Detection of Staphylococcus quorum sensing using Gaussia luciferase

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Abstract

Resistance to first-line antibiotics to treat a number of Gram positive pathogen's such as *Staphylococcus aureus* infections is widespread. Infection with MRSA (methicillin-resistant *Staphylococcus aureus)* has been estimated to be 64% more likely to end in fatality than when infected with a non-resistant form of the infection1, therefore, development of alternative drug therapies is crucial.

Quorum sensing (QS); bacterial cell-cell communication, is used by a number of pathogens including *S. aureus,* to determine cell density and activate production of virulence factors, which are detrimental to a host. Importantly, quorum sensing is not essential for bacterial growth and survival. Inhibition of QS would stop the production of virulence factors but not affect bacterial growth, reducing selective pressures that result in bacterial resistance.

Here we have developed and optimised an in-cell, *Gaussia* luciferase (GLuc) based bio-reporter, which can be used to detect quorum sensing activity. We have demonstrated that this system can be activated with the addition of exogenous auto-inducing peptides (AIP), and similarly inhibited with previously reported QS inhibitors. Importantly, we have also shown that this system is a good alternative to the more common *lux* based reporters of QS the readouts from which can be affected by the compounds themselves, resulting in false positives. We have shown that QS inhibitors that have an effect on *lux* signal can be reliably assayed using GLuc, demonstrating that GLuc is a good alternative output for bacterial reporter systems.

Keywords: Gaussia luciferase, MRSA, Staphylococcus aureus, Gram positive pathogen, Quorum Sensing

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