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Test for Genetic Recombination in Kappa Particles of *Paramecium aurelia*, Variety 4

Kappa particles are microscopically visible structures, about a micron in length, which are distributed at random in the endoplasm of certain strains of paramecia. Furthermore, these particles, numbering several hundred per paramecium, are self-reproducing and mutable, and they contain deoxyribonucleic acid and are capable of infecting other paramecia under certain conditions (1). It is clear that the kappa particle shows many properties of a microorganism; hence, another property, genetic recombination, was also looked for.

At least two pairs of characters which do not lie at the same genetic locus must be studied to detect recombination. With kappa particles two such pairs are (i) ability, or lack of it, to produce the poison paramecin and (ii) ability, or lack of it, to persist in paramecia under certain culture conditions. The reason for assuming that these characters are not at the same locus is that they mutate independently of one another. Specifically, *slow hump kappa* particles (2) produce paramecin but are lost from animals grown at maximal fission rate at 31°C; *pi* particles (3) do not produce paramecin and are not lost under the growth conditions just described. Both types are mutants of the *normal hump kappa* particles found in stock 51 of *Paramecium aurelia*, variety 4. Normal hump kappa particles, like slow hump kappa, produce paramecin, but, like pi are not lost from well-fed paramecia grown at 31°C.

The test for recombination is to determine whether, following placement of slow hump kappa and pi particles in a common cytoplasm, there will appear particles capable both of producing paramecin and of persisting in host organisms grown at maximal rate at 31°C. That is, will normal hump kappa-like particles appear? This test was made as follows. Three types of paramecia, containing pi and slow hump kappa particles, containing only slow hump kappa particles, and containing only normal hump kappa particles, were all grown under conditions which would result in the marked decrease or loss of slow hump kappa particles, as indicated by a

marked decrease or loss of poison production. Then the progeny of all three sets were tested for production of paramecin. The animals containing pi and slow hump kappa particles gave results comparable to those given by animals containing only slow hump kappa, both groups showing little or no paramecin production, whereas the normal hump kappa animals produced large amounts of the poison.

If the animals containing both pi and slow hump kappa particles had shown paramecin production similar to that of the normal hump kappa animals, then appearance of a recombinant type of particle in the former would be a possible explanation. In the absence of such a finding, the simplest conclusion is that under the conditions of this experiment no recombination occurs. This experiment assumed that the recombinant would behave as normal hump kappa do in the presence of pi—that is it would become abundant in each organism (4). However, it is possible that the recombinant might be of a new type which would exist only in a very low frequency. The experiment, as executed, does not test this possibility (5).

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References and Notes

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5. This article is contribution No. 647 from the Zoology Department of Indiana University. During the course of this investigation, I was a predoctoral fellow of the National Science Foundation. This work was aided in part by a grant from the Rockefeller Foundation for work in genetics at Indiana University, and in part by a grant-in-aid to Professor T. M. Sonneborn from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

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Acetylcholine Hydrolysis in Psychiatric Patients

In a recent report (1) I suggested the possibility that the mechanism underlying the relationship between scotopic threshold changes and psychiatric disorders may be a deficiency in the acetylcholine-cholinesterase balance.

Granger (2) reported that schizophrenics manifested a significant elevation of the dark-adaptation curve along the log-luminance axis, without alteration of shape, as compared with normals. Rubin and Goldberg (3) employed Sarin (isopropyl methylphosphonofluoride), an anticholinesterase, in experiments designed to determine the effect

on scotopic visibility of measured quantities of inhaled material and found significant elevations of the absolute visual threshold. A second study (4) indicated that conjunctival instillation had no significant effect on dark adaption, while significant elevation of the dark-adaptation threshold did occur when both eyes were protected from the atmosphere containing Sarin and in both eyes although only one had been protected. Rubin *et al.* (5) then performed another test of the hypothesis that the eventuation of the threshold response was localized in the central nervous system. Following exposure to Sarin, it was found that the tertiary atropine salt (atropine sulfate) reduced the elevated threshold to the preexposure level while the quaternary methosalt of atropine (atropine methyl nitrate) had no effect on the Sarin-produced elevated threshold. The ability of the tertiary salt to pass the blood-brain barrier while the quaternary salt does not suggested that the cholinergic blocking effect observed was acting centrally. It was further suggested that acetylcholine-cholinesterase concentrations are important determinants of the dark-adaptation process. These results suggested that the elevated dark-adaptation thresholds observed in schizophrenia could be attributed to some biochemical imbalance between the enzyme and its substrate.

With this paradigm in mind, it was posited that the hydrolysis rate of acetylcholine by erythrocyte cholinesterase should be different for normals and for patients admitted to a psychiatric institute (6). Blood samples (5 ml) were obtained from 10 volunteers among the hospital staff and from 23 patients within 24 hours after admission and prior to the administration of any kind of therapy. Michel's electrometric method (7) was employed to determine the activity of the cholinesterase (8). The rate of hydrolysis of acetylcholine by erythrocyte cholinesterase for the normals and institutionalized patients is presented in Table 1. The standard error of regression for the normals was found to be $s_b = \pm 0.0003$, and the fiducial limits of the slope at the 5-percent level of confidence for $(n-2)df$ was found to be $1_1 = -0.0106$ and $1_2 = -0.0088$. The slope for each patient was calculated and then evaluated relative to the fiducial limits calculated for the normal sample. Six out of 23 patients had slopes that fell within the fiducial limits of the sample, while 17 distributed themselves into two groups that differed significantly from the linear regression that characterized the sample of normals. Ten patients showed significantly slower, and seven patients showed significantly faster, hydrolysis of acetylcholine by erythrocyte cholinesterase. Of the six patients whose slopes were in the normal hy-