Reports

Tumor-Inducing Factor in Drosophila

Abstract. Attempts to repeat experiments reported to demonstrate the existence of a tumor-inducing factor in the *tu-e* mutant of *Drosophila* were not successful.

In view of the continued references (*1*) to earlier work in this laboratory (*2*) concerning the purification and properties of a reputed tumor-inducing factor (TIF) from the *tu-e* mutant of *Drosophila*, it seems desirable to comment on the investigations described and on additional experiences.

Initially I served as adviser to F. Friedman and L. Burton on the purification of TIF with the assumption that the biological assay was satisfactory. However, shortly before the departure of these investigators from this laboratory they were presented with coded samples containing only buffer solution or buffer plus various concentrations of "purified TIF." The results of their assay demonstrated clearly that they could not distinguish buffer solution from TIF solutions. Because of the possible validity of some of the explanations offered for this, and because of some subsequent experiments of a similar nature, I undertook a repetition of tumor transmission experiments with both crude and purified extracts. Control series totaling 1047 animals, surviving to adults after injections, yielded 216 (20.4 percent) with melanotic inclusions, whereas 207 (18.5 percent) were observed among 1120 animals surviving injections of preparations from the *tu-e* mutant. Percentage survival varied widely, as did percentage "tumors" (2 to 80 percent), in different experiments, but controls did not differ significantly from experimentals when injections were made at the same time.

Since various arguments can be invoked, neither these results, nor other details not given here, prove that a tumor-inducing factor does not exist in the *tu-e* mutant of *Drosophila*. Nevertheless, I would be pleased to be forgotten as a collaborator in the work described earlier (*2*).

HERSCHEL K. MITCHELL
Biology Division, California Institute of Technology, Pasadena

References

1. L. Burton, F. Friedman, R. Kassel, M. L. Kaplan, A. Rottino, *Trans. N.Y. Acad. Sci.* **21**, 707 (1959); R. Kassel, L. Burton, F. Friedman, A. Rottino, *Proc. Soc. Exptl. Biol. Med.* **101**, 201 (1959); F. Friedman, R. Kassel, L. Burton, M. L. Kaplan, R. Rottino, *ibid.* **103**, 16 (1960).
2. L. Burton, F. Friedman, H. K. Mitchell, *Cancer Research* **16**, 880 (19[illegible] F. Friedman, L. Burton, H. K. Mitchell, *Ann. N.Y. Acad. Sci.* **68**, 349 (19[illegible] L. Burton, F. Friedman, H. K. Mitchell, *ibid.* **68**, 356 (1957); F. Friedman, L. Burton, H. K. Mitchell, *Cancer Research* **17**, 208 (1957).

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Rapid Effect of Sodium Cyanide and Dinitrophenol on Mammalian Nerve

Abstract. Strips of rat nerve from dorsal roots were immersed in solutions containing sodium cyanide and α-dinitrophenol. The inhibitors extinguish the action potential of such strips within minutes. The rapid action on mammalian nerve is contrasted with the slow effect of inhibitors on amphibian and invertebrate nerve.

The application of cyanide to the squid giant axone (*1*) or to frog peripheral nerve (*2*) does not block conduction or depress the resting potential for at least 2 hours. Presumably the effect of inhibitors on sheathed nerve that has been reported (*3*) may be explained as resulting from the increased leakage of ions into the extracellular space around nerve fibers; the ions having been restrained from diffusion by the envelope of sheaths surrounding the nerve fibers would become more concentrated and cause depolarization. The slow action of the inhibitors on invertebrate and frog nerve has been offered as evidence that the action potential is not directly dependent upon metabolic energy. We have attempted to assess the generality of these results by applying sodium cyanide and α-dinitrophenol to mammalian nerve.

Rats were anesthetized with ether, the lumbar roots were exposed, and thin strips of nerve were dissected from these roots. The rootlets were placed on silver stimulating and pickup electrodes; they were then stimulated with a 0.1-msec pulse, and the action potential was photographed with a Polaroid Land camera from a Dumont 304H oscilloscope after preamplification with a Grass P-4 amplifier. The strips were kept in Ringer's solution (20° to 25°C) for a 1-hour control period and immersed in Ringer's solution to which an inhibitor was added. The strips were tested periodically until the potentials disappeared; they were then placed quickly in Ringer's solution to check the reversibility of inhibition.

Strips were immersed in 0.005*M* solutions of sodium cyanide and 0.001*M* solutions of α-dinitrophenol within a *p*H range of 6.8 to 7.6. Figure 1 is a graph of the amplitude of the action potentials obtained for 17 strips immersed in cyanide (open circles) and ten strips placed in α-dinitrophenol (solid circles). The effect on individual strips may occur more rapidly than the average values indicate. The shortest disappearance of the action potential occurred in about 1 minute with a strip in cyanide solution. The longest survival time was 15 minutes. Such a range may be attributed to the variability in strip diameters.

After disappearance of the potentials, the strips were again immersed in Ringer's solution. The cyanide-poisoned nerves recovered almost the full amplitude of the action potential within 2 to 3 minutes; the strips treated with α-dinitrophenol did not recover at all, even after prolonged washing in Ringer's solution. Nerves may be treated with cyanide and reversed repeatedly, provided washing is performed immediately after disappearance of the potential.

The inhibitors cyanide and α-dinitrophenol, in contrast to their action on frog and squid nerve, rapidly extinguish the action potential of mammalian nerve. The experiments of Dettbarn and Stämpfli (*4*) have shown that α-dinitrophenol does not affect the resting potential of rat nerve. If cyanide is similarly ineffective, the inhibitors do not act by depolarizing nerve. Schoepfle and Bloom (*5*) have suggested that the effect of cyanide on frog nerve is to alter the *h* factor before altering the sodium or potassium equilibrium poten-

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Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].