

isolated from 1 g wet liver tissue. There was an insignificant decrease of the mitochondrial nitrogen in all experimental groups with the exception of the rats with HyE or HyE + PHE. In the right-hand column, oxygen consumption by mitochondria isolated from the liver tissue is expressed per mg mitochondrial nitrogen. A significant decrease was noted in sham-operated rats (after 24 h, $P < 0.05$), in those with PHE (after 24 h, $P < 0.001$; after 48 h, $P < 0.001$), with HyE plus laparotomy ($P < 0.05$) and HyE plus PHE ($P < 0.05$). HyE alone was without effect; similarly, laparotomy alone showed no influence after 48 h.

The decrease of succinate oxidase activity calculated per unit liver weight in the first 48 h after partial hepatectomy is more pronounced than the respective decrease of mitochondrial nitrogen. This suggests that the drop in activity of the succinate oxidizing system cannot be explained by the decrease of the number of mitochondria. The overall oxygen uptake for the oxidation of hydrogen atoms removed from succinate decreases considerably following PHE, whereas succinate dehydrogenase activity in mitochondria and especially in the fluffy layer² has a rising tendency. If one assumes, with GREEN¹⁶, that the relative proportions of the components of the terminal electron transport chain are constant, it would be inevitable to conclude that the concentration of other components does not drop either. The decrease in activity of the overall system might then be explainable by the change of the cofactor concentration or by the presence of inhibitors or, possibly, by the change of spatial orientation of the individual components. Our further analysis of the phenomenon reported here follows these lines. Pituitary

function does not seem to be in causal relationship with the decrease of succinoxidase activity. In further study of the metabolism following PHE, it will be necessary to pay attention to possible nervous regulatory links or to the direct influence of the concentration changes of substances in blood or liver. As the results obtained with laparotomized rats show, the drop in succinate oxidase activity after PHE may partly be accounted for by the surgery itself.

Zusammenfassung. Bei den 24 und 48 h nach partieller Hepatektomie (Resektion von 65–70% der Leber) aus der Rattenleber isolierten Mitochondrien wurde eine Abnahme der sukzinoxidaseaktivität beobachtet. Dasselbe wurde auch bei Ratten beobachtet, bei welchen gleichzeitig mit der partiellen Hepatektomie eine Hypophysectomie durchgeführt wurde. Die Veränderung der Sukzinoxidaseaktivität ist nicht auf eine Erniedrigung der Mitochondrienzahl pro Gewichtseinheit Leber zurückzuführen.

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¹⁶ D. E. GREEN, 6th Intern. Congr. Biochem., New York Abstr. VIII-S7 (1964), p. 615.

The Effect of Fluorouracil and Fluorodeoxyuridine on the Genetic Recombination in *Schizosaccharomyces pombe*

Fluorodeoxyuridine, an inhibitor of DNA synthesis¹, is known to have a stimulating effect on the genetic recombination in a number of organisms^{2,3}. During a study on the genetics of the Ad_2 locus of the fission yeast *Schizosaccharomyces pombe*, methods were investigated with which the relatively small frequencies of recombination, observed at this locus, could be increased. To this end the effect of fluorouracil (FU)⁴ and fluorodeoxyuridine (FdUR)⁴ on the frequencies of recombination in an intergenic cross, involving the two closely linked mating type genes⁵ and an intragenic cross involving two spontaneous mutants at the Ad_2 locus⁶, was investigated.

The strains used for the first set of crosses were the two wild type strains 972 and 975, and for the second set, the mutants ad_2 -R-67 and ad_2 -R-113.

The drugs, in sterile filtered solutions, were added to the autoclaved crossing medium containing 3% malt extract and 2% agar. The cells were mixed in equal proportions, spread on the crossing medium slants, and incubated at 25°C. After 7 days of incubation the crosses were treated with ethanol⁷. The ascospores from the mating type crosses were plated on malt extract plates which were incubated for 6 days at 25°C. In order to differentiate the recombinant homothallic colonies from the non-recombinant colonies, the plates were treated with iodine

vapour⁸. The ascospores from the ad_2 crosses were plated on minimal and on adenine supplemented plates. After 6 days of incubation at 30°C the colonies were scored and the frequencies of recombinant prototrophs calculated.

Figure 1 shows the results of the mating type crosses. The frequency of recombination was increased almost twentyfold at the highest concentration of FU used. The effect of FdUR was less pronounced, only a twofold increase being observed. Figure 2 summarizes the data of the adenine mutant crosses. Here too a stimulation of the genetic recombination by FU and FdUR could be demonstrated.

In control experiments the mutagenicity of FU and FdUR in the strains used in the recombination experiments was tested. The results of these tests were negative. It seems that both drugs are recombinagens and not mutagens for *S. pombe*.

It is assumed that both FU and FdUR, which in vivo probably undergo a transformation to the corresponding

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⁸ U. LEUPOLD, Pathologia Microbiol. 18, 1141 (1955).

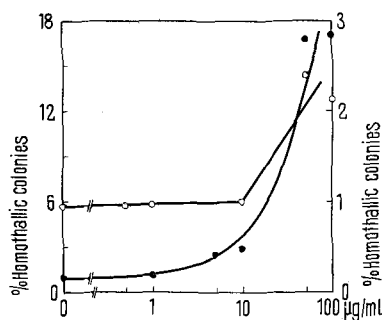


Fig. 1. The effect of fluorouracil (FU) and fluorodeoxyuridine (FdUR) on the frequency of recombination between the two mating type genes of *S. pombe* expressed in % of recombinant, homothallic colonies from ascospores of FU and FdUR treated crosses. FU and FdUR at the given concentration were added to the crossing medium.

● FU = fluorouracil; ○ FdUR = fluorodeoxyuridine.

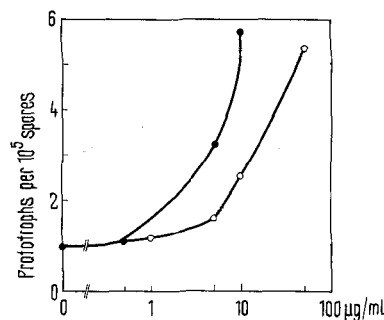


Fig. 2. The effect of FU and FdUR on the frequency of recombination between two allelic mutants *ad₂-R-67* and *ad₂-R-113* at the *Ad₂* locus of *S. pombe*. FU and FdUR at the given concentration were added to the crossing medium. ● FU = fluorouracil; ○ FdUR = fluorodeoxyuridine.

ribotides and deoxyribotides respectively, inhibit the DNA synthesis in *S. pombe*. It seems therefore reasonable to assume that recombination in *S. pombe* occurs in the absence of DNA synthesis and the mechanism of recombination in this organism is of the breakage and rejoining and not of the copy choice type⁹.

A mechanism, similar to that observed in *B. subtilis*¹⁰, by which FU and FdUR induce single strand breaks in the DNA molecules, could also operate in *S. pombe*. Such breaks would facilitate genetic recombination. Alternatively one could speculate that FU and FdUR treatment of cells undergoing meiosis prolongs the period of chromosome pairing, thus increasing the probability of recombination.

Zusammenfassung. Die Rekombinationshäufigkeit, in inter- und intraallelen Kreuzungen bei *Schizosaccharomyces pombe*, wird durch Zugabe von Fluorouracil oder Fluorodeoxyuridin zum Kreuzungsmedium stark erhöht.

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Lipid-Mobilizing and Hypoglycaemic Activity of Pituitary Homogenates from Alloxan-Diabetic Rats

The presence of substances with a lipid-mobilizing and hypoglycaemic activity in the pituitary has been known for 30 years^{1,2}; nevertheless attempts to investigate these activities in the pituitary in relation to the physiological condition of the animal are still rare.

In the present work we investigated the lipid-mobilizing and hypoglycaemic effect of pituitary homogenates of intact and alloxan-diabetic rats. For the experiments male Wistar rats with an initial weight of 197 ± 10 g were used. Diabetes was induced by administration of alloxan hydrochloride, 250 mg/kg, in two subcutaneous injections in the course of 4 h. The diabetic rats lost $8.3 \pm 4.6\%$ of their weight within 8 weeks, their blood-sugar level varied from 275–563 mg%. The control animals gained in the same period $58.5 \pm 5.1\%$ of their body-weight. The pituitaries were removed immediately after decapitation and homogenized in a Potter-Elvehjem glass homogeniser in 0.02M sodium phosphate solution (pH 8.6). In the experiments, pooled specimens of pituitary homogenate from 5–6 rats were examined. The activity of the homogenate was tested on male mice (strain H); as an index of lipid-mobilizing activity changes in the liver fat content and free fatty acid blood level 6 h after the subcutaneous administration of pituitary homogenate was used. The

free fatty acids were estimated by TROUT's modification³ of DOLE's method⁴, the fat content of the liver gravimetrically after extraction, as described by FOLCH⁵, the blood sugar level by a modification of Somogyi-Nelson's method⁶.

Figure 1 summarizes the results of two separate experiments from which it appears that the administration of 1–3 mg pituitary tissue of alloxan-diabetic rats to mice led to a significantly smaller fatty infiltration of the liver and a smaller rise of the free fatty acid level in blood in comparison with the corresponding weight of control pituitaries. Similar results were obtained also in the subsequent experiment with rat pituitaries, and in a preliminary experiment with pituitaries from normal and alloxan-diabetic rabbits. From Figure 2 it appears also that the hypoglycaemic activity, which usually runs parallel with the lipid-mobilizing activity, is markedly reduced in the homogenates from diabetic rats; while,

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