Project proposal template
Graduate School studentships
March 2015

Project title	Synthesising novel pharmacological inhibitors of Rab7 to promote islet beta cell expansion for diabetes therapy.
First Supervisor	Dr — Adam Le Gresley
Second Supervisor	Dr Natasha Hill
School	Pharmacy and Chemistry
Other member of supervisory team (no more than three KU supervisors in total)	Dr Alex Sinclair
Specific requirements beyond 2:1 degree	

Project summary

(max 4,000 characters)

urpose of this study is to develop novel pharmacological inhibitors of the protein Rab7 and to ıte their effectiveness in promoting islet beta cell expansion. Rab7 is a member of the Rab family of ses that regulate intracellular trafficking. Specifically, Rab7 regulates the trafficking of internalised ors to the lysosome for degradation rather than recycling these receptors back to the cell surface. us data by our collaborators on this project has shown that Rab7 inhibition is a very promising novel ach to promoting beta cell expansion for diabetes therapy.

e (50+) series of ester derivatives of CID 1067700 will be synthesised to evaluate activity in cell assays. The series of esters have been proposed as they would improve cell membrane ability and in the case of the acetoxymethyl derivative will undergo rapid hydrolysis in the cytosol to ne active compound CID 1067700. The approach will either involve the inclusion of the desired ester roup (R) at the initial stages of the synthesis or could be included after the synthesis of CID 1067700 event that the ester functionality is intolerant to the benzoyl isothiocyanate addition.

ldition, there exists the potential for a cyclisation reaction to occur under mild conditions, which may ult in inactivity in the cell based assay. A CID 1067700 derivative will be synthesised which will not rgo this cyclisation to test this hypothesis. This studentship will involve developing skills in synthetic emistry and biology and will be run jointly between the school of Pharmacy and Chemistry and the ol of Life Sciences.The chemistry element will be conducted within the Le Gresley/Sinclair group and the biology section will be supervised by Dr Natasha Hill.