Engineered enzymes to disrupt bacterial communication and reduce virulence

Engineered enzymes that inhibit bacterial virulence factors by breaking down bacterial communication molecules.

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Virulence factors

Bacteria are a major source of infections in both plants and animals, as well as contamination of food products. The consequences of rampant bacterial growth can range from loss of product and capital (in the livestock and agricultural industries) to illness and loss of life (in animal and human health). Quorum sensing mediated by acyl homoserine latonces (AHLs) has been implicated in regulating bacterial virulence factors in pathogens including *Vibrio cholerae* (cholera), *Pseudomonas aeruginosa* (infections in cystic fibrosis) and *Staphylococcus aureus* (hospital-acquired infections). The pathogenicity of bacterial plant pathogens including *Pectobacterium spp*. (soft rot and blackleg disease), *Erwinia amylovora* (fire blight disease) and *Pseudomonas syringae* (opportunistic plant pathogen) is also regulated by quorum sensing. Given the widespread occurrence of antibiotic resistance it is imperative to find new modalities to combat pathogenic bacteria. Targeting AHLs to decrease or limit the expression of virulence factors could be a powerful tool to combat costly plant, animal and human pathogens. Lactonase enzymes that degrade AHLs are being explored as a novel way to inhibit expression of virulence factors and reduce the pathogenicity of bacteria.

Breaking lines of communication

Bacterial pathogenicity is linked to robust expression of virulence factors. AHL signaling molecules that are widely secreted by bacteria for quorum sensing are implicated in activating the expression of virulence genes and exacerbating infections. Lactonases, enzymes that degrade AHLs, are a viable and novel strategy to interrupt quorum sensing and therefore mitigate against bacterial infections. University of Minnesota researchers have engineered lactonases in order to maximize enzyme stability and activity against a wide variety of AHLs. These enzymes are capable of disrupting bacterial communication and reducing virulence. The improved solubility, stability and longevity profile of these enzymes makes them ideal anti-infectives. Specifically, they can be incorporated in a variety of solvents or coatings, thus rendering them readily deployable on most surfaces. Engineered lactonases are also appealing since their mode of action is outside the cells and are unlikely to elicit survival mechanisms that increase the likelihood of resistance development. These enzymes have been found to be non-toxic in animal feed studies and could be used to control microbial infections in the livestock industry, in crop production and post-harvest crop storage. Engineered lactonases have the potential to mitigate crop and livestock contamination without the introduction of chemical antibiotics into the food chain.

Phase of Development

Proof of concept. Experiments have shown that the enzymes can successfully inhibit quorom sensing (and associated biofilm formation and biocorrosion of submerged steel).

Features & Benefits

- **Lowers pathogenicity of microbes:** Lactonase breaks down the AHL lactones used for quorum sensing by bacteria, an important regulator of virulence factor expression.
- **Non-toxic:** Based on research and animal feeding studies, no environmental or health hazards have been identified, which are commonly associated with biocidal compounds.
- **Robust and useable in diverse environments:** The enzymes are temperature, protease, acid and age resistant, retaining activity even in organic solvents.
- **Conventional production methods:** Scalable enzyme production using fermentation.

Applications

- Animal feed additive to prevent livestock infections
- Crop treatment to prevent pre- or post-harvest plant pathogens
- Anti-microbial coating
- Prevention of food contamination (spray/coat food products)
- Dietary supplement or skin application to alter/control microbial community of the gut or skin

Researchers

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Publications

Evaluation of biological and enzymatic quorum quencher coating additives to reduce biocorrosion of steel
PLOS ONE, May 16, 2019

Ready for Licensing

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