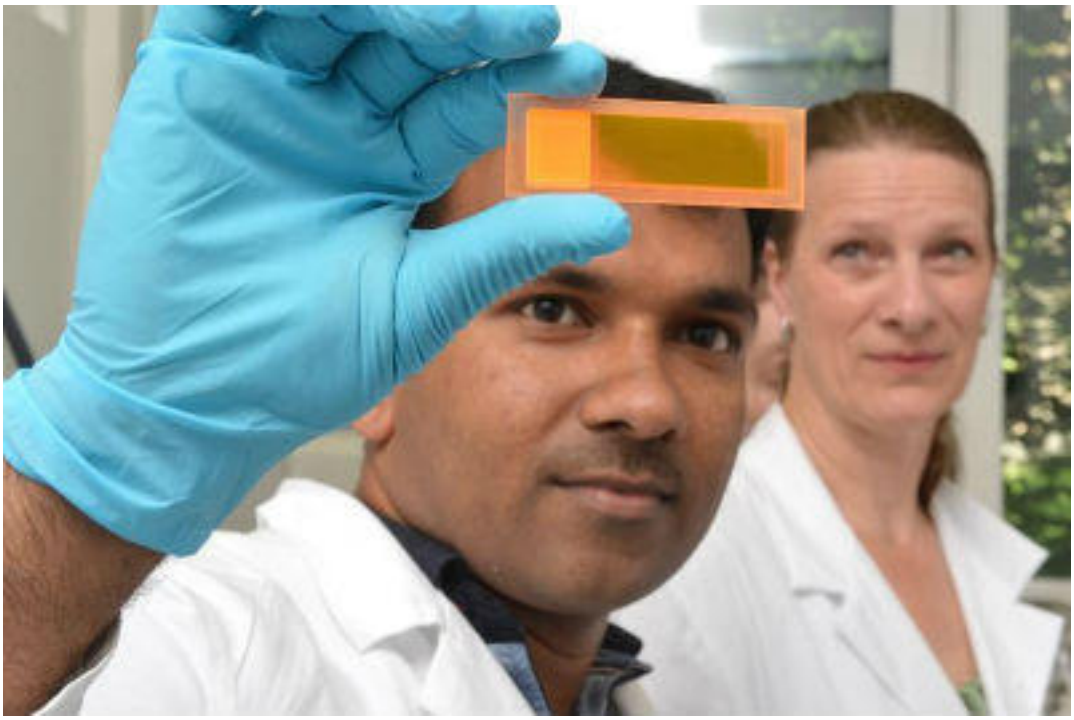
A Quick Test for the Black Death

Max-Planck-Gesellschaft

Sugar-based detection method enables easy and accurate identification of the Yersinia pestis bacterium



Diagnosing the presence of Yersinia pestis, the cause of plague, may soon be easier than ever before. Scientists working with Peter Seeberger, Director at the Max Planck Institute of Colloids and Interfaces (MPIKG) in Potsdam and Professor at the Freie Universität Berlin, have come up with a simple, inexpensive and reliable method of detecting the bacterium. The research team, specializing in glycochemistry and glycobiology, first identified and synthesized an oligosaccharide structure on bacterial surface before combining it with a protein to heighten the immunological effect. The presence of antibodies against this surface glycan in the blood of infected patients can be a biomarker of diagnostic value in Yersinia pestis infections. The Potsdam-based scientists also used the antigen to create antibodies which can directly detect the plague pathogen in infected samples.

The Black Death is best known as a devastating medieval disease which affected Europe, Central Asia and China. The plague killed more than 200 million people through the ages. Yet it is by no means completely eradicated. In 2002 there was an outbreak of plague in the Indian state of Himachal Pradesh, and 2008 saw 18 cases reported in Madagascar. Ziketan, a city in north-west China, was quarantined after an outbreak in 2009, and in the same year there were 16 cases in Tobruk, Libya. Cases are also repeatedly reported in New Mexico, USA. As it is extremely infectious and indeed deadly, plague is one of the most dangerous bioweapons.

Although plague can be treated with antibiotics, survival rates decrease with every hour the disease remains undetected. Left untreated, plague can often lead to death within a very short time, depending on the disease type. “Early identification of an infection is of paramount importance for survival,“ says Chakkumkal Anish, Leader of the Glycobiology Research Group at the Max Planck Institute in Potsdam, “So our work may have direct and positive consequences on patient survival rates.“

In order to specifically detect the plague pathogen, the scientists first had to identify an oligosaccharide in a lipopolysaccharide on the surface of Yersinia pestis. This oligosaccharide would serve as a specific antigen. They then synthesized the complex compound in a multi-step process. Subsequently, the chemists bound the sugar molecule to a protein which is used in many vaccines to heighten the immune reaction. The resulting glycoprotein produced by the sugar-protein compound was used to trigger an immune reaction in mice. The scientists used this circumstance to create antibodies to the plague pathogen using murine immune cells.

The antibodies can identify plague bacteria with high selectivity (accuracy) without the result being distorted by other bacteria biochemically related to plague. Thus the scientists have effectively produced a quick test for the Black Death. There are, in fact, many ways of using this particular research finding in medical practice. On the one hand, the glycan or its glycoconjugates can be applied to test strips where it acts as an antigen and catches antibodies from the blood of infected patients. The antigen-antibody complexes are very easy to detect with fluorescing proteins. On the other hand, the antibodies could provide a way of directly detecting the plague pathogen in infected tissue. Here, too, fluorescing proteins are used to identify whether the antibodies have docked onto the bacterial surface.

“These reliable tests are simple and economical to administer,” says Peter Seeberger. This gives the new approach major advantages over the testing methods used to date. In the past, plague pathogens were detected by phenotyping or gene testing. The problem with these methods is that they are complex, expensive and slow - and, what’s more, they have a high failure rate.

The new method is a direct result of research successes in glycomics. This field is dedicated to the study of carbohydrates, which includes all sugars, and their role in biology. Scientists are now able to identify and synthesize ever more complex carbohydrate molecules. “We have the ability to synthesize complex molecules from simple chemical building blocks, much like children using Lego bricks to build a space ship,” explains Chakkumkal Anish. “This is just the start – we have only just begun exploiting the opportunities this brings.” The chemical methods signify much more than just scientific advances. They also help scientists to come up with new methods of diagnosis and treatment, and to develop vaccinations for various diseases. “Basic research has an intrinsic value,” says Peter Seeberger. “But in the field of glycomics, we are increasingly able to translate our research directly into applications with a practical value, very much like the value our latest development has for the medical world.”

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