

This Week's Citation Classic

Korn E D. Clearing factor, a heparin-activated lipoprotein lipase. I. Isolation and characterization of the enzyme from normal rat heart. *J. Biol. Chem.* **215**:1-14, 1955. (Lab. Cellular Physiol., Natl. Heart Inst., NIS, US Public Health Serv., Bethesda, MD]

This paper showed that the 'clearing factor' that appears in blood plasma following the injection of heparin is a lipoprotein-specific lipase normally present in heart and other tissues where it functions in the transport of fats from the blood into cells. [The SC[®] indicates that this paper has been cited over 565 times since 1961.]

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"A few months before I was to leave Jack Buchanan's laboratory at the University of Pennsylvania for postdoctoral training with H.A. Barker at Berkeley, it became necessary to make other plans. Arthur Kornberg kindly invited me to join him at Washington University but, wishing to gain experience with problems unrelated to my doctoral research on purine biosynthesis, I declined and thus made my contribution to a Nobel prize. Parenthetically, 16 years later, when Kornberg and I met and shared space in Alec Bangham's laboratory in Babraham, England, he remembered the incident. Paul Berg was to come to his laboratory that year and Kornberg had anticipated a publication coauthored by Korn, Berg, and Kornberg (an aborted *Citation Classic*?).

"Instead, I went to the National Heart Institute. Chris Anfinsen, a graduate student with Buchanan under Baird Hastings at Harvard, had established a group of young investigators to study the structure and metabolism of plasma lipoproteins, then recently implicated by John Gofman and others in the etiology of coronary artery disease.¹ One

of the clinical associates was Don Fredrickson, now director of the National Institutes of Health.

"Ten years previously, P.F. Hahn had observed that fat that appears in blood following a meal is removed more rapidly when the anticoagulant heparin is injected intravenously.² Moreover, when postheparin lipemic plasma is removed from the animal, the opalescent plasma continues to 'clear' in the test tube. This phenomenon had aroused considerable interest among clinical investigators and physiologists but was unknown to biochemists, most of whom, like me, had never heard of chylomicrons and low density lipoproteins; we were still eating eggs!

"To an enzymologist, it seemed obvious that, since the turbidity of lipemic plasma was caused by an increased level of triglycerides, the 'clearing factor' must be a lipase that catalyzed their hydrolysis to less turbid molecules. It was a simple matter to demonstrate an increase in fatty acids and glycerol accompanying 'clearing' *in vitro* (glycerol is water-soluble; fatty acids become so by binding to serum albumin). Moreover, since addition of heparin to lipemic plasma *in vitro* had no effect, injected heparin must cause the release of the lipase from tissues. It was routine enzymology to demonstrate that lipoprotein lipase is present normally in heart and other tissues.

"I like to think my first independent publication, one year out of graduate school, became a *Citation Classic* because it explained an important physiological and medical problem in molecular terms, the only way in which such problems can be understood. More likely, the many later workers who discovered most of what is now known about the biochemistry of plasma triglycerides just felt obligated to refer to the paper in which lipoprotein lipase was christened. A review of this field was recently published in the *Annual Review of Biochemistry*.³

1. **Gofman J W.** Biophysical approaches to atherosclerosis. *Advan. Biol. Med. Phys.* **2**:269-80, 1951.
2. **Hahn P F.** Abolishment of alimentary lipemia following injection of heparin. *Science* **98**:19-20, 1943.
3. **Nilsson-Ehle P, Garfinkel A S & Schotz M C.** Lipolytic enzymes and plasma lipoprotein metabolism. *Annu. Rev. Biochem.* **49**:667-93, 1980.