Popular Science abstract

Staphylococcus aureus, a major health threat according to the WHO, has become increasingly resistant to antibiotics over the years, with Methicillin-resistant Staphylococcus aureus (MRSA) presenting a particularly challenging problem. Exploring fresh avenues for antibiotic targets requires a profound understanding of *S. aureus* unique biology and identifying vulnerabilities for therapeutic intervention. While cell wall synthesis has been a known target, the realm of cell wall degradation remains promising but largely uncharted. Bacteria utilize hydrolytic enzymes, called peptidoglycan hydrolases (PGH), to modify their cell walls during growth and divisions. If we can learn to control these enzymes at the protein level, we might redirect their activity against the bacteria. Despite the challenges posed by the redundancy of PGHs, their potential is not ruled out. Activating their hydrolytic activity offers a ground-breaking strategy in antibacterial development.

LytM, a staphylococcal autolysin, initially exists in a latent form but can be activated *in vitro*, proving highly effective against staphylococci. The hurdle lies in translating this potential into a practical antibacterial strategy by uncovering the key to activating LytM *in vivo*. Our focus is on understanding the intricacies of LytM activation – when and how it transitions from a latent state to an active one. Our scientific quest involves identifying the triggers for LytM activation, delving into environmental conditions like pH shifts, the presence of specific ions, and other factors that might influence its performance. Using advanced techniques, we will dissect LytM molecular structure and unravel the complex interactions between bacterial cell walls. We plan to explore various activation scenarios for LytM. Is it a straightforward proteolytic activation or a nuanced structural change induced by molecular interactions? Our approach combines traditional lab experiments with computational simulations to piece together the puzzle.