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A special issue dedicated to Dr. Bruce N. Ames: Introduction

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Innovative, creative, and never afraid to plunge into a new research area or express a controversial opinion, **Dr. Bruce N. Ames** is a brilliant and amazingly productive scientist. His research has covered a remarkable range - from biochemical and genetic analyses of fundamental molecule mechanisms, to designing a widely used test for environmental mutagens and carcinogens, to evaluations of carcinogenic potency, to the studies of the effects of diet on human health and aging. Bruce has published more than 550 papers and is one of the few hundred most-cited scientists in all fields. On the occasion of his 90th birthday, it is an honor to introduce this special issue dedicated to Bruce and his outstanding contributions to science and the scientific community.

Bruce was born in 1928 and grew up in New York City. However, it was during summers spent in the Adirondack Mountains that he developed both his fascination with biology and his habit of reading voraciously about a wide range of topics (1). Both were to stand him in good stead during his career. Bruce received his B.A. degree in chemistry and biochemistry from Cornell University. He then moved to Cal Tech for graduate school where he worked with Herschel K. Mitchell, a former postdoc of George Beadle, and used *Neurospora* histidine-requiring mutants to study histidine biosynthesis. Bruce was able to order steps in the pathway and show that they fit with the known biochemistry, receiving his Ph.D. in 1953. To strengthen his knowledge of enzymology, Bruce then became a postdoc with Bernard L. Horecker at NIH where he switched to using *Salmonella typhimurium* as a model organism because of a collaboration with Phil Hartman at Johns Hopkins University.

In 1954, Bruce was appointed as an independent investigator at NIH and focused on studying histidine biosynthesis in *Salmonella*. In 1960 Bruce married Giovanna Ferro-Luzza, herself a highly accomplished scientist, and ever since Giovanna has been a huge support to Bruce in both his personal and professional lives. After spending a sabbatical year split between Francis Crick's lab and Jacob Monod's lab, an experience Bruce has described as "*honeymoon year both personally and intellectually*," he returned to NIH in 1962 as Section Chief (1). Gerry Fink, John Roth, and Bob Martin were his first postdocs. To Gerry

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Conflict of Interest
No conflict of interest.

Fink (2)“ *the Ames lab in building 2 at NIH was heaven, but a very small heaven*” as Bruce and he shared on of the two tiny adjoining labs, one of which also served as Bruce’s office.

The roots of the Ames Test, Bruce’s most widely known accomplishment, go back to 1964 when Bruce read the ingredients list on a box of potato chips and began to wonder about whether preservatives and other chemicals might cause genetic damage to humans (1). Bruce recognized that it would be useful to have a short-term test for chemical mutagenesis and realized he could design such a test by taking advantage of the literally thousands of the histidine-requiring *Salmonella* mutants that were available, many of them isolated by Phil Hartman. Bruce soon discovered that certain *Salmonella his* mutants reverted especially well to His⁺ with particular classes of mutagens. Thus, he used a small set of *his* mutants to develop his test and improved their sensitivity by eliminating *uvr*-dependent nucleotide excision repair.

Bruce then moved to the University of California, Berkeley in 1967 as a Professor of Biochemistry, where he continued to work on the regulation of the histidine operon, but also got funding from the Atomic Energy Commission to support the development of his short-term mutagen-detection test. Bruce’s gifts as an inspirational mentor were on full display as, aided particularly by his postdoc Joyce McCann and his technician Edie Yamasaki, he worked with a succession of talented undergraduate students to continue to develop the Ames Test. A critical final improvement was the introduction of the plasmid pKM101, which was derived from the naturally occurring plasmid R46 by Kristien Mortelmans (3). pKM101 increased the sensitivity of the strain to mutagenesis by a wide variety of chemicals to such an extent that Bruce was able to describe the Ames Test to the world in *PNAS* papers published in 1975 and 1976 (4, 5) (4, 5) Several of the papers in this volume discuss the Ames Test and its implications.

I was a graduate student at the University of Illinois in the early 1970’s doing nucleic acid chemistry and a little biochemistry but had decided that, if I wanted to work on really interesting biological problems, I would need to learn genetics and physiology as well. I heard Bruce give a talk at the University of Illinois when I was graduate student and remembering thinking “*Bruce knows how to think like a cell. I think I’d like to do postdoctoral work in his lab and learn how to do that.*” I joined Bruce’s lab at the University of California, Berkeley in 1974. I thought that it would be interesting to try to determine what pKM101-encoded function(s) was responsible for increasing mutagenesis and so decided to focus on that project. That turned out to be a very good decision as it led me, and later on my own lab at MIT, into studies that helped elucidate the molecular basis of the SOS response to DNA damage and also contributed to the eventual discovery of translesion synthesis (TLS) DNA polymerases.

I stayed in Bruce’s lab until 1976, which meant that I was present when many reporters and journalists visited the lab after the public release of the Ames Test. Every few mornings, as I walked down the hall I would see bright lights coming out of the lab doors and would know that another TV crew had arrived. They would always initially say just to carry on our normal activities, but it usually ended up with me and various lab members repeatedly pipetting sterile medium into empty test tubes as that gave the best visuals. I also remember

how the director of videotaping would usually ask Bruce to give a short talk explaining the Ames Test within a time interval that tended to range from 30 seconds to four minutes. Bruce would always decline to practice, and I remember the lab members holding our watches and watching with wonderment as Bruce would always smoothly deliver the talk while finishing virtually exactly at the requested time.

After introducing one new improvement to the Ames Test in the 1990's, Bruce's interests continue to evolve and diversify. His growing interest in cancer prevention and toxicology grew out of the mutagenicity tests. Working with Lois Gold, he developed the Cancer Potency Database in an effort to systematize the literature on the quantitative aspects of animal tests (1). Bruce's work showed that carcinogens could vary by about a million-fold in their potency and he and Lois Gold went on to publish more than 100 papers analyzing that database. Bruce's studies of the mutagenicity of naturally occurring chemicals led him to shift his previous viewpoint and to conclude that these were likely very important for cancer, while synthetic chemicals were likely to represent only small fraction of important mutagens/carcinogens except for situations involving high doses from occupational exposure or medicinal drugs.

In 1999, Bruce shifted his lab from UC Berkeley to the Children's Hospital of Oakland Research Institute (CHORI). The breadth of Bruce's research continued to grow and expand as he became interested in relationships between diet and health. This interest was stimulated in part by Jim MacGregor's observations that, similar to ionizing radiation, folic acid deficiency caused chromosomal breaks in mice (1). Bruce's molecular characterization of these breaks led him to look more broadly into an array of vitamins and essential minerals, to examine the importance of antioxidants, and to explore the relationship of mitochondrial decay to aging and age-related degenerative diseases. Ever practical, Bruce developed a mix of vitamins and other compounds that he felt could help to fend off aging (6). I don't have the requisite background to critically evaluate this aspect of Bruce's research. However, when I attended Bruce's 90th birthday symposium at CHORI in March 2019, I brought a photo of Bruce and myself that was taken in 1975 when I was a postdoc in his lab. I couldn't help but notice that I clearly had aged substantially, whereas Bruce seemed to have changed very little over the intervening 44 years!

At his 90th birthday symposium, Bruce summarized his approach to research as being “*You follow your nose until you find something interesting and then you follow up.*” The approach has been remarkably successful for Bruce and his accomplishments have been recognized by a large number of professional honors. Bruce is member of the *National Academy of Sciences*, the *American Academy of Arts and Sciences*, the *Japan Cancer Association*, the *Royal Swedish Academy of Science* and is a Fellow of the *American Association for the Advancement of Science*, the *Academy of Toxicological Sciences*, and the *American Academy of Microbiology*. The numerous awards that Bruce has received include the *National Medal of Science*, the *Japan Prize*, the *Thomas Hunt Morgan Medal (Genetics Society of America)*, the *Gairdner Foundation Award (Canada)*, the *Glenn Foundation Award*, and the *Society of Toxicology Lifetime Achievement Award*.

Ever enthusiastic, ever innovative, ever generous with his ideas and help, and ever fearless of entering a new field, Bruce has been a huge inspiration to so many who have worked with him or encountered him in the course of their professional careers. Whenever I have had the chance to see Bruce over the past decades, he would always tell me, (as he tells everyone!), that he is doing the best science of his life. About a year before Bruce's 90th birthday symposium, he sent me a message about his latest research in which he wrote, "*you may ask why I am still working at my age?*" To answer his own question, Bruce paraphrased the Nobel-Prize winning economist Friedrich Hayek as saying, "*I tried old age and decided I didn't like it.*"

Congratulations, Bruce, on a brilliant career and may you keep doing the best science of your life. We all hope you will enjoy reading the collection of papers in this issue.

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Biography

References

1. Ames BN. 2003 An enthusiasm for metabolism. J Biol Chem 278:4369–4380. [PubMed: 12496254]
2. Fink GR. 2009 Getting along with a little help from my friends. J Biol Chem 284:23885–23890. [PubMed: 19515841]
3. McCann J, Spingarn NE, Kabori J, Ames BN. 1975 Detection of carcinogens as mutagens: Bacterial tester strains with R factor plasmids. Proc. Natl. Acad. Sci. U.S.A 72:979–983. [PubMed: 165497]
4. McCann J, Ames BN. 1976 Detection of carcinogens as mutagens in the *Salmonella*/microsome test: Assay of 300 chemicals: discussion. Proc. Natl. Acad. Sci. U.S.A 73:950–954. [PubMed: 768988]
5. McCann J, Choi E, Yamasaki E, Ames BN. 1975 Detection of carcinogens as mutagens in the *Salmonella*/microsome test: Assay of 300 chemicals. Proc. Natl. Acad. Sci. U.S.A 72:5135–5139. [PubMed: 1061098]
6. Ames BN. 2018 Prolonging healthy aging: Longevity vitamins and proteins. Proc Natl Acad Sci U S A 115:10836–10844. [PubMed: 30322941]

Highlight

A brief introduction to Bruce Ames, to whom this volume is dedicated.

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