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Campbell A. Sensitive mutants of bacteriophage λ. *Virology* **14**:22-32, 1961.
[Department of Biology, University of Rochester, NY]

Suppressible, thermosensitive, acid-sensitive, and alkali-sensitive mutants of coliphage λ were isolated and used to identify and map most of the genes determining functions necessary for plaque formation. The suppressors allowing phage growth were shown to include genuine suppressors of host mutations. [The *SCI*® indicates that this paper has been cited in over 595 publications since 1961.]

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In 1957, while working at Cold Spring Harbor Laboratories, I accidentally found that two small plaque mutants of phage λ isolated on one substrain of *Escherichia coli* K-12 (C600) failed to plate at all on another K-12 strain (W3350). During the next two years, first at Cold Spring Harbor and then at the Institut Pasteur in Paris, I isolated a total of 15 such mutants from mutagenized λ stocks. They mapped in widely scattered locations along the λ chromosome and belonged to 12 different complementation groups. I had little idea of the basis of their conditional lethality, but they were extremely useful markers in my investigations of defective, galactose-transducing variants of λ.[1]

When I returned to the US in 1959, I encountered Bob Edgar[2] (then at the California Institute of Technology), who informed me that Dick Epstein had found mutants of phage T4 (which they called "amber" mutants) that had the same host range among K-12 strains as my mutants. We agreed that this sounded as though C600 had an allele-specific, gene-nonspecific suppressor. Edgar pointed out that such mutants might provide a means for identifying all the genes essential for phage growth, and I recalled the earlier relevant work of Horowitz and Leupold[3] on thermosensitive mutants of *Neurospora* and *E. coli*.

In my new position at the University of Rochester, I decided to isolate enough suppressible λ mutants to exhaust the complementation groups accessible by this means and to carry out several tests of the basic ideas Edgar and I had discussed. First, I wanted to show that mutations rendering λ sensitive to extreme conditions (high temperature, high or low pH) would generate the same complementation groups as the suppressible mutants did. Second, I wanted to verify that some bacterial mutants isolated for their ability to suppress a bacterial gene would allow the phage mutants to plate, as C600 did. Third, I wanted to identify the function and product of at least one such gene. For this last purpose I chose lysis and endolysin. When these goals had apparently been accomplished, I published the results. My success in exhausting the complementation groups proved to be incomplete. I found 18 groups; 7 more have been identified since.[4] After the work was completed, I returned to my studies of prophage integration and specialized transduction, for which the mutants were invaluable.

The paper has occasionally been cited for its part in the history of conditionally lethal mutations. The paper of Epstein *et al.*[5] is cited much more often because its impact was far greater. By the time it was written, the mechanism of translational suppression was somewhat understood, and it included a much deeper analysis of the gene functions associated with various T4 complementation groups that I had produced with λ. Interest in similar studies on λ was sparked by a later paper by Katherine Brooks,[6] a graduate student of mine, who investigated the effect of some λ mutants on DNA replication as estimated from genetic pool size. Most of the citations to my paper are references to the origin of the mutants, which were widely distributed among λ workers and remain in use. Some authors also cite the paper as the original reference for specific λ genes that they are studying.

1 **Campbell A.** Ordering of genetic sites in bacteriophage λ by the use of galactose-transducing defective phages *Virology* 9 293-305, 1959 (Cited 40 times)
2 **Edgar R.** Conditional lethals (Cairns J, Stent G & Watson J, eds.) *Phage and the origins of molecular biology* New York Cold Spring Harbor Laboratory, 1966 p 166-72
3 **Horowitz N H & Leupold V.** Some recent studies bearing on the one gene-one enzyme hypothesis *Cold Spring Harbor Symp* **16** 65-74, 1951 (Cited 60 times since 1955.)
4 **Hendrix R, Roberts J, Stahl F & Weisberg R.** *Lambda II* New York Cold Spring Harbor Laboratory, 1983. 694 p
5 **Epstein R H, Bolle A, Steinberg C, Kellenberger E, Boy de la Tour E, Chevalley R, Edgar R, Susman M, Denhardt G & Lielausis A.** Physiological studies of conditional lethal mutations of bacteriophage T4D *Cold Spring Harbor Symp* **28** 375-94, 1963 (Cited 865 times)
6 **Brooks K.** Studies in the physiological genetics of some suppressor-sensitive mutants of bacteriophage λ *Virology* **26** 489-99, 1965 (Cited 105 times)

