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Sugar coating reveals black death

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Even today, the lives of humans and animals are claimed by plague. A new antibody-based detection method can be used to reliably and sensitively identify plague in patient serum and other biological samples. The antibody specifically recognizes a particular carbohydrate structure found on the cell surfaces of the bacterium that causes plague, as reported by German researchers in the journal *Angewandte Chemie*.

"Black death" took the lives of over 200 million humans over the course of three pandemics in the last 1500 years. More recently, cases of plague have been detected in Africa and Asia. Because of the high danger of transmission and the severity of the infection, Yersinia pestis, the pathogen behind the plague, is classified as a category A biological weapon. When inhaled as an aerosol it causes pneumonic plague, which usually results in death if it is not treated fast. Rapid and reliable diagnosis is thus critical.

"Currently, Y. pestis is detected by polymerase chain reaction based assays or traditional phenotyping," explains Peter Seeberger of the Max Planck Institute of Colloids and Interfaces in Potsdam. "These methods of detection are reliable, but they are also often complex, expensive, and slow." The recognition of surface proteins by antibodies is a highly promising and less complicated alternative method for the detection of plague, but it has a high failure rate and low selectivity with regard to related strains of bacteria.

Seeberger and his team have now found a way around this problem: Gram-negative bacteria like Y. pestis have molecules called

lipopolysaccharides (LPSs), made of fat and carbohydrate components, on their outer cell membranes. "The inner core of the Yersinia LPS has a unique structure that differs from that of other Gram-negative bacteria," says Seeberger. "This could be a suitable region for detection by means of specific antibodies for rapid point-of-care diagnosis."

Because isolation of Y. pestis LPS is a laborious undertaking, the researchers chose to synthetically produce one typical motif from the molecule, a segment consisting of three sugar molecules, each of which has a framework of seven carbon atoms. The researchers attached these segments, called triheptoses, to diphtherietoxoid CRM197, which acts as a carrier protein. This protein is a typical component of licensed vaccine formulations and triggers the formation of antibodies. The researchers immunized mice and isolated antibodies from their blood.

Various immunoassays demonstrated that the resulting antibodies detect the plague pathogen with high selectivity and sensitivity, and selectively differentiate between Y. pestis and other Gram-negative bacteria. The researchers hope to be able to use this to develop applications for patient diagnostics. The development of corresponding tests is the focus of their current research.

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