

Ames B N, McCann J & Yamasaki E. Methods for detecting carcinogens and mutagens with the salmonella/mammalian-microsome mutagenicity test. *Mutat. Res.* 31:347-64, 1975. [Department of Biochemistry. University of California. Berkeley, CA]

This paper describes the detailed methods and theory for the Salmonella/mammalian microsome mutagenicity test. It presents the techniques for handling and growing the histidine-requiring bacterial mutants, the function of the various mutations in the tester strains, and the preparation and storage of the rat liver homogenate and co-factor mix [The *SCI*<sup>®</sup> indicates that this paper has been cited in over 2,705 publications since 1975.]

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January 12, 1984

"One day in 1964 after reading a label on a potato chip package, I began to think about all of the new chemicals entering the environment. Being a geneticist as well as a biochemist, I thought it important to screen chemicals to which humans were exposed for mutagenicity. This led to our work on the development of a simple test for mutagens.

"My mutagenicity work started as an offshoot from my basic research on the molecular biology of *Salmonella* bacteria. I was studying how genes are switched on and off in response to the presence of the amino acid histidine and the effect of mutations which perturbed this control mechanism. I was using a large collection of histidine-requiring mutants, mostly made by Philip E. Hartman of Johns Hopkins University. The development of the test system for detecting mutagens using these mutants and our work on mutagenesis were done first at the National Institute for Arthritis and Metabolic Diseases, where I was until 1968, and then at Berkeley, where I have been since then.

"During the course of this work on mutagenesis, I became convinced that one essential aspect of carcinogens was their ability to damage DNA. We

kept lists of popular carcinogens and kept working to make improvements in the test which could detect them as mutagens. One key development was the addition of a rat liver homogenate and cofactors to our petri plates. With this plus other improvements we had made in our tester strains we were able to detect over 80 percent of carcinogens as mutagens. The initial work on the test was mostly done with undergraduate students at Berkeley, particularly Frank Lee and Bill Durston. Joyce McCann, a postdoctoral fellow, then worked on the problem and made major contributions as did Edie Yamasaki, my unusually able technician.

"By 1975, over 500 laboratories were using our system (it is up to about 3,000 now) and we were inundated with letters and telephone calls. McCann, Yamasaki, and I decided to write a methods paper to help in dealing with these inquiries. We were reinforced in this decision because in 1975 McCann and I reviewed our own and other work on validating the test for detecting carcinogens as mutagens and we expected this review would lead to even more use of the test. We tried to make the methods paper, as we called it, definitive: it is the main paper now cited when people use our test. We recently wrote a new methods paper<sup>1</sup> incorporating modifications, by both ourselves and others, and discussing our new tester strains.<sup>2,3</sup> The new paper should make the 1975 paper obsolete. We have been surprised how few changes have been made in the procedure over eight years. We hope the additional tester strains<sup>2,3</sup> will make the test even more comprehensive. One of its major uses has been the detection of new classes of mutagens from complex mixtures, such as cooked food, plants, cigarette smoke, water, food, and urine, and man-made chemicals, such as hair dyes and flame retardants. Many of these mutagens have later been shown to be carcinogens. The test has been useful to industry as large numbers of chemicals are being screened in the development of new drugs and industrial chemicals. In addition, it has become widely used for investigating the metabolic pathways of carcinogens to their active forms. The most important theoretical contribution from our work has been support for the idea that damage to DNA is one essential aspect of carcinogenesis."

[This work led to the John Scott award in 1978.\*]

1. Maron D M & Ames B N. Revised methods for the *Salmonella* mutagenicity test. *Mutat. Res.* 113:173-215, 1983.
2. Levin D E, Hollsteln M, Christman M F, Schwlers E A & Ames B N. A new *Salmonella* tester strain (TA102) with A:T base pairs at the site of mutation detects oxidative mutagens. *Proc. Nat. Acad. Set. US—Biol. Sci.* 79:7445-9, 1982.
3. Levin D E, Yamasaki E & Ames B N. A new *Salmonella* tester strain. TA97, for the detection of frameshift mutagens: a run of cytosines as a mutational hotspot. *Mutat. Res.* 94:315-30, 1982.

\*Garfield E. Since 1816 the John Scott and other Philadelphia awards have recognized "useful" scientific discoveries—James Black and Benjamin Rubin head a list of recent distinguished recipients. *Essays of an information scientist*. Philadelphia: ISI Press, 1983. p. 686-94.