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UV-induced inactivation and mutation-
induction 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 ad-3A and ad-3B loci, comparisons have been made between our standard auxotrophic strain 74-OR31-16A (al-2; Cot-1; pan-2) and various UV-sensitive derivatives bearing uvs-1, uvs-2, uvs-3, uvs-4, uvs-5, uvs-6, and upr-1. 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

uvs-2 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-OR60-29A (his-2 ad-3A ad-36 nit-2; ad-2; inl) and 74-OR31-16A (al-2; cot-1 pan-2), both point mutations (ad-3A^R and ad-3B^R) and multilocus deletions (ad-3A^{IR}, ad-3B^{IR} and {ad-3A, ad-3B}^{IR}) in the ad-3 region can be recovered (de Serres and Malliny 1971, Chemical Mutagens 2:311). To determine the effect of uvs-2 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 uvs-2.

The strain numbers and genotypes of this new heterokaryon are as follows: 74-OR276-40A (his-2 ad-3A ad-36 nit-2; ad-2; uvs-2; inl) and 74-OR244-3A (al-2; cot-1 uvs-2; pan-2). 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 ad-3 region. This experiment showed that, whereas heterokaryon 12 has a multihit survival curve with a broad shoulder (de Serres and Kilbey 1971, Mutation Res. 12:221), heterokaryon 59 has greater sensitivity to UV-induced inactivation with a simple exponential survival curve. 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 curves for the overall induction of ad-3 mutants shows no difference between the slopes of the curves; both curves increase as the square of UV exposure. In a comparison of the UV exposures required to give comparable forward-mutation frequencies (in the range of $10-100 \times 10^{-5}$ survivors), the higher yield of ad-3 mutations in heterokaryon 59 results in an RBE of 4.0. Genetic analysis of ad-3 mutants induced in heterokaryon 59 will reveal whether the spectrum of ad-3 mutants is qualitatively different from that found 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 Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, North Carolina 27709