

## Project proposal template

### Graduate School studentships

### March 2015

<i>Project title</i>	<input type="text" value="NMR analysis of HsaD and inhibitor screening for the treatment of M. tuberculosis"/>
<i>First Supervisor</i>	Dr <input type="text" value="Adam Le Gresley"/>
<i>Second Supervisor</i>	<input type="text" value="Dr Alex Sinclair"/>
<i>School</i>	<input type="text" value="Pharmacy and Chemistry"/>
<i>Other member of supervisory team (no more than three KU supervisors in total)</i>	<input type="text" value="Dr Ali Ryan, Dr Mark Howard, University of Kent"/>
<i>Specific requirements beyond 2:1 degree</i>	<input type="text"/>

**Project summary**  
**(max 4,000 characters)**

The rise of antibiotic resistance is one of the most pressing issues in modern science. This project will focus on novel targets for antibiotics in *M. tuberculosis*. In *M. tuberculosis* the study will focus on HsaD a key hydrolase enzyme that has been show to be crucial to the survival of the bacterial pathogen. This makes HsaD an excellent target for new antibiotic therapy against tuberculosis. It is thought that one-third of the population has been infected with tuberculosis with new infections occurring in approximately 1% of the population, year on year.

The aim of the project is to recombinantly produce HsaD protein and use this product to screen potential inhibitors that can be developed as potential drugs. The project will centre on the expression of HsaD protein with and without isotopic enrichment (<sup>13</sup>C, <sup>15</sup>N and <sup>2</sup>H) in the first year. The necessary protein expression and purification skills will be acquired through an existing inter-university collaboration with Dr Mark Howard, an expert in Protein NMR at the University of Kent. The successful applicant will be seconded to Dr Howard's research group to develop these skills including specific amino acid labeling and protein NMR spectroscopy. The second year of the PhD will involve using the Bruker Avance 600 MHz NMR spectrometer at Kingston to obtain data assign the primary, secondary and tertiary structure of the isotopically labelled protein using 3D triple resonance NMR techniques in addition to performing assignment using computer packages such as CCPNmr/NMRView Analysis. The third year will involve the screening of potential inhibitors using <sup>15</sup>N HSQC titrations and Saturation Transfer Techniques to evaluate a library of potential sulphonamide inhibitors. There will also be access to a 589-compound Maybridge <sup>19</sup>F NMR library at Kent to assess fragment hits. This interdisciplinary project would use expertise and resources in biotechnology and enable the student to develop skills in structural biology, taking advantage of our research-dedicated highfield NMR suite. In addition, this would further cement an inter-university collaboration that will provide data to support joint funding applications to research councils and charities in addition to driving a project with enterprise and impact opportunities.

