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Genetically-engineered enzyme biosensor for the healthcare industry

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During Gram-negative bacterial infection, endotoxin (or lipopolysaccharide, LPS) released from the outer membrane of the gram-negative bacteria, interacts with host sensor/receptor proteins to drive inflammation and pyrogenic reaction. In severe persistent infections, excessive LPS may induce septic shock and death. The ubiquity of endotoxin poses a threat to the biotechnology, pharmaceutical and healthcare industries. The quality assurance for injectable drugs and medical devices, for endotoxin-free applications, started with the slow, less efficient and expensive pyrogen test using rabbits. In the mid-1970s, the US Food and Drug Administration (FDA) approved the Limulus amoebocyte lysate (LAL) for testing endotoxin contamination. However, the LAL test requires the harvesting and bleeding of the horseshoe crab, and LAL suffers seasonal and geographical variations in sensitivity to endotoxin. Problems with the specificity of LAL to endotoxin and the threats on horseshoe crab extinction called for an alternative more reliable endotoxin test. This paper shows genetic engineering efforts to clone and express recombinant Factor C (rFC), the endotoxin-inducible enzyme biosensor in LAL, which establishes a synthetic rapid diagnostic test for endotoxin. The rFC-based PyroGene® is US FDA-approved. Based on the identified LPS-binding motifs in rFC, we innovated short sushi peptides for LPS-removal (for depyrogenation) from parenteral fluids and also to generate novel future antibiotics.