If each spermatogonial generation were equally labelled initially the concentration of label in sperm would be halved every 3 days (with each successive mitosis). This is just what is happening in Table 1. Together with other details to be published elsewhere, this shows how exact is the progression of spermatogenesis in the mouse, with very little overlap between sperm derived from successive generations of spermatogonia.

In all matings other than those from which sperm autoradiographs were made, the females were dissected on the thirteenth day of pregnancy and the frequency of dominant lethals recorded. The simplest estimate of mutation-rate is the ratio of deciduomata to other implants[1] given in Table 1 for each day's mating. There is a remarkable day-by-day parallelism with the degree of labelling of the sperm.

That tritiated thymidine is mutagenic for the nuclei into the deoxyribonucleic acid of which it is incorporated is only to be expected, though we believe this is the first demonstration of the phenomenon in a mammal. What is remarkable to us is the quantitative aspect: that it requires a concentration of tritium which gives 25 grains per sperm in three weeks' exposure to produce one dominant lethal mutation per sperm. From injection to mating was approximately 5 weeks. On geometric grounds it has been argued (Taylor, J. H., personal communication) that about 40 per cent of the transmutations of tritium will be represented as grains. The number of transmutations in the 5-week period to mating will therefore be $100/40 \times 5/3$ ($= 4{\cdot}167$) times the number of grains. This estimated number of transmutations per sperm has been entered in Table 1. From this it appears that only about 1 per cent of the transmutations of tritium incorporated into DNA thymidine produces a dominant lethal mutation (which we may roughly equate to a chromosome break). It should be noted that the dose is chronic (continuous over 5 weeks) and partitioned between spermatocytes, spermatids and sperm (with their different responses to radiation) in the ratios of approximately 2 : 1 : 2.

It would be very difficult to express tritium-labelled thymidine in terms of rem and thus to calculate its relative biological efficiency. In any event we do not feel competent to do so. It can be concluded, however, that the great majority of transmutations fail to produce a chromosome break either at the site of the transmutation or in the track of the electron (max. energy, 18 keV.; mean, 6 keV.). Whether this is due to the absence of initial damage or to the high rate of recovery (repair or restitution) we cannot say.

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Transformation in Yeast: Evidence of a Real Genetic Change by the Action of DNA

In a previous paper[1] a successful transformation of yeast akin to the transformation of bacteria was reported and it was shown by the normal Mendelian segregation that the newly acquired abilities were localized exclusively in the nucleus.

Deoxyribonucleic acid (DNA) was extracted from *Saccharomyces chevalieri* (W_{332}) and dissolved in brewery wort, which was used as culture medium for the yeasts R_7 and $K_{83}S_{58}$; the donor yeast can ferment sucrose and raffinose 1/3, but the acceptor can ferment only mono-saccharides. After the DNA treatment, cells were isolated which had acquired the ability to ferment sucrose or both sucrose and raffinose. Back crosses with the recessive yeast showed a regular Mendelian segregation.

Harris and Thompson[2], repeating these experiments, were unable to confirm the results, although they used the same yeasts and the same extraction method. Laskowski and Lochmann[3] also failed to obtain a transformation in yeast, but these latter workers did not report sufficient technical details to allow judgment of their results in contrast to the former.

Instead of going into the minor differences between the technique used by Harris and Thompson and by me, a general comment may be made which might account for the negative results published. According to my experience, it is not yet possible to predict the biological activity of a DNA preparation. Sometimes the extract is active, and hereditary characters from one yeast are transferred into the other yeast, whereas at other times no results can be obtained. This might be ascribed either to (*a*) inactivation of the extract, or to (*b*) incompetence of the yeast. These varying results are obtained without any indication of the cause and without any demonstrable change of the extraction method. Attempts to trace the origin of this peculiar phenomenon have been unsuccessful and work on the subject is proceeding. Nevertheless, some of the experiments have shown a transforming activity[4,5].

The purification of the extracted DNA without loss of activity has been attempted by fractionation by means of the ion-exchange 'Ecteola'-cellulose column. As estimated by the absorption spectrum curves, very pure fractions of DNA were obtained; but the hope of being able to fractionate in this way the DNA into fractions containing only one gene or a restricted number of genes was not realized. In these experiments two haploid yeasts (*Sacch. cerevisiae*) deficient in adenine and tryptophan respectively were treated with these purified fractions of DNA prepared from the diploid non-deficient yeast *Sacch. chevalieri*. The former can ferment maltose, the latter cannot ferment this sugar. The treated cultures were sporulated on Fowel's agar and in most instances many asci were found, indicating the diploid state. Single cell cultures which could not ferment maltose were often obtained and were able to synthesize adenine or tryptophan.

These experiments permit the conclusion that both dominant and recessive characters can be transferred. Experiments with a negative result, that is, without a transformation effect, point to the absence of mutagenic factors in the DNA preparations. Thus I have been able to hybridize non-sporulating yeasts, for example, the bottom yeasts used in the brewing industry, by the transformation procedure.

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