This proposal is representative of the projects currently on offer in our group. For more details of active research projects, please visit our webpage at: http://www.chem.leeds.ac.uk/andrew-wilson/wilson-group.html

Studentship in Synthesis and Chemical Biology - Inhibitors of Protein-Protein Interactions Involved in Cancer Development and Progression

The purpose of this project is to develop methods for the design and synthesis of inhibitors of key protein-protein interactions (PPIs) involved in the development and progression of cancer.

In order to effectively intervene in biological processes, it is necessary to inhibit protein-protein interactions (PPIs). However, it is difficult to design small molecules that cover 800-1100Å² of a protein surface and complement the poorly defined projection functional groups on a flat or moderately convex surface (Fig. 1). The project is concerned with the development of scaffolds that posses the required size and shape to cover the large discontiguous projection of functional groups found at protein-protein interfaces. These scaffolds will be amenable to rapid modular or dynamic synthesis. The student will have opportunities to develop, synthesise and test both novel aromatic oligoamides as proteomimetics and ruthenium (II) tris-chelates as protein-surface mimetics.

Current cancer targets include: p53/HDM2, Bcl-xL/BID, Mcl-1/NOXA-B, androgen receptor/co-activator and growth factor/ growth factor receptor interactions. Inhibitors of these targets are being sought to decrease tumour growth, with potential clinical applications in a broad range of cancers, including breast cancer, prostate cancer and small cell lung carcinoma.

This multidisciplinary project will provide opportunities for the student to receive training in organic synthesis in addition to molecular biology, molecular modelling and biophysical analysis. Significant opportunities exist to tap into active collaborations across the University of Leeds and beyond. This opportunity is associated a larger ERC starting investigator project led by Dr Andy Wilson Please contact Dr. Andy Wilson (A.J.Wilson@leeds.ac.uk) for further details about this project.

References