Ahlquist R P. A study of the adrenotropic receptors.
Amer. J. Physiol. **153**:586-600, 1948.

This paper proposed that there were two different kinds of receptors for the neurotransmitter norepinephrine. This concept has resulted in new insights into physiological control mechanisms and a whole new class of drugs useful for cardiovascular disease. [*The SCI*® indicates that this paper was cited 1383 times in the period 1961-1977.]

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January 24, 1978

"The work on which my paper was based was carried out during the 'golden age' of biomedical research: no lab technicians, no statistical analysis, drugs of doubtful purity, smoked paper kymographs, inexpensive animals and a heavy teaching load. The only 'modern' instrument available was a home-made, high-frequency-response, optical manometer designed by W. F. Hamilton. The total budget for the project was about $3500; this included my annual salary.

"The concept of two receptors for the adrenergic neurotransmitter was the result of pure serendipity. The experimental work was done to find a drug that would relax the human uterus; the clinical objective was to find a cure for dysmenorrhea.

"I have described the concept of *alpha* and *beta* receptors in a short essay.[1] The following is a quotation from this. 'The original paper was rejected by the *journal of Pharmacology and Experimental Therapeutics,* was a loser in the Abel Award competition, and was finally published in the *American journal of Physiology* due to my personal friendship with the great physiologist W.F. Hamilton. It was ignored for five years. The reasons for this are obvious today; the concept did not fit with ideas developed since 1890 on the actions of epinephrine.'

"The utility of the concept was first recognized by pharmacology teachers. Adrenergic drugs could be classified according to which receptor they acted on. The actions, uses and side-effects of these drugs could be predicted. Physiologists started to use this concept to study control systems in the body. The beta receptor was the starting point for the discovery of cyclic AMP and adenyl cyclase by E.W. Sutherland and coworkers.

"At the time this paper was published, three classes of drugs that acted on these receptors were known: *alpha* agonists, *beta* agonists and *alpha* blocking agents. The fourth class, the *beta* blocking agents, was unknown, but their actions were completely predictable. Although I searched diligently for drugs of this type, someone else found them ten years later. The history of the *beta* receptor blockers is too long to cover here completely. Propranolol was introduced by James Black as a treatment for angina pectoris in 1963. Subsequently the *beta* blockers were found to be useful in arrhythmias, thyrotoxicosis, tremor, migraine, and essential hypertension. Although only one beta blocker, propranolol, is available in this country, at least 18 are available throughout the rest of the world.

"In my opinion, the most important contribution of my concept was to repopularize the idea of receptors. These had been described in the early part of this century but for some reason had been forgotten. Now there are receptors for hormones, peptides and drugs."

REFERENCE

1. **Ahlquist R P.** Adrenergic receptors: a personal and practical view.
Perspect. Biol. Med. **17**:119-22, 1973.