Clodomiro Picado, Facultad de Microbiología, Universidad de Costa Rica, San José, Costa Rica

Snakebite: a neglected tropical disease

Snakebite envenoming is a major cause of death and morbidity in tropical parts of the world. Current therapies are based on animal-derived antisera that are associated with a high degree of immunogenicity, high cost, and batch-to-batch variation. Here, we report the results of our ongoing efforts of developing the world’s first fully recombinant antivenom based on human IgGs targeting the key toxins from the notorious black mamba (*Dendroaspis polyplepis*).

Discovery of human scFvs by phage display

Based on a combined toxicovonomics and phage display selection approach, 431 human scFv binders were isolated from a phage display library against the medically relevant neurotoxins and dendrotoxins of *D. polyplepis*.

Conversion of unique scFv binders to IgG

Following expression of 147 scFvs with unique Vh CDR3 regions in E. coli and evaluation of binding strength, the 24 most promising scFvs were selected and converted to IgG format. Of these, 20 displayed good binding after successful expression in HEK cells.

Human oligoclonal recombinant antivenoms

Currently, the binding affinities and the neutralization potential of these 20 toxin-targeting IgGs is being investigated with the aim of being able to design a cost-effective recombinant oligoclonal mixture of IgGs that can effectively neutralize the lethal effects of the synergistically-acting venom of *D. polyplepis*.

Reference


Acknowledgements

This work was funded by the Novo Nordisk Foundation (NNF14OC102481), Elsfleth Rejsestipendium, Otto Fonden, Lundbeckfonden, Foundation for Lethal Envenomation Therapy, Knud Halberg’s Food, Christian og Odda Reumathemtisk Fonden, Foundation for Biological Research and to Instituto Clodomiro Picado for financial support.

Contact information

DTU Bioengineering
Technical University of Denmark
Kgs. Lyngby Phone: +45 45 25 34 65
DTU Bioengineering
Kgs. Lyngby Phone: +45 45 25 34 65

References