A PHYSIOLOGICAL BASIS FOR SOME SUPPRESSOR MUTATIONS AND POSSIBLY FOR ONE GENE HETEROSIS*

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A mutant strain of Neurospora which requires sulfonamides for growth at 35° frequently becomes altered so that it can grow at that temperature without sulfonamides. In each instance analyzed, the developed ability to grow without sulfonamides has resulted from mutation of genes distinct from that responsible for the sulfonamide requirement. Each "reverted" strain has proved to be a heterocaryon, composed of two kinds of nuclei, both of which carry the gene (sfo) for sulfonamide requirement, but one also carries a new "suppressor" gene. At least two independent suppressor genes have been involved in such reversions. Homocaryotic strains have been isolated, some carrying both sfo and the suppressor, others carrying the suppressor alone. None of these isolates has the growth characteristics of wild type, but each shows some peculiar relationship to the p-aminobenzoic acid requirement, the nature of which is still obscure. In a few instances, artifically constructed heterocaryons between the sulfonamide-requiring strain and a strain carrying both the sulfonamide-requiring gene and a suppressor have resulted in better growth on minimal medium than either strain is capable of by itself, thus reconstituting the situation observed in the original "reverted" heterocaryons.

As long as it was believed that sulfonamides were used as metabolites by the sulfonamide-requiring strain it was difficult to picture a possible physiological basis for the circumvention of the drug requirement by mutation of some entirely different gene. Recently Zalokar\(^2\) has shown that the "sulfonamide-requiring" strain can grow in the absence of sulfonamides provided the available p-aminobenzoic acid is reduced to a particular concentration, growth being inhibited by both higher and lower
concentrations. It now appears that in the sulfonamide-requiring strain some reaction catalyzed by \( p \)-aminobenzoic acid is detrimental in that growth is prevented unless the effective amount of \( p \)-aminobenzoic acid is decreased, either by the competition of sulfonamides,\(^1\) or by a reduction in the amount synthesized by the strain.\(^2\) It follows then that any mutation which would have the effect of reducing the available \( p \)-aminobenzoic acid content might permit growth of the sulfonamide-requiring strain in the absence of sulfonamides, and this could happen even if the mutant gene was carried by only part of the nuclei in a heterocaryon.

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**FIGURE 1**

Growth curves of the sulfonamide-requiring mutant strain (\( sfo, + \)), the double mutant sulfonamide requiring, \( p \)-aminobenzoicless (\( sfo, pab \)), and of heterocaryons between them, on minimal medium at 35°. Changes in growth rates in the heterocaryons are presumably due to changing relative frequencies of the two types of nuclei at the growing tips.
To test this possibility, artificial heterocaryons were made between a double mutant strain carrying the sulfonamide-requiring gene (sfo) and a gene (pab) which prevents the synthesis of p-aminobenzoic acid, and a strain carrying sfo and the wild type allele (+) of pab. Neither of these strains sfo, pab or sfo, + grows appreciably on minimal medium at 35°C, but as indicated in figure 1 the heterocaryons between them do.

These are not the ordinary sort of heterocaryons (cf. Beadle and Coonradt3) in which growth results because each of the two sorts of nuclei carries the wild type allele of the mutant gene carried by the other, since in these there are no nuclei carrying the wild type allele of sfo. In this case growth results from a balance between the production of p-aminobenzoic acid by one type of nucleus and the lack of production by the other to give an amount tolerated by strains carrying sfo, yet still sufficient for growth.

A heterocaryon of this sort, composed of two kinds of haploid nuclei, both carrying sfo, and one carrying pab the other +, is roughly equivalent to a diploid organism heterozygous for a single pair of alleles pab/+; the homocaryotic strains mixed to form the heterocaryons can be compared to the corresponding homozygous diploids pab/pab and +/++. The augmented growth of the heterocaryon reminds one of the instances of single gene heterosis in maize reported by Jones.4

It is not the intent of this note to suggest that most instances of one gene heterosis and most occurrences of suppressor mutations result from competitive systems such as must be involved in the case just described, but such a possibility must be borne in mind.

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