Project proposal template
Graduate School studentships
March 2015

Project title	Investigation of the physiological role of azoreductases in Pseudomonas aeruginosa
First Supervisor	Dr — Ali Ryan
Second Supervisor	Mark Fielder
School	Life Sciences
Other member of supervisory team (no more than three KU supervisors in total)	
Specific requirements beyond 2:1 degree	

Project summary

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P. aeruginosa is a major nosocomial pathogen accounting for some 17% of nosocomial infections worldwide. Resistance rates against common antibiotics can reach 40% and multidrug resistant strains accounted for more than 400 fatalities in the US in 2013. *P. aeruginosa* remains a major cause of morbidity in cystic fibrosis sufferers where around 80% of adults suffering from the condition are infected and 20% are infected with multidrug resistant strains of the bacterium.

Azoreductases are a diverse family of flavoproteins found in a range of pathogenic bacteria [1]. They are broad spectrum reductases whose physiological substrate has yet to be identified. Current theories on their function are centred around the bacteria's response to toxic quinones produced by plants in response to bacterial infection [1]. Gene deletion studies in *P. aeruginosa* have shown they are also required for bacterial infection in mammals [2] and our results have shown they also play an important role in the resistance of bacteria to antibiotics. Although we know the effect of deletion of the azoreductases has on the bacterium how they exert this function. This initial data does though make the azoreductases an interesting target for novel antibiotic therapies.

Through the use of recombinant protein technology we have been able to characterise a large number of azoreductases from *P. aeruginosa* [1,3] and identify inhibitors. This data provides useful tools to allow further scrutiny of the role of these enzymes within the cell.

This project will continue established work which has received funding by the Society for Applied Microbiology and will use a combination of molecular biology, microbiology and protein chemistry techniques to help answer the question what fundamental role do the azoreductases play in bacteria. The candidate will have the opportunity to work in a state of the art multidisciplinary research laboratory working as part of an international consortium which includes labs in Oxford, Hanover and Munich.

[1] Ryan et al. 2014 PloS One (9) e98551

[2] Skurnik et al. 2013 PloS Path (9) e1003582

[3] Ryan et al. 2010 J Mol Biol (400) 24-37