DNA damage and the ability to repair such damage have critical roles in cancer pathogenesis and also in tumour response to treatment. There are 5 major DNA repair pathways by which cells protect their genome, nucleotide excision repair, base excision repair, mis-match repair, double strand break repair and direct reversal. Inherited defects in these pathways have long been recognised as causing susceptibility to form tumours and it also known that loss of key elements in DNA repair pathways are associated with many sporadic cancers.

However, the ability of tumour cells to repair DNA damage using these pathways is a cause of resistance to radiotherapy and many of the standard cytotoxic agents. DNA repair thus acting as a double edged sword in cancer cell biology, loss of effective repair being a predisposing cause and effective repair protecting cancer cells from many treatments.

In recent years there has been a rapid expansion in interest in these pathways, both in terms of understanding tumour biology and also as targets for novel cancer treatments. A number of DNA repair inhibitors have entered the clinic, or are in late preclinical development, targeting at least 3 pathways. It was initially believed that DNA repair pathway inhibitors would be used in combination with DNA damaging agents to overcome resistance but the emergence of data of single agent activity in the context of synthetic lethality has greatly expanded the potential of these agents. The field of DNA repair research is rapidly emerging as one of the most exciting in cancer drug development and in translational research to identify the molecular profile of patients who may benefit from this strategy.

This educational lecture will review the major pathways and their roles, exploring the areas where cancer drug development has been focussed and setting the scene for the clinical updates from other speakers in the session.