the presence of atypical cells[2] by counting 500 cells in each instance.

The partial reversal of toxic effects of 5-AzCR by cytidine and by uridine is evident from Table I. Both metabolites in 5-AzCR treated normal mice diminish the loss of thymus and of body weight, the depletion of blood leucocytes and of bone marrow myeloid cells as well as the occurrence of atypical bone marrow cells[2].

In further studies, experiments were designed to disclose whether 6-azauridine would have the same effect as uridine and cytidine. The partial reversal of toxic effects of 5-AzCR by 6-azauridine in normal mice is shown in Table II. The mice used in this instance were of lower average weight by about 2-3 g than in the preceding experiment. This may be the reason for the smaller extent of protection afforded by 6-azauridine in the case of myeloid bone marrow cells. All of the remaining experimental results are very similar to those given in Table I.

The biochemical mechanism of action of 6-azauridine has been elucidated to a considerable degree[3]. 5-Azacytidine is known to undergo phosphorylation and incorporation into various mouse ribonucleic acids[4]. In vitro, in appropriate concentrations, it increases the number of chromosomal breaks[5]. Its cytological effects on lymphocytes and especially on their nuclei have been described elsewhere[6]. The blocking of its action by uridine and cytidine is probably due to the ability of these nucleosides to compete with 5-azacytidine for phosphorylation and for subsequent incorporation into cell nucleic acids.

Mammalian cells, however, do not incorporate 6-azauridine, and for this reason it seems that the reversal effect of 6-azauridine in alleviating the toxicity of 5-azacytidine is mainly due to the competition of both substances at the level of kinase system.

To our knowledge, the reversal of toxic effects of one pyrimidine antimetabolite by another pyrimidine antimetabolite has not been reported up to now. This phenomenon may be of considerable interest for the chemotherapy of cancer.

Zusammenfassung. Die partielle Blockierung der toxischen Effekte von 5-Azacytidin in normalen Mäusen mit Uridin, Cytidin und 6-Azauridin wird beschrieben. Die Hemmung der toxischen Effekte eines Antimetaboliten durch einen anderen kann für die Krebschemotherapie von Bedeutung sein.

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Recombination Among UV-induced Adenine-1 Mutants of *Schizosaccharomyces pombe*

Intragenic recombinational mapping has been reported for several of the genes controlling adenine biosynthesis in the fission yeast *Schizosaccharomyces pombe*[1-10].

The present study was carried out using ten adenine auxotrophs of independent origin, kindly provided by Professor U. Leupold. These ten mutants are located at the adenine-1 locus and had been isolated following irradiation of the wild-type strain, of h^+ mating type, with UV-light (Leupold[11]). Adenine-1 mutants are blocked at one of the early steps in purine biosynthesis, before the formation of 5-aminoimidazole ribonucleotide (AIR), and do not accumulate a red pigment when grown on media containing limiting adenine[2,11].

The isolation numbers of the ten UV-induced adenine-1 mutants are 3, 25, 40, 51, 107, 153, 169, 199, 233, and 249. Mutants 169 and 199 are temperature-sensitive auxotrophs.

The ten mutants were tested for their ability to recombine, in an attempt to produce an intragenic recombination map of the adenine-1 locus.

The results of the crosses[1,12] involving all the possible pairwise combinations of the ten adenine-1 mutants in h^+ and h^- mating types are given in the Table. Recombination frequencies are expressed as numbers of adn^+ recombinants per 10^6 viable ascospores plated on minimal medium agar (MMA). It was impossible to determine frequencies of adn^+ recombinants in the crosses involving mutant 233 with mutants 25, 51, 107, 169, and 199 due to the growth of mainly unstable complementing diploids and aneuploids on the MMA plates (Leupold[12]).

The results obtained show quite clearly that the ten UV-induced adenine-1 mutants tested represent damage at ten distinct sites within the adenine-1 locus. Seven of the ten are clustered towards one end of the locus, two (numbers 233 and 3) are close together in the central part of the adenine-1 locus, and mutant 40 is located towards the other end of the locus. Additional UV-, spontaneous-, and diethyl sulphate-induced mutants also belong mainly to the same cluster containing the seven mutants (25, 51, 107, 153, 169, 199, and 249) tested in the present study, or to a central cluster which includes mutants 3 and 233 of the ten tested here (Leupold[12]). Taken together with

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Adenine-1 recombination results

Serial no. of mutant	3	25	40	51	107	153	169	199	233	249
3	0 (*1.84*)	74 (*1.76*)	166 (*3.29*)	132 (*3.77*)	130 (*1.71*)	160 (*1.73*)	265 (*1.89*)	159 (*1.30*)	11.7 (*2.13*)	136 (*4.31*)
25		0.29 (*3.41*)	206 (*5.29*)	15.7 (*11.01*)	8.8 (*6.24*)	49.5 (*3.28*)	32.8 (*5.98*)	17.4 (*6.52*)	Comple-mentation	16.2 (*6.22*)
40			0.62 (*4.87*)	260 (*8.99*)	327 (*5.78*)	130 (*8.09*)	325 (*6.27*)	316 (*5.51*)	116 (*6.27*)	237 (*7.21*)
51				0 (*7.70*)	6.05 (*11.57*)	10.4 (*8.52*)	9.7 (*10.84*)	2.1 (*10.96*)	Comple-mentation	6.2 (*12.43*)
107					0 (*3.42*)	13.8 (*6.90*)	13.2 (*8.98*)	6.95 (*4.90*)	Comple-mentation	2.15 (*8.82*)
153						0 (*2.89*)	7.65 (*8.77*)	4.24 (*13.44*)	85 (*8.14*)	25.9 (*12.2*)
169							0 (*3.69*)	5.35 (*4.86*)	Comple-mentation	22.2 (*8.56*)
199								0 (*2.89*)	Comple-mentation	7.8 (*6.68*)
233									0 (*1.8*)	98 (*5.60*)
249										0 (*5.68*)

Adn$^+$ per 10^6 spores (weighted mean values, based on 2–5 estimates per cross). All mutants induced by UV. Example: 159 (*1.30*) = 159 adn$^+$ recombinants per 10^6 viable spores. $1.30 \cdot 10^6$ viable spores plated.

additional data[6,12], a probable order for the ten UV-induced adenine-1 mutants is 40...(233, 3)...(25, 107, 249, 51, 199, 169, 153) where those mutants in brackets are clustered together.

The recombination frequencies obtained are not strictly additive. Probably dilution and plating errors will have affected the estimates of adn$^+$ recombinants per 10^6 viable ascospores, and there may be present also errors resulting from the presence of low frequencies of diploid cells in the haploid strains which were crossed[12]. In this context it is interesting to compare the three sets of data available for some crosses between adenine-8 mutants[2,8,9]. HOLLIDAY[13] has recently postulated mechanisms by which non-additivity in intragenic recombination frequencies can occur.

Zusammenfassung. Zehn der von LEUPOLD isolierten UV-induzierten Mutanten beim Adenin-1-Gen von *Schizosaccharomyces pombe* sind in zehn verschiedenen Stellen im Gen lokalisiert.

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Deamino[1]-phenylalanine[2]-arginine[8]-vasopressin: A Peptide with Highly Selective Antidiuretic Activity

During the last ten years, the effect of slightly modifying the chemical structure of the neurohypophysial hormones on their principal biological activities has been rather extensively investigated[1,2].

Such studies have revealed that the suppression of the phenolic OH-group[1,3–12] in position 2 as well as the removal of the amino group[1,13–19] in position 1 leads to highly active compounds with interesting pharmacological profiles. Some of these compounds possess qualities which – from the therapeutic point of view – confer advantages over the naturally occurring neurohypophysial hormones.

We therefore investigated the influence of both these modifications together on human antidiuretic hormone by synthesizing and biologically testing deamino[1]-phenylalanine[2]-arginine[8]-vasopressin.

Methyl L-phenylalaninate was reacted with 2,4,5-trichlorphenyl N-benzyloxycarbonyl-L-phenylalaninate to