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A dual coding *Staphylococcus aureus* RNA produces two secreted peptides that unequally lyse host cells and competing bacteria

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In bacteria, messenger RNAs usually produce proteins of homogeneous sequences and functions. Stable SprG1 RNA produced from the pathogenicity islands of *Staphylococcus aureus* clinical isolates encodes and expresses two peptides from a single internal reading frame. Both peptides accumulate at the membrane and stimulating their expression induces *S. aureus* death. Replacement of the two initiation codons into termination signals is required to reverse toxicity. During growth, a convergent RNA, SprF1, is expressed to reduce SprG1 levels, preventing death. The peptides are excreted and lyse human host erythrocytes, the longer peptide as the more efficient. The secreted peptides also inactivate Gram negative and positive bacteria, the shorter peptide as the more effective against competing *S. aureus*. A toxin–antitoxin pair expressed from a human pathogen produces two secreted virulence factors from an individual RNA that contains two functional initiation codons. This is a case of the alternative expression of a single internal ORF of a RNA to produce two distinct peptides.

- *Staphylococcus aureus* cells express a dual coding stable RNA
- SprG1 reading frame expression induces death reversed by mutating the two AUG codons
- The two peptides are excreted to destroy host cells and competing bacteria
- Inducing the expression of these peptides in S. aureus could be effective antibiotics.

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