

# This Week's Citation Classic

Judd B H, Shen M W & Kaufman T C. The anatomy and function of a segment of the *X* chromosome of *Drosophila melanogaster*. *Genetics* 71:139-56, 1972.  
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**A cytogenetic analysis of the organization of all the genes in a *Drosophila* chromosome segment shows essentially a one function-one polytene band relationship. This suggests that the average gene size is about 25 times larger than needed to encode an average polypeptide. [The *SCI*<sup>®</sup> indicates that this paper has been cited over 190 times since 1972.]**

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"The first series of experiments reported in this paper were done in 1962. I had been working on the white locus of *Drosophila melanogaster* and had given a talk to the genetics group at Texas about the interaction of white with the neighboring zeste locus. We were all stimulated by the concept of the bacterial operon that Jacob and Monod had recently formulated,<sup>1</sup> and I suggested that the zeste-white system might represent the eukaryotic equivalent of an operon. These loci are more than half a map unit apart on the chromosome and no mutants were known that mapped between them. Was it possible that the entire region was a huge operon-like cluster? It was from a conversation with Wilson Stone that the idea to saturate the region was generated. The rationale was to obtain a mutant representative of every gene in the segment and test each for an interaction with zeste or white.

"The first summer's work identified five complementation groups but none showed any zeste or white interactions. Margaret Shen joined me in 1964 and it was her endless patience and meticulous work that kept the project moving. By 1967, we had identified 12 groups and we knew that there

was good correspondence between complementation groups and the bands in the polytene chromosomes. We were at first reluctant to accept this because there are only 5,000 to 6,000 bands and yet the amount of DNA in a *Drosophila* cell is the equivalent of about 100,000 genes the size of those in viruses and bacteria.

"Tom Kaufman became interested in the problem when he arrived as a graduate student in 1967. He set about trying to induce mutants with a series of chemical mutagens we had not previously used. Much hard work uncovered no new groups, and because of the large number of mutants we had produced, we became convinced that we were approaching saturation of the region.

"If our estimate of gene number proved correct, then gene size in *Drosophila* is very large indeed. If we were wrong, what is the nature of the genes for which we could get no mutants? Interesting questions about gene organization can be framed on either alternative, but we were confident that our efforts had indeed detected a majority of the genes in the region and we focused on why gene size was so unexpectedly large.

"To me the most satisfying aspect of the work is that it drew attention, particularly from molecular biologists, to the possibility that genes may consist of much more information than that which encodes a polypeptide. We had failed to uncover the sought after operon, only to discover that a single eukaryotic gene may, in some instances, be as large and complex as several operons or even an entire viral chromosome.

"I believe this paper is frequently cited because it reported one of the most direct measures of gene size and number in a eukaryote. It also raised questions about the organization and complexity of genes at a time when molecular analyses of DNA sequences were just beginning. Our suggestion that genes are much larger than expected because much of the information in them is used in regulation was somewhat controversial. These questions are not yet answered, but work with cloned genes makes it clear that many eukaryotic genes are large mosaic structures with sequences that contribute to a single mRNA interspersed with sequences of unknown functions."<sup>2</sup>

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1. Jacob F & Monod J. On the regulation of gene activity. *Cold Spring Harbor Symp.* 26:193-211, 1961.

2. Axel R, Maniatis T & Fox C F, eds. *Eukaryotic gene regulation*.

New York: Academic Press, 1979. 661 p.