

**PROCESSING OF STRUCTURALLY DIFFERENT DNA LESIONS
BY NUCLEOTIDE EXCISION REPAIR**

L.H.F. Mullenders, A. van Hoffen, M. van Oosterwijk, Harry Vrieling,
A.T. Natarajan, Albert A. van Zeeland, Leiden University, The
Netherlands.

We have investigated the contribution of the global genome (GGR) and the transcription-coupled repair pathway (TCR) to the removal of structurally different DNA lesions. The repair kinetics of UV-induced CPD and 6-4PP as well as NA-AAF induced adducts dG-C8-AF and dG-C8-AAF were determined in (in)active genes in normal human, xeroderma pigmentosum group C and Cockayne's syndrome cells. Our results can be summarized as follows:

- * All bulky lesions investigated are targets for TCR. However, in the case of normal human cells the contribution of TCR to repair of 6-4PP, dG-C8-AAF and dG-C8-AF in active genes is minor.
- * Results of experiments with different UV-doses suggest that (i) TCR of UV-induced photolesions takes place in a processive way and that (ii) the significance of TCR for the removal of lesions depends on the dose.
- * CS cells are sensitive to both UV-light and NA-AAF. The UV sensitivity is explained by the lack of TCR of CPD in CS cells. However, the kinetics of repair of dG-C8-AF in normal and CS cells are the same; yet CS cells are unable to recover NA-AAF inhibited RNA synthesis. Therefore, it is questionable whether the absence of recovery of the transcription process in CS cells in the presence of DNA damage is due to a defect in TCR. An alternative model will be discussed.