LOCALIZATION OF GENES INVOLVED IN DNA REPAIR
ON HUMAN CHROMOSOMES BY USING CELL FUSION

M. Stefanini*, W. Keijzer, A. J. J. Reuser,
A. Geurts Van Kessel, T. Verkerk, A. Westerveld,
J. F. Jongkind, and D. Bootsma

Department of Cell Biology and Genetics
Erasmus University
Rotterdam, The Netherlands

The use of somatic cell hybrids in human gene mapping is based on the fact that human chromosomes are preferentially lost in proliferating hybrids formed between human cells and tissue culture adapted rodent cells. When it is possible to discriminate between homologous human and rodent gene products, correlation of the expression of the human phenotype in the hybrids with their human chromosome pattern allows the assignment of genes to a specific chromosome. In the case of DNA repair, the gene products are unknown and the analysis has to rely on less specific characteristics and differences between the human and rodent repair systems, like the level of repair DNA synthesis. We report differences in repair systems between normal human and Chinese hamster cells and analysis of the repair capacity of proliferating human-Chinese hamster cells.

The UV-induced repair activity was analyzed in Chinese hamster Wg3-h, E36, and CHO cells. We found that the level of repair DNA synthesis (Unscheduled DNA synthesis UDS) measured by autoradiography in these three Chinese hamster cell lines was about 50% of that observed in normal human fibroblasts (Fig. 1).

We have used this difference in our studies of DNA repair in proliferating hybrid cells: these hybrids can be used to localize

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Present address: Istituto di Genetica Biochimica ed Evoluzionistica, C.N.R., Via S. Epifanio, 14-27100 Pavia, Italy.

761
Fig. 1. Repair synthesis as a function of UV dose in two normal human fibroblast strains (C5RO, GM) and in three Chinese hamster cell lines (CHO, E36, Wg3-h). Repair synthesis is expressed as mean number of autoradiographic grains over nuclei in G₁ and G₂ phase. The arrows indicate the standard error of the mean. The cells were incubated in the presence of ³H-thymidine 1 h and 2 h after UV-irradiation. Autoradiographic preparations were made as described in reference 9.

human repair genes if it is possible to differentiate between human and rodent components in the repair capacity of the hybrid cells.

The level of repair as a function of UV dose in normal human fibroblasts, Chinese hamster cells and two human–Chinese hamster hybrids is shown in Fig. 2. These hybrids have intermediate levels of repair. UDS was measured in a total of 8 proliferating hybrids between E36 and normal human cells and variable repair levels were found between those of the Chinese hamster and human cells.

Different UDS values were measured in hybrids with different human chromosome content but, taking into account the heterogeneity observed within the same hybrid population, the differences are too small to be correlated directly with the presence or the absence of a specific human chromosome. Furthermore, the repair activity in the hybrids turned out to depend also on the Chinese hamster DNA content: in fact we observed that the UDS level in Chinese hamster tetraploid cells was about twice as high as in diploid cells obtained from an asynchronous population by flow sorting.