Project Title:	Understanding environmental determinants of microbial virulence as a route to design anti-infectives		
Application Deadline:	**Applications accepted all year round**		
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Contact email:	hy3@le.ac.uk	**Funding:**	Self-funded

Summary

Streptococcus pneumoniae can colonise our tissues without any harm, but for incompletely understood reasons it can also cause life-threatening diseases. It is not known exactly why this happens but our hypothesis is that disease-causing potential of *S. pneumoniae* is largely determined by the environmental conditions they are exposed to in different host tissues, such as the different concentration of oxygen, sugar, and pH.

We hypothesise that the Rgg type transcriptional regulators play a fundamental role in pneumococcal adaptation. The proposed project aims to investigate the role played by Rgg regulators in pneumococcal adaptation to different sugars, oxygen concentration, and acidity levels. For your project, you will be trained to create mutants, measure gene expression using different technologies including qRT-PCR, RNAseq, LacZ reporter assays, and in vitro and in vivo models of pneumococcal infection.

References:

1: Kadam A, Eutsey RA, Rosch J, Miao X, Longwell M, Xu W, Woolford CA, Hillman T, Motib AS, Yesilkaya H, Mitchell AP, Hiller NL. Promiscuous signaling by a regulatory system unique to the pandemic PMEN1 pneumococcal lineage. PLoS Pathog. 2017 May 18;13(5):e1006339.

2: Kahya HF, Andrew PW, Yesilkaya H. Deacetylation of sialic acid by esterases potentiates pneumococcal neuraminidase activity for mucin utilization, colonization and virulence. PLoS Pathog. 2017 Mar 3;13(3):e1006263.

3: Al-Bayati FA, Kahya HF, Damianou A, Shafeeq S, Kuipers OP, Andrew PW, Yesilkaya H. Pneumococcal galactose catabolism is controlled by multiple regulators acting on pyruvate formate lyase. Sci Rep. 2017 Feb 27;7:43587.

4: Paixão L, Oliveira J, Veríssimo A, Vinga S, Lourenço EC, Ventura MR, Kjos M, Veening JW, Fernandes VE, Andrew PW, Yesilkaya H, Neves AR. Host glycan sugar-specific pathways in Streptococcus pneumoniae: galactose as a key sugar in colonisation and infection [corrected]. PLoS One. 2015 Mar 31;10(3):e0121042.

5: Hajaj B, Yesilkaya H, Shafeeq S, Zhi X, Benisty R, Tchalah S, Kuipers OP, Porat N. CodY Regulates Thiol Peroxidase Expression as Part of the Pneumococcal Defense Mechanism against H(2)O(2) Stress. Front Cell Infect Microbiol. 2017 May 24;7:210.