

## **Penny Jeggo**

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### Selected Publication

Barazzuol L., Rickett, N, Ju L-M and Penny Jeggo Endogenous and X-ray induced DNA double-strand breaks sensitively activate apoptosis in adult neural stem cells. *J. Cell Science* 128; 3597-3606 (2015).

### Research Aims and Interests

For many years, my laboratory has studied the DNA damage response to DNA double strand breaks (DSBs). We have especially focused on the DNA repair processes (DNA non-homologous end-joining (NHEJ) and homologous recombination (HR)) but have also studied the signalling response to DSB formation and how it influences DSB repair. In recent studies, we have examined factors regulating the choice and interplay between NHEJ and HR. We have shown that in non-replicating G0/G1 phase cells, there is a fast and slow component to NHEJ and have gained evidence that the slow DSB repair component represents a form of NHEJ involving a restricted level of resection, akin to the process described as microhomology mediated end-joining. This work is ongoing via collaborations. More recently, we have become interested in how chromatin architecture impacts upon NHEJ and have collaborated with Jessica Downs in the GDSC to examine roles for chromatin remodelling complexes. These studies are connected with evaluating how the DSB repair machinery interfaces with other transactions involving DNA such as transcription, silenced DNA regions and replication. The laboratory also has a fundamental interest in understanding how the DNA repair and signalling responses affect human health and development. We have identified and characterised disorders with defects in NHEJ proteins and carry out routine diagnosis for such disorders, interfacing with the two major hospitals in the UK who treat such patients. We have established and characterised a mouse model for deficiency in DNA ligase IV, the ligase required for NHEJ. This work has led us to examine the responses to DSBs in stem cell compartments, and especially the neural stem cells, which represents a major current interest of the laboratory. Finally, since radiation exposure induces DSBs, a personal interest of Penny Jeggo is the response to low dose radiation exposure and issues affecting radiation protection. The response of stem cells to low dose radiation exposure is a particular current interest.