Understanding the Dynamics of NFkappaB transcription factor complex formation

Project ID: 315

Supervisory team

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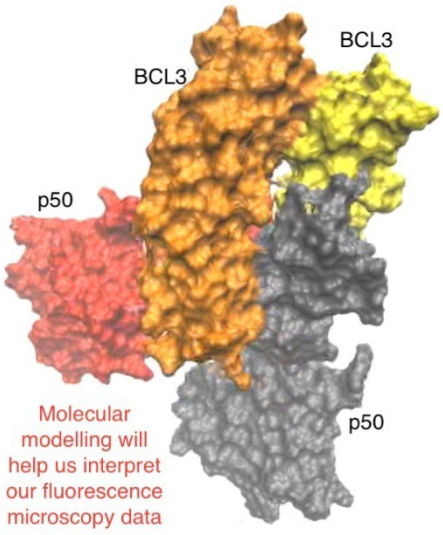
Host institution: Cardiff University



Project description: Protein-protein interactions (PPIs) play crucial roles in many biological processes with ~20,000 proteins making ~650,000 interactions in humans alone. Disruption of PPIs also underlie many diseases. PPIs comprise association of identical proteins (homo-oligomerisation) or different proteins (hetero-oligomerisation), with a combination of both contributing to functional complexes such as transcription factors. As with many protein complexes, transcriptional factors are inherently dynamic both in terms of their protein composition and location within the cell. NFkappaB is one of the most important transcription complexes, responsible for controlling immune response, replication and cell death; its dysregulation is linked to many diseases including autoimmune disease and cancer. However, our understanding of how NFKappaB controls these vital cellular processes is limited as we do not fully understand the dynamic events that underlie assembly of the complex. The components that comprise NFKappaB vary, but the composition ultimately determines function and thus gene regulation. The core of NFKappaB comprises a dimer but at least 5 different protein forms can constitute this dimer with both homo and hetero-dimer forms capable of forming. Furthermore, additional proteins can bind to the core dimer, which in turn affects function and cellular location.The aim of the PhD project is to investigate NFkappaB complex assembly within the cell and generate models to understand what drives the formation of particular complex forms. Such molecular level of information will in turn help develop next generation therapeutics that target NFKappaB. The project will apply and further develop engineered fluorescent proteins produced by the project team that can monitor homo and hetero-oligomerisation events in situ. Coupled with advanced fluorescence microscopy, the location and composition of NFKappaB complexes in the cell can be tracked in real time. Based on experimental data, molecular models will be built to understand what drives the formation of particular complexes. The PhD project will thus provide new and unprecedented detail on how NFKappaB functions dynamically within the cell.The student will learn a variety of techniques including molecular biology, protein engineering, cell biology, advanced fluorescence microscopy, structural modelling and molecular dynamics. While the current project focuses on NFKappaB, the knowledge and skills learnt can be applied more broadly within both academic and industrial sectors to investigate the plethora of protein:protein interactions that underlie biology and disease.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.