Project proposal template
Graduate School studentships
March 2015

Project title	Mutation Mapping: characterising the emergence of antibiotic resistance in Gram positive organisms
First Supervisor	Professor — Mark Fielder
Second Supervisor	Dr G Forster-Wilkins,
School	Life Sciences
Other member of supervisory team (no more than three KU supervisors in total)	Dr Simon Gould
Specific requirements beyond 2:1 degree	2:1 degree or above Good microbiology or molecular biology/genetics skills.

Project summary

(max 4,000 characters)

The rise of antibiotic resistance has been widely reported in the media in recent years and compounded by the report of the Chief Government medical officer Prof Dame Sally Davies. It is clear that our use of antimicrobials needs to be controlled and the development of new drugs vital. What was also clear from the report was a need to understand how resistance actually develops. If possible 'trigger points' that lead to the development of resistance can be predicted in both Gram positive and Gram negative bacteria, we could potentially identify novel therapy targets. Work from Kishony Lab in Harvard USA has already shown that we can monitor the exact point where resistance emerges. This project will move onto the next step using next generation sequencing technologies to characterise the mutation that has occurred in Gram positive bacteria and use this data to model the frequency and type of resistance seen to determine the emergence of resistance biomarkers that can be used to inform prediction models. The focus on Gram positive organisms allows for a detailed analysis of some of the most well established pathogens in human and animal infections. The study will examine both hospital acquired strains as well as the newly defined MRSA ST398 strains. The project will use novel methods to induce chromosomal mutations in the test organisms against an increasing concentration of a clinically relevant antibiotic. The resultant mutation will then be mapped and the developing resistome recorded. Changes in phenotype, metabolism and mutation will be used to determine the type and frequency of chage observed. The data derived will be used to help predict the type and location of the mutations and SNPs so as to be used as potential biomarkers for resistance or novel therapy targets in the future. This project is timely as we are facing a potential catastrophe with regard to controlling and treating infection this project provides opportunity to undertake applied research to help address a real clinical problem, using cutting edge methodologies.