

# This Week's Citation Classic

Sbarra A J & Karnovsky M L. The biochemical basis of phagocytosis. I. Metabolic changes during the ingestion of particles by polymorphonuclear leukocytes. *J. Biol. Chem.* **234**:1355-62, 1959.  
[Depts. Bacteriology and Biological Chemistry, and Biophysical Lab., Harvard Med. Sch., Boston, MA]

**In this study we report that the uptake of particulate material by leukocytes is accompanied by a number of stimulated metabolic events. It is concluded that phagocytosis is an energy requiring process. [The SCI® indicates that this paper has been cited in over 765 publications since 1961.]**

Anthony J. Sbarra  
Department of Medical Research  
and Laboratories St.  
Margaret's Hospital for Women  
and  
Department of Obstetrics and Gynecology  
Tufts University School of Medicine  
Boston, MA 02125

May 4, 1983

"From 1953 to 1956, I was an associate biologist in the Biology Division at the Oak Ridge National Laboratory. In the fall of 1955, my sister Lucia wrote to me from her home in New York, pointing out that I had been away from the East Coast long enough and that I should be thinking of moving back home!

"I mentioned my desire to return East to a colleague, who worked in the lab next to mine, and who had recently finished a doctorate at Harvard University. She immediately wrote her former mentor, asking him whether he might have a place in his laboratory for a person with my interest. He, in turn, referred her request to Suter and Karnovsky at Harvard Medical School, with the result that Suter offered me a post in his laboratory.

"At that time, this laboratory had an ongoing program concerned with a study of the interactions between *Mycobacteria* and guinea pig exudate cells! This was great; however, there was one complication. Suter had just accepted a new post, and would be leaving Harvard on July 1st. I headed East anyway.

"For the first month or two I read papers, but in the spring I began to do a few experiments with Karnovsky. Meanwhile, I wondered what I would do in July. In the midst of pondering my future, Karnovsky announced that he was planning to

stay in the phagocytosis field for two more years. and invited me to join him; I happily did.

"The study which led to our frequently cited paper was originally designed simply to look at the metabolic activities of guinea pig exudate cells, and specifically at the polymorphonuclear neutrophilic leukocyte (PMN), in both the absence and presence of particulate material. It was Karnovsky's contention that by using inert material, our system would be 'cleaner' and might generate more significant data. The first result of the addition of these particles to PMN was an immediate and dramatic increase in oxygen uptake, glucose-1-<sup>14</sup>C oxidation, and lactic acid production. These findings were not entirely unexpected.<sup>1,2</sup> The use of inert particles and the omission of serum in the reaction, however, allowed us 'better' control of the ensuing reactions. And, most importantly, we noted a correlation between the stimulated metabolic events and actual particle entry.

"The actual significance of these metabolic stimulations was not obvious at the time. In order to learn more about them, the use of so-called 'respiratory' and 'glycolytic' inhibitors was introduced to the study for the first time. The finding that oxygen uptake, glucose-1-<sup>14</sup>C oxidation, and particle uptake were not affected by the respiratory inhibitors, but were affected by the glycolytic inhibitors, was exciting. But again, the precise physiological significance of the findings was still not clear. A few years later, when Bob Good sent Art Page to Harvard to become familiar with the techniques used in our paper, we felt that something was 'breaking.' A few years later, Holmes, Page, and Good<sup>2</sup> reported, in a classic paper, that PMN collected from children with chronic granulomatous disease did not show stimulated oxidative activities when challenged with particles as control PMN did. In addition, they were not able to kill certain bacteria; and, finally, the children so afflicted experienced frequent and repeated infections with these organisms. These later observations shed considerable light on the physiological significance of our findings,<sup>3,5</sup> and were certainly contributory to the frequent citation of our paper.

"In light of all of the above, the opportunity to have worked in Karnovsky's laboratory was an experience I shall always remember and cherish."

1. Stähelin H, Suter E & Karnovsky M L. Studies on the interaction between phagocytes and tubercle bacilli. I. Observations on the metabolism of guinea pig leukocytes and the influence of phagocytosis. *J. Exp. Med.* **104**:121-36, 1956.
2. Holmes B, Page A R & Good R A. Studies of the metabolic activity of leukocytes from patients with a genetic abnormality of phagocytic function. *J. Clin. Invest.* **46**:1422-32, 1967.  
[The SCI indicates that this paper has been cited in over 485 publications since 1967.]
3. Sbarra A J & Strauss R R, eds. *The reticuloendothelial system. II. Biochemistry and metabolism.* New York: Plenum Press. 1980. 456 p.
4. Rossi F, Patriarca P L & Romeo D, eds. *Movement, metabolism, and bactericidal mechanisms of phagocytes.* Padua, Italy: Piccin Medical Books, 1977. 410 p.
5. Karnovsky M L & Bolis L, eds. *Phagocytosis—past and future.* New York: Academic Press, 1982. 592 p.