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Abstract

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UV-induced inactivation and mutationinduction in a new two-component

heterokaryon (59) homozygous for the

excision-repair deficient mutant UVS-2

To determine the effect of various mutations which confer sensitivity for UV inactivation and mutation-induction at the <u>ad-3A</u> and <u>ad-3B</u> loci, comparisons have been made between OUT standard auxotrophic strain 74-OR31-16A (al-2; Cot-1; pan-2) and various UV-sensitive derivatives bearing <u>uVS-1</u>, <u>uVS-2</u>, <u>uVS-3</u>, <u>uVS-4</u>, <u>uVS-5</u>, <u>uVS-6</u>, and <u>upr-1</u>. The comparative sensitivities of these 8 strains to inactivation and the induction of ad-3 mutants are being published elsewhere (de Serres; de Serres et al.; Inoue et al. --Mutation Res. in press). The excision-repair deficient strain containing <u>uVS-2</u> was more sensitive to radiation (UV, x-rays, and

u-rays) and Various chemical mutagens (MNNG, ICR-170 and 4NQO) than the auxotrophic strain both with regard to inactivation and the induction of ad-3A and ad-3B mutations.

In heterokaryon 12 which consists of the following two strains: 74-0R60-29A (his-2 ad-3A ad-36 nit-2; <u>ad-2; inl</u>) and 74-0R31-16A (<u>al-2; cot-1</u> pan-2), both point mutations (<u>ad-3A</u>^R and <u>ad-3B</u>^R) and multilocus deletions (ad-3A ^{IR}, <u>ad-3B ^{IR}</u> and {<u>ad-3A</u>, ad-3B ^{IR}) in the <u>ad-3</u> region can be recovered (de Serres and Malliny 1971, Chemical Mutagens 2:311). To determine the effect of <u>uvs-2</u> on the recovery of both of these classes of mutations, a new heterokaryon (59) was constructed that has the same genotype as heterokaryon 12 except that it is homozygous for <u>uvs-2</u>.

The strain numbers and genotypes of this new heterokaryon are as follows: 74-0R276-40A (<u>his-2 ad-3A</u> <u>ad-36 nit-2; ad-2; uvs-2; inl</u>) and 74-0R244-3A (<u>al-2; cot-1 UVS-2; pan-2</u>). The sensitivity of this new heterokaryon to UV was compared with that of heterokaryon 12 for inactivation of the heterokaryotic fraction as well as the induction of mutations in the <u>ad-3</u> region. This experiment showed that, whereas heterokaryon 12 has a multihit survival CUTVE with a broad shoulder (de Serres and Kilbey 1971, Mutation Res. <u>12</u>:221), heterokaryon 59 has greater sensitivity to UV-induced inactivation with a simple exponential survival CUTVE. A comparison of the UV exposures required to give 50% survival, for example, gives a relative biological effect (RBE) for inactivation of 46.7. A comparison of the dose-response CUTVES for the overall induction of <u>ad-3</u> mutants shows no difference between the slopes of the curves; both curves increase as the square of UV exposure. In a COMPATISON of the UV exposures required to give comparable forward-mutation frequencies (in the range of $10-100 \times 10^{-9}$ survivors), the higher yield of <u>ad-3</u> mutations in heterokaryon 59 results in an RBE of 4.0. Genetic analysis of <u>ad-3</u> mutants induced in heterokaryon 12.

These experiments report the development of a new two-component heterokaryon that is excision-repair deficient and demonstrates its expected sensitivity to both inactivation and the induction of specific locus mutations in the ad-3 region. - Office of the Associate Director for Genetics, National Institute of Environ mental Health Sciences, P. O. Box 12233, Research Triangle Park, North Carolina 27709