Toxin targets discovered

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Research that provides a new understanding of how bacterial toxins target human cells is set to have major implications for the development of novel drugs and treatment strategies.

Cholesterol-dependent cytolysins (CDCs) are toxins produced by major bacterial pathogens, most notably *Streptococcus pneumoniae* and group A *streptococci*, which collectively kill millions of people each year.

The toxins were thought to work by interacting with cholesterol in target cell membranes, forming pores that bring about cell death.

Published today in the prestigious journal *Proceedings of the National Academy of Sciences*, the research is an international collaboration between Professor Michael Jennings from Griffith University and Professor James Paton, University of Adelaide in Australia, and collaborators at the University of Queensland and Department of Microbiology, New York University School of Medicine.

The team has, for the first time, shown that these toxins require binding to specific glycans (sugar structures) on the cell surface for efficient targeting of the host.

This explains why some cell types are more susceptible to the toxins than others, and also provides opportunities to develop novel drugs capable of blocking toxin-glycan interactions, thereby protecting host cells from toxin-mediated damage.

Professor Michael Jennings, Deputy Director of the Institute for Glycomics, says these findings open up a completely novel approach to developing drugs which may block toxin action.

"Understanding how toxins target particular cells in the human body is the first step in understanding their mechanism of action and how to block them from causing cell death."

Professor James Paton, Director of the University of Adelaide's Research Centre for Infectious Diseases, says: "interactions between CDCs and glycan receptors on immune cells also explains why these toxins have additional effects on host responses to infection, which enable the pathogenic bacteria to 'fly under the radar' of host immune defences."

More information: The cholesterol-dependent cytolysins pneumolysin and streptolysin O require binding to red blood cell glycans for hemolytic activity, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1412703111

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