

Dr S Shackleton - Nuclear architecture and its role in human disease

The DNA of eukaryotic cells is contained within the nucleus and is separated from the cytoplasm by a double membrane structure, known as the nuclear envelope. Protein components of the nuclear envelope play a critical role in the structural organization of the nucleus and also in communication between the nuclear interior and the cytoplasm. Their importance is highlighted by the fact that nuclear envelope proteins have been associated with a wide range of human inherited disorders including muscular dystrophies, lipodystrophy (fat wasting), neuropathy and premature ageing syndromes (progeria).

Although around 20 nuclear envelope proteins have now been identified, their precise functions remain poorly understood. The aim of our research is characterize the functions of nuclear envelope proteins and, through this, to gain a better understanding of how mutations in these proteins cause such diverse inherited disorders.

Projects available fall into three main areas. Firstly, we are studying the fat wasting disorder, familial partial lipodystrophy (FPLD). FPLD involves wasting of subcutaneous fat, leading to diabetes and an increased risk of coronary heart disease. We are using transgenic and stem cell technologies to investigate the mechanism of fat loss and identify the molecular defects occurring. Secondly, we are investigating how different defects in lamin A result in the devastating premature ageing syndrome, Hutchinson-Gilford progeria and related phenotypes, using a range of cell biology techniques. Thirdly, we are investigating a novel family of nuclear envelope proteins with a conserved "SUN" domain, that are involved in nuclear-cytoskeletal attachment and nuclear positioning within the cell. We are using a combination of in vitro, cell biology and transgenic techniques to study SUN protein interactions and their roles in nuclear positioning and human disease, in particular muscular dystrophies.

Applications for PhD studentships are welcome from candidates who hold or expect to hold a first or upper second class degree. Further information is available from the Website at

<http://www.le.ac.uk/biochem/>