Formation and Repair of DNA Double-Strand Breaks

Andris Abramenkovs

Ionizing radiation is widely used in diagnostics and cancer treatment. Although, the effects of ionizing radiation on biological systems have been investigated for decades, full understanding is not achieved. Ionizing radiation generates reactive oxygen species that damage lipids, sugars and proteins. However, the danger of ionizing radiation has mainly been associated with DNA damage. It is known that ionizing radiation can induce base modifications, a-basic sites, single-strand breaks and, most importantly, double-strand breaks (DSBs). DSBs have been regarded as highly dangerous lesions and even one DSB can result in cell death, therefore, requiring fast repair of DSBs. In mammalian cells, two different repair pathways are responsible for DSB repair. These repair pathways have different repair rate and fidelity.

The modification of the methods used to study repair of DSB in cells led to discovery of heat-labile sites (HLS) that were induced by ionizing radiation and chemical agents. The nature of HLS is still under debate and as well it is unknown if HLS can transform into DSBs in live cells. To date there are two controversial theories describing the importance of HLS in live cells. Therefore, further understanding of these lesions is of great importance for new drug discovery and prognostic purposes in cancer treatment.

In this study the transformation of chemically induced HLS into DSBs were investigated. Also the importance of chemically and ionizing radiation induced HLS repair and transformation into DSBs in live cells was assessed in DSB repair inhibited cells. The activation of DSB related proteins was investigated as well.

Degree project in biology, Master of Science (2 years), 2013
Examensarbete i biologi, 45 hp till masterexamen, 2013
Biology Education Center and Department of Biomedical Radiation Sciences, Uppsala University
Supervisor: prof. Bo Stenerlöw