Edward Lawrie Tatum
1909–1975

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EDWARD LAWRIE TATUM[1,2]

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Edward L. Tatum's contributions to the founding of biochemical genetics and of bacterial genetics were instrumental in the transformation of modern biology, which increasingly has focused on the flow of information through nucleic acids and the protein structure of the cell.

Tatum was most effective in collaborative investigations, in which he played the role of microbiologist and biochemist, meeting challenges of profound genetic interest. In these studies, he was instrumental in the development of microorganisms such as *Neurospora* and *Escherichia coli* as tools for fundamental genetic investigations. In 1958, he shared the Nobel Prize in Physiology and Medicine with G. W. Beadle and J. Lederberg, having been a principal partner in these separate, major lines of research.

Tatum was born December 14, 1909, at Boulder, Colorado, the first son of Arthur L. and Mabel Webb Tatum. At that time, Arthur was just beginning a career in academic pharmacology that would take him, by 1925, to the University of Wisconsin, where Edward received both his undergraduate and graduate education. His PhD thesis, under the supervision of W. H. Peterson and Marvin Johnson, concerned the nutritional requirements of propionic-acid bacteria. This work, the first to show that thiamin, long known as a vitamin for man and for yeasts, was also a growth factor for a bacterium, led to Tatum's preoccupation with comparative nutrition and biochemistry which illuminated the remainder of his career.

[1]This chapter is adapted from the *Year Book* of the American Philosophical Society for 1977.
[2]This memoir is a progress report on a biographical effort for which I am still seeking documentary material. I would be particularly grateful for correspondence, class notes, or other contemporary documents that could add further precision to this history, particularly for the period 1936–1945, beyond what has been published. A considerable collection of supporting records has already been deposited at the Rockefeller Archive Center.

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While Tatum was completing his research training as a postdoctoral fellow at the University of Utrecht in the laboratory of F. Kogl, which was notable for the characterization of biotin as a vitamin, he received word that G. W. Beadle was recruiting a biochemist to join him at Stanford University. The research, founded on the recent collaboration of Beadle with B. Ephrussi, was a chemical characterization of the precursors of the eye pigments of the fruit fly, *Drosophila.* For many years, genetic mutants with variant eye color had been well-known markers for studies of the transmission of the genes on the chromosomes. This research attempted to probe gene action in more proximate biochemical terms. As it turned out, Tatum joined Beadle at Stanford as a biochemical research associate in the fall of 1937, and set about the task of isolating crystallizable quantities of the pigment precursors from *Drosophila* mutants—a task of no little tedium and technical difficulty. The work was simplified by the discovery of a (contaminant) bacterial strain that also produced a similar substance, and culminated in the isolation of pure crystalline samples with biological activity. The material was subsequently identified as kynurenine-sucrose. However, before Beadle and Tatum could complete their arduous work, they were scooped by Butenandt who, by a routine survey of compounds metabolically related to tryptophane, discovered that kynurenine was active.

This experience led Beadle and Tatum to reexamine their basic research strategies. They decided that it was essential to find an organism more suitable than *Drosophila* for the extraction of biosynthetic enzymes and the isolation of intermediates, even though Tatum had pushed the microchemical art to its limits (before the widespread development of chromatographic methods). Furthermore, they realized that it would economize on the efforts of geneticists if they could have access to biosynthetic pathways that had already received attention from other biochemists.

During this reappraisal, Tatum was starting a new course on comparative biochemistry. In his lectures, which Beadle attended whenever possible, and which provoked many perambulatory discussions, Tatum reviewed available knowledge of the nutrition of bacteria and fungi. In particular he mentioned the work of Nils Fries, his former colleague in Kogl's laboratory. By this time, a number of ascomycetes had been cultivated on defined media, requiring some combination of biotin, thiamin, or a few other water-soluble vitamins as their only required growth factors. Beadle was already familiar with the genetic studies on *Neurospora,* which B. O. Dodge had pioneered, and which C. C. Lindegren had pursued with T. H. Morgan's prompting. It occurred to Beadle that *Neurospora* might indeed be the ideal experimental material for their research program.

Once they procured the necessary cultures, in March 1941, the first task was to verify the nutritional requirements of *Neurospora.* Fortunately, these requirements are quite simple, and within a few days, Tatum was able to establish that biotin was the only required growth factor. Over the period of the next three months, cultures were irradiated, and strains were isolated and tested for their ability to grow on the basic medium. By early July 1941, No. 299 had turned up as a nutritionally demanding mutant and again in extraordinarily simple experiments was shown to have a specific requirement for pyridoxine. These procedures have become the basis for some of the most fundamental analytical techniques in experimental biology, as well as for industrial processes of enormous economic import.

The findings were also the basis both for elaboration of theories of gene action, which Beadle focused on in later work, and for the dissection of biosynthetic pathways, Tatum's more natural province.

Tatum was appointed an assistant professor in 1941. Warren Weaver, of the Rockefeller Foundation, who played such an important role in the development of molecular biology, noted the substantial opposition to the concept that a chemist had a place in a department of biology! He remained at Stanford until 1945, but lacking substantial encouragement at that time, he accepted an invitation (and promotion) from Yale University to establish a program in biochemical microbiology within the Department of Botany. Before he moved east, however, he had already begun studies on biochemical mutation in bacteria, which gave nutritional mutants similar to those found in *Neurospora.*

This work came to the attention of Professor F. J. Ryan at Columbia, and in turn his apprentice (also medical student) Joshua Lederberg. At that time, the idea that bacteria lacked sexual processes was essentially unquestioned. Hence it was not clear how one could go further in genetic analysis of these mutants. Lederberg wrote to Tatum suggesting an experimental protocol to challenge the asexuality of bacteria, and applied for a fellowship to work with him at Yale in this pursuit. Doubtless having already formulated some similar objectives, Tatum agreed to accommodate Lederberg in his laboratory, during a break in the medical school curriculum, from March through August 1946. That cooperation resulted in the discovery of genetic recombination in *Escherichia coli* strain K-12 and the opening up of genetic analysis by crossing in bacteria generally.

Tatum's own research interests turned more to the use of biochemical mutants to analyze synthetic pathways, and he did the pioneering work for such important end metabolites as tryptophane, biotin, and several amino acids. Despite the manifest advantages of bacteria for many of these lines of investigation, he continued to prefer *Neurospora.* This fungus was, after

all, a eucaryote and appeared to offer many advantages for simple models of morphogenesis.

In 1948, a new administration at Stanford and its Department of Biology invited Tatum to return to Stanford, with the offer of a secure and esteemed position. From this time, his attention was increasingly devoted to organizational and administrative matters. For example, he played a significant part in the integration of the Stanford Medical School with the main university campus, and in the establishment of a new Department of Biochemistry, which symbolized the new prestige of this discipline. However, in part owing to complications of his personal affairs, he left Stanford in early 1957 for a professorship at The Rockefeller University in New York.

At Rockefeller, Tatum continued to nurture the scientific development of a number of remarkable young investigators, while his own attentions were increasingly devoted to the advancement of research at an institutional and national level. His work for the National Science Board was particularly notable for its emphasis on the development of scientific talent, on the human resources of science rather than the bureaucratized framework of projects and programs.

The last years of his life were marred by increasingly poor health, substantially self-inflicted by a notorious smoking habit. His mental outlook was further scarred by the agonizing death of his second wife.

Edward Tatum died in New York on November 5, 1975. He was eulogized at the Rockefeller University some few weeks later. Every speaker stressed the generosity and affection with which Tatum nurtured young scientists, and the help that he gave them—often at the expense of his own reputation—to embark on their own careers.

The readers of this *Annual Review* also know the important part that Edward Tatum played as a founding member of the editorial committee of the *Annual Review of Genetics,* on which he served for the first six volumes. Long prior to that time he had been a close personal and professional associate of J. Murray Luck, and had helped him and Annual Reviews as its Assistant Managing Editor for two years prior to leaving Stanford for New York.

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Almost 40 years have elapsed since the landmark discovery of 1941 (Beadle & Tatum 1941). Just how did it change the course of biology's history?

Most of the central ideas were already firmly planted in the contemporary scientific worldview. That genes affected metabolic pathways, doubtless via enzymes, had been Garrod's thesis 30 years earlier. *Neurospora* genetics was already figured in Sturtevant & Beadle's textbook issued in 1939 (Sturtevant & Beadle 1939). The relationship of nutrition to biosynthesis

had been the main concern of microbial biochemistry for the previous decade, and of the laboratories at Wisconsin where Tatum worked on his doctorate.

The novelty of Tatum's work was the integration of these conceptual strands into an effective new experimental methodology: This was the aggressive pursuit of laboratory mutations as tools for the dissection of biochemical pathways and their genetic control. This approach is so deeply engrained in all experimental biology today, whether of viruses or of man, that an act of historical will is needed to remind us that it once had to be discovered.

This report is far from a complete analytical biography, which would require not only access to personal information but also skills in their interpretation that surpass the author's competence. Enough is manifest to show how the professional and personal lives of scientists are interwoven in ways that are not revealed just in their bibliographies.

Literature Cited

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