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Japan develops novel test to tackle hospital acquired infections

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New advances could help reduce the use of endangered horseshoe crabs for detecting lipopolysaccharide

Proteins developed at Kyushu University in Japan may soon make tests for identifying the presence of particular endotoxins on bacteria easier to manufacture by ending the dependence on substances from horseshoe crabs.

Found in the outer layer of a number of bacteria, lipopolysaccharide is an endotoxin that can trigger inflammatory responses leading to a condition called sepsis, which can be especially life-threatening in intensive care units. To monitor for contamination of lipopolysaccharide in non-oral drugs, medical devices, and biologics, testing for the molecules has been increasing. However, current tests depend on raw materials from the limited natural resource of horseshoe crabs.

Named after the species name of the American horseshoe crab, the *Limulus* test uses substances produced by breaking down horseshoe crab amebocytes—the equivalent to mammalian white blood cells—to detect lipopolysaccharide. In response to a minute quantity of bacterial lipopolysaccharide, three precursors of enzymes—referred to as ProC, ProB and ProCE—found in the broken-down cell material cause a chain reaction to form a clot, indicating the presence of the endotoxin.

As an alternative approach, the research team led by Shun-ichiro Kawabata, professor of Kyushu University's Faculty of Science, has been developing a next-generation *Limulus* test using recombinant proteins that can be produced from cells grown in the lab as a substitute for the three enzyme precursors. While they have previously made functional recombinant proteins of two of the components, they now report the successful preparation of an alternative for the remaining component, ProCE.

The protein was found to greatly promote the coagulation process and gives the researchers a complete set of alternatives for ProC, ProB and ProCE that could be applied to a next-generation *Limulus* test to contribute to the development of a very sensitive mixture for the detection of lipopolysaccharide for a variety of biomedical uses without depending on horseshoe crabs.