

This Week's Citation Classic®

CC/NUMBER 39
SEPTEMBER 29, 1986

Edelman R & Hartroft P M. Localization of renin in juxtaglomerular cells of rabbit and dog through the use of the fluorescent-antibody technique.

Circ. Res. 9:1069-77, 1961.

[Department of Pathology, Washington University School of Medicine, St. Louis, MO]

This paper provides strong evidence that the source of renin in the kidney is the juxtaglomerular cell. By using adsorbed, antirenin sera coupled to fluorescein dyes, and then staining kidneys from sodium-deficient animals, specific fluorescent staining of renal juxtaglomerular granules was demonstrated. [The SC⁹ indicates that this paper has been cited in over 180 publications.]

Robert Edelman
Clinical and Epidemiological
Studies Branch
Microbiology and Infectious
Diseases Program
National Institute of Allergy
and Infectious Diseases
Bethesda, MD 20205

July 10, 1986

I worked as a Student Research Fellow in the laboratory of Phyllis Hartroft in the Pathology Department of Washington University Medical School the two summers preceding my freshman and sophomore years of medical school in St. Louis. Hartroft introduced me to the problem of renin, hypertension, and salt metabolism and gave me my first opportunity to develop my own research project.

I chose to use the fluorescent-antibody technique in an attempt to localize the site of renin in the kidney. Jack Davies and Paul Lacy at Washington University had just demonstrated insulin in the mammalian pancreas by the fluorescent-antibody method, and although Hartroft had failed to localize renin using the same technique the year before, she encouraged me to try my luck. At least I would learn what it was to do research. So I learned

to make antirenin, couple it to fluorescein dyes (which Davies and I synthesized in his Anatomy Department laboratory—reliable commercial preparations were not readily available in 1959), and prepare animal tissues for staining. I nearly poisoned myself several times inhaling the phosgene gas needed to synthesize the fluorescein isocyanide.

My first attempt was unsuccessful; that is, I was not able to visualize specific staining in kidneys using our fluoresceinated antirenin antibody. The breakthrough came when I hit upon the idea of making renal juxtaglomerular (JG) cells more prominent by feeding animals a sodium-deficient diet. Using a freshly prepared antirenin fluorescein conjugate on a sodium-deficient kidney, I visualized brilliant apple-green fluorescent staining of JG cell granules. The sudden, intense thrill of that discovery remains fresh in my mind and has helped sustain my research career for the past 25 years.

Because immunologically pure renin was not available in 1959-1960, the possibility remained that the specific staining may have been the result of an unknown protein (and its antiprotein) from JG cells present in the renin extracts. With the help of Harry Goldblatt and Edwin Haas of Cleveland, who supplied us renin and additional lots of antirenin, we were able to relate in individual rabbit kidneys the renin content with the degree of granulation of JG cells and the frequency and prominence of JG cells showing specific fluorescent staining with antirenin. We could go no further at that time. Later, immunologically pure renin became available and others confirmed and expanded our discovery.¹⁻³

This research helped me earn my medical degree *cum laude* when I graduated two years later. It also helped other investigators in the field of hypertension and salt metabolism focus their research, which led eventually to the elucidation of the renin-angiotensin system. I suppose this is the principal reason why our discovery has been cited so often.

1. Barajas L. The juxtaglomerular apparatus: anatomical considerations in feedback control of glomerular filtration rate. *Fed. Proc.* 40:78-86, 1981.
2. Yokosawa H, Holladay L A, Inagami T, Haas E & Murakami K. Human renal renin: complete purification and characterization. *J. Biol. Chem.* 255:3498-502, 1980.
3. Ballermann B J, Levenson D J & Brenner B M. Renin, angiotensin, kinins, prostaglandins and leukotrienes. (Brenner B M & Rector F C, Jr., eds.) *The kidney*. Philadelphia: Saunders, 1985. Vol. 1. p. 281-340.

1A-14