Cancer Genetics and DNA Damage

Growth and maintenance of tissues is regulated by balanced mechanisms of cell division, quiescence and death. The biochemical network that controls these mechanisms is in turn tightly regulated and complex. During human development the code for this complexity, the genome, is stably maintained in the majority of cells. Later in life, however, changes and errors can arise in the genome which affect the control of cell growth and death and are associated with the development of cancer and other morbidities.

In this theme we are studying proteins that protect the genome from error and instability. These include proteins whose genes give rise to syndromes that cause cancer predisposition and/or immunodeficiency when they are mutated; for example, Ataxia-Telangiectasia (ATM), familial breast cancer (BRCA1, BRCA2), RIDDLE and Nijmegen Breakage Syndromes (RNF168 and NBS1). Our research examines the pathways these proteins are involved in (such as DNA repair, DNA replication and checkpoint signalling), their regulatory network of protein: protein interactions (such as MDC1, 53BP1 and ATR), post-translational modifications (such as phosphorylation, ubiquitination and sumoylation) and the way in which some viruses subvert these processes.

Clinically, the processes that protect the genome are central to the actions of many DNA damaging anti-cancer therapeutics and, therefore, we are exploring these pathways for potential therapeutic targets. For example, we are asking how DNA repair mechanisms allow cancer cells to overcome the severe obstacles that DNA-damaging anti-cancer treatments pose to replication forks and exploring synthetic lethal approaches in the treatment of B-cell chronic lymphocytic leukaemia (B-CLL) and acute lymphoblastic leukaemia (ALL).

The shared aims of the research theme are to better understand the pathways that maintain genome stability and to elucidate the consequences of their deregulation thus improving diagnosis and treatment of human disease.

Research groups

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