**GENOMIC AND EPGENETIC CHANGES**

**EPGENETIC CHANGES** include structural changes in the chromatin and chemical modifications of the DNA. This results in heritable changes in gene expression. Epigenetic regulation is frequently altered in cancer and acts in combination with genetic changes during cancer initiation and progression.

The best-known epigenetic marker is DNA methylation, which occurs primarily at CpG dinucleotides. Its dysregulation in cancer usually leads to genomic instability, activation of oncogenes and inhibition of tumour suppressor genes.

**GENOMIC CHANGES** include deletions, insertions and translocations of DNA as well as fusion of different DNA sequences. This can lead to genes being gained or lost or being under the control of the wrong elements. Increased expression of oncogenes or decreased expression of tumour suppressor genes can lead to cancer.

We use a method called FISH (fluorescent in situ hybridisation) to detect these fusions by using fluorescent probes that are specific to particular DNA sequences.

**DNA DAMAGE RESPONSE**

We wish to measure the response of prostate cancer stem cells to cancer therapies including radiation and chemotherapy.

Initial therapies for prostate can be successful at shrinking the tumour. However, in some cases a secondary tumour emerges and this is typically resistant to therapy.

We hypothesise that prostate cancer stem cells are resistant to radiation and chemotherapy and are responsible for secondary tumours.

**HOW TO MEASURE DNA DAMAGE?**

DNA damaging agents:
- Radiation
- Chemo therapeutic drugs

Cell detects DNA break using proteins that go to site of break. These proteins either signal repair or if damage is too great, the cell will commit suicide.

Protein is visualised by immunofluorescence as dots in the nucleus of the cell indicating sites of DNA damage. By counting the cells with these foci we can quantify damage. Blue dye shows DNA.