This Week's Citation Classic

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Babior BM Oxygen-dependent microbial killing by phagocytes. *N. England J. Med*. 298:659-68, 1978.
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This paper reviews the highly reactive oxidizing agents that are used by phagocytes to kill microorganisms and discusses the ways in which these oxidizing agents are generated via the superoxide radical (O_2-) and H_2O_2 [The SCI indicates that this paper has been cited in over 780 publications since 1978]

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McCord and Fridovich's initial description of superoxide dismutase[1] clearly implied that the superoxide radical must be a harmful by-product of certain biological reactions and suggested to me the corollary notion that phagocytes, then known to kill bacteria by oxygen-dependent mechanisms, might conceivably make superoxide and use it as a microbicidal agent. At that time, I was working on a different problem, so I set the phagocyte/superoxide idea aside, thinking vaguely that I might look into it in the future. Eighteen months later, that future arrived in the form of John Curnutte, a tutee who was doing his undergraduate thesis in my lab at Boston City Hospital.

After working without success for nearly an entire summer on another project, John told me in the most tactful way possible that his interest in that project was waning and that, while he was prepared to continue beating his head against the wall if I insisted on it, he would really rather work on something more related to human disease. The phagocyte study I had been postponing for so long seemed to fulfill this requirement, so I suggested this study to John, who immediately learned how to play with neutrophils and within a week had done the critical experiments. Our first paper[2] appeared eight months later, but it took almost three more years before our work was confirmed in a full paper by another group[3] (although early abstracts in *Clinical Research* showed that they had started working on the project around the same time that our group did). By 1978, interest in oxygen radical production by phagocytes had become substantial, so I was invited by the *New England Journal of Medicine* to write the article summarized here. The topic has been reviewed many times since then.[4]

Of course, I had no idea that the initial review would meet with the reception it did. The production of superoxide by neutrophils appeared to me to be a biological curiosity – a clue perhaps to the nature of the respiratory burst of phagocytes, but hardly a phenomenon of general interest. It does seem, however, that the review captured the attention of a much wider audience than I had anticipated. It may be that this wider audience was initially attracted by the term "superoxide", a word not then familiar to biologists and one that evokes images of heroic beings from the planet Krypton. I suppose, though, that most of the interest in the article reflected a need for a short review on the topic that was felt by biologists working in the many fields that overlap the rather specialized area of phagocyte oxygen metabolism. Those who found the paper useful include immunologists and microbiologists, who are interested in phagocytes per se; biochemists and cell biologists examining signal transduction, who regard superoxide production by neutrophils as a useful system for studying this problem; and biologists of all kinds who became interested in oxygen radicals through McCord and Fridovich's ground-breaking discovery and who are now looking into oxygen radicals in relation to everything from lignification and fruit spoilage to atherosclerosis, aging, and cancer.

1. McCord JM and Fridovich I. Superoxide dismutase. An enzymic function for erythrocuprein (hemocuprein) Journal of Biological Chemistry 244(22): 6049-55 1969. [See also McCord JM. Citation Classic / Current Contents Life Sciences (17): 17-17 1981
2. Babior BM, Kipnes RS, Curnutte JT. Biological Defense Mechanisms – Production by Leukocytes of Superoxide a potential bactericidal agent. Journal of Clinical Investigation 52(3):741-744. 1973 (Cited 740 times)
3. Johnston RB, Keele BB, Misra HP et al. Role of superoxide anion generation in phagocytic bactericidal activity – studies with normal and Chronic Granulomatous Disease leukocytes. Journal of Clinical Investigation 55(6):1357-1372, 1975 (Cited 376 times).
4. Babior BM, Crowley CA. Chronic Granulomatous Disease and other disorders of oxidative killing by phagocytes. (Stanbury JB, Wyngaarden JB, Frederickson DS, Goldstein JL and Brown MS. Eds) The Metabolic Basis of Inherited Diseases, 5th Ed. McGraw-Hill Book Company, New York, 1983. p.1956-1985.