# *Exjobb/ Master thesis project*

## DNA repair by non-homologous end-joining

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DNA double-strand breaks (dsb) pose a major threat to the integrity of the genome. Unrepaired dsb can lead to cell death or be involved in the development of a malignant cell. Among agents causing dsb ionising radiation is one of the most effective. The mammalian cell has at least two alternative pathways for the repair of dsb; non-homologous end-joining (NHEJ) and homologous recombination (HR). NHEJ is the major repair pathway in human cells and cells lacking the keyproteins
are extremely sensitive to ionising radiation. The exact sequence of activation of these proteins, and the interaction of NHEJ proteins with other proteins involved in repair and signaling, are not understood.
The project focuses on how the NHEJ proteins Ku70/80, DNA-PKcs and XRCC4/ligase IV are organised within chromatin and how they interact with other protein complexes in response to dsb. We recently showed that the absence of Ku70/80 and DNA-PKcs almost completely blocked the repair of dsb and you will study how this complex activates signalling and repair in response to dsb. These proteins are abundant in the cell nucleus and their interactions with other proteins are difficult to analyse. The idea is to use novel techniques to detect close protein-protein interactions after exposure to ionising radiation and cytotoxic drugs. You will use cultured normal or mutated human cells, rodent knockout cell lines and techniques as pulsed-field gel electrophoresis, WB, chromatin extraction, immunocytochemistry, proximity ligation, in situ detection of proteins by fluorescence/confocal microscopy, etc.