Circuit design for limiting Mycoplasma growth to bioreactors

Summary

Inducible systems are genetic switches based on transcriptional activators or repressors that regulate the expression of a target gene, depending on their binding to small molecules or ions, or some other stimuli like heat. In model bacteria there are several inducible systems that have been described and are well-characterised. Here, inducible systems have been developed for use in *Mycoplasma* species. These tools will contribute to the exploitation of *Mycoplasma* as a synthetic biology asset. Particularly, these tools have been used to engineer new synthetic gene switches for better and safer live attenuated vaccines against mycoplasma infections.

Applications

Imperial inventors have created novel gene circuits suitable for manipulating Mycoplasma growth in vivo. In the absence of natural inducible systems, three well-known repressor systems have been engineered to be genetic switches in *M. pneumoniae*. Accordingly, expression of these three transcriptional factors has been optimised for *M. pneumoniae* and new synthetic inducible promoters have been designed for each case.

Imperial inventors have additionally developed a set of synthetic gene switches that can be used to provide genetic barriers preventing growth and proliferation of *Mycoplasma* in vivo. Switches are designed so that they may limit *Mycoplasma* growth to bioreactors in the presence of added compounds. This can, for example, enable selective in vivo attenuation of a *M. pneumoniae* chassis used for live vaccines, thus maximising vaccine immunogenicity while increasing biosafety.

Intellectual property

This technology is subject to a Priority patent application.

Benefits

- Novel genetic engineering tools that can be applied to Mycoplasma expanding its utility as a synthetic biology asset.
- Combined auxotrophic, killswitch synthetic circuits to allow Mycoplasma chassis to be grown in bioreactors in the presence of added compounds, while preventing growth and proliferation in vivo.
- This enables selective in vivo attenuation of M. pneumoniae for live vaccines, thus maximising immunogenicity while increasing biosafety..

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Technology reference: **8985**