*Purifying the guardian of your genome HSSB1*

Cells frequently encounter DNA damage; with DNA double-strand breaks (DSBs) being among the most cytotoxic of these lesions. Chromosomal instability may occur even from a single DSB, if it is repaired incorrectly, and this may ultimately lead to cell death. It is essential that DSBs in human cells are detected, signalled and repaired efficiently in order to prevent the accumulation of damage, which can lead to chromosomal instability or malignant transformation. DSBs may be induced by a number of factors including ionizing radiation (IR), reactive chemical species and via normal cellular processes such as DNA replication. Once a DSB is detected, DNA repair proteins are recruited to the site of the DSB and a multi-faceted DSB pathway is activated. This complex signalling network includes altered transcriptional and translational regulation and the induction of DSB repair and cell cycle arrest via the activation of checkpoints.

One element of the repair machinery is the MRN complex which works with kinases, for example ATM (ataxia-telangiectasia mutated), to phosphorylate various protein targets to repair the damage. MRN is proposed to tether together broken DNA ends and promote ATM activation via mediating the recruitment of ATM to sites of DNA damage. ATM in turn stimulates nuclease activity to carry out early limited resection at the sites of DSBs.If the damage cannot be repaired, they direct the cell to apoptosis. The MRN complex as well as repair kinases are also involved in telomere maintenance and genome stability.

hSSB1 is a recently discovered single-stranded DNA binding protein that is essential for efficient repair of DNA double-strand breaks (DSBs) by the homologous recombination pathway. Dr. Richard’s research data suggests that hSSB1 is a crucial component of MRN mediated resection. The development of many anti-cancer drugs is now focusing on the inhibition of DNA repair processes. Future studies into the mechanism of the hSSB1: MRN interaction, particularly as it acts at the earliest stages of the DNA damage response, could provide valuable information to aid drug development.

In this project students will work with researchers from Dr. Richard’s team to amplify and purify the protein hSSB1 for use in the study of DNA repair processes.