

Beadle G W & Tatum E L. Neurospora. 2. Methods of producing and detecting mutations concerned with nutritional requirements. *Amer. J. Botany* **32**:678-86, 1945.

The authors describe various methods of inducing, identifying and characterizing large number of gene mutations in the red bread mold Neurospora that are concerned with the synthesis of vitamins, amino acids and other essential metabolites. [The *SCI*[®] indicates that this paper was cited 271 times in the period 1961-1977.]

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"Our approach to a better understanding of genes, enzymes and chemical reactions goes back to the turn of the century when, shortly after the rediscovery of Mendel's work, the biochemist-physician Garrod demonstrated a relation between the genetic disease alcaptonuria and a postulated enzyme. Unfortunately his findings soon dropped out of the genetic literature.

"As a graduate student with the plant geneticist R.A. Emerson in the 1930's, I recall his futile attempts to interest plant physiologists and biochemists in making use of genetic traits in corn known to be concerned with the synthesis of chlorophyll and its role in photosynthesis.

"As a National Research Council Fellow at the California Institute of Technology, I was much influenced by researchers there, especially by Boris Ephrussi, a Rockefeller Foundation Fellow from Paris, who was interested in the role of genes in development and function. The organisms of choice for genetic studies, *Drosophila* for example, seemed less suited for studies of

development than were sea urchins or frogs, favorites of embryologists.

"But the genetics of eye pigments in *Drosophila* did offer promise of bringing the two approaches together. By devising techniques of transplanting larval embryonic eye-buds we did identify two enzymatic steps in brown eye-pigment synthesis, with evidence that each was the immediate control of a single gene, a relation that prompted the slogan 'one gene-one enzyme.' We then attempted to understand the biosynthesis of brown eye pigment, Ephrussi with Kouvine in Paris and I with Tatum at Stanford. Tatum and Haagen-Smit isolated a crystalline precursor of brown pigment, later identified by Butenandt and Weidel as kynurenine.

"Serendipity then came to our aid. Tatum was familiar with the work of Mills Fries in Sweden who had worked out the nutritional requirements of a number of filamentous fungi. I knew the genetic advantages of the red bread mold *Neurospora*, also a filamentous fungus but one Fries had not investigated. Tatum soon determined that *Neurospora* would prosper on a simple chemically defined medium including biotin which had just become available commercially.

"We were thus in a position to induce an array of mutants as described in this paper. At the time it was written, we had identified the nutritional requirements of 43 mutant lines, these representing 23 vitamins, amino acids and other metabolites.

"The accomplishments recorded in this article represent the efforts of many investigators, most, but not all of whom are listed in the summary of mutant strains, Table 5 of the article, and in the literature cited. No longer could doubt continue as to the indispensable relations of genes, enzymes and biochemical reactions."