# High-tech breakthrough in snakebite antivenom

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An experimental antivenom has been developed against dendrotoxins from the world's most feared venomous snake, the black mamba, which can be found in Africa. The experiments were carried out in

collaboration between DTU and Instituto Clodomiro Picado in Costa Rica, and IONTAS in Cambridge, U.K., and the findings were recently published in the journal *Nature Communications*.

Andreas Hougaard Laustsen, associate professor at DTU Bioengineering, estimates that these findings may lead to a paradigm shift in snakebite treatment.

"The leap forward in our experiments is that we used a biotechnological method to find and then propagate human antibodies in the laboratory to enable use in the treatment of experimental black mamba envenoming. The method we employed can be used to discover human antibodies in the lab by simulating of the human immune system, so we can avoid injecting patients with snake venom to raise antibodies by immunization," says Andreas Hougaard Laustsen.

The antibodies for the experimental black mamba antivenom were discovered using an antibody library containing human antibody genes extracted from white blood cells in donor blood. These genes were inserted into genetically modified virus particles that can express the desired human antibodies on their surfaces. These virus particles were then used to screen and find human antibodies that can bind to black mamba dendrotoxins. After the correct antibodies were found, the antibody genes were inserted into mammalian cells acting as cell factories with a large output of monoclonal antibodies.

The discovered antibodies can be used in the industrial setting for large-scale production in huge fermentation tanks, similar to insulin production today. Insulin underwent similar development in the early 1990s, when production went from pig-based insulin to fully human insulin manufactured using recombinant DNA technology.

Andreas Hougaard Laustsen estimates that it will still take years before

production of antivenom based on human antibodies is ready to go beyond the laboratory.

"We have shown that it is possible to produce an experimental human-based antivenom against important toxins from one snake species, the black mamba. Before clinical testing of the antivenom on humans will make sense, it is relevant to develop more antibodies for the antivenom to give it a broader spectrum against several types of snake venom," says Andreas Hougaard Laustsen.

The researchers are therefore working to develop an antivenom against several species of snakes. If the research is successful, physicians will be able to use the antivenom in the many cases of snakebite in which the snake species is unknown. This can potentially save many lives, not only in Africa, but all over the world.

More than 100,000 people annually die of snakebite envenoming, and many more are disabled. Given that most snakebites occur in poor areas of the world, this is not a main focus area for the pharmaceutical companies. In order to attract more attention and more funds to the area, the World Health Organization (WHO) in 2017 added snakebites to the list of neglected tropical diseases.

Andreas Hougaard Laustsen Andreas Hougaard Laustsen is an associate professor at DTU Bioengineering, where he conducts research on therapeutic antibodies and is working towards developing antivenoms against snakes, scorpions, and spiders, designed in such a way that they do not cause adverse reactions in patients. In 2017, Andreas Laustsen became a member of the WHO Working Group on Snakebite Envenoming.

**More information:** Andreas H. Laustsen et al, In vivo neutralization of dendrotoxin-mediated neurotoxicity of black mamba venom by

oligoclonal human IgG antibodies, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06086-4

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