Synopsis of Original Research Paper

Studies on the Changes in Chromatin Structure during Aging of Human Skin Fibroblasts and the Mechanism of DNA Repair

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Our previous experiments suggest that the length of the linker DNA which connects nucleosomal core particles becomes to be heterogeneous by aging, both in *vivo* and *in vitro* in human skin fibroblasts. In order to get some insight on the relation between growth capacity and the regularity of nucleosome structure, we examined the structural change of lymphocyte chromatin upon growth stimulation with FHA. When chromatin of lymphocytes from peripheral blood was digested with the nuclease, unclear pattern of electrophoresis was observed. However, discrete ladders of nucleosomal DNA were detected in the case of lymphocytes stimulated with FHA for 48h and 96h. Their digestion patterns were similar to those of lymphoma cell lines. These results indicate that the regularity of chromatin structure is closely related to the activity of cell proliferation.

As for the UV damage on the skin, we are investigating the mechanism of nucleotide excision repair. We have purified to homogeneity a repair complex by *in vitro* complementation of the XP-C defect in a cell-free repair system containing UV-damaged SV40 minichromosomes. The complex has a high affinity for ssDNA and consists of two tightly associated proteins of 125 and 58kd. Subsequent cDNA cloning revealed that the 125kd subunit is a N-terminally extended version of previously reported XPCC gene product which is thought to represent the human homolog of the *S. cerevisiae* repair gene *RAD4*. The 58kd species turned out to be a human homolog of yeast RAD23. The 58kd species and yeast RAD23 share a ubiquitin-like N-terminus. The nature of the XP-C defect implies that the complex exerts·a unique function in the genome overall repair pathway which is important for prevention of skin cancer.