The reason for the 13-year delay in publication was that Lerner felt uncomfortable in not understanding these remarkable results. Fortunately, however, evidence accumulated that methyldopa lowered blood pressure by a central nervous system site of action through a receptor similar to that in the frog skin, as suggested in this paper. Still, even though he provided the support, the technician, and the laboratory, Lerner declined coauthorship, claiming that the ideas were uniquely mine.

During 1976 and 1977 this unique α-adrenergic receptor was becoming more interesting to me. I asked Spencer Berthelsen, a medical student working in my laboratory on a summer fellowship, to review the scientific literature for evidence of other α-adrenergic receptors with similar characteristics. This review revealed a widespread similarity among α-adrenergic receptors in other experimental systems. This similarity led to our description of the pharmacologic characteristics of and the classification of α1- and α2-adrenergic receptors.

There are several reasons the work was so highly cited. First and foremost, the α2-adrenergic receptor regulatory role is important in many systems involving cyclic AMP as a mediator of plasma membrane receptor effects. Examples include regulation of lipolysis, insulin release, sodium and water excretion in the kidney and GI tract, and mood and depression and are abnormally regulated in the kidney of genetically hypertensive rats. Second, as simple as our concept was in retrospect, no one had previously put the whole picture together. Once we did this with the melanocyte granule dispersion data, the inhibition of norepinephrine release, and so on, in this Citation Classic, the picture was so obvious that nearly everyone accepted it immediately. Finally, timing was obviously important. Prior to our publication everyone thought of α-adrenergic receptors as postsynaptic and presynaptic rather than pharmacologically distinct. Our concept of a broad distribution of α1-adrenoceptors located on effector organs that mediate apparently suppressive effects (through inhibition of adenylate cyclase) was immediately accepted by most investigators. Within a few weeks of publication, I had many calls and letters from fellow researchers because the concept explained and simplified apparently diverse and conflicting data and perspectives.

I have received the Burroughs Wellcome Scholar Award in Clinical Pharmacology, the Rawls Palmer Progress in Medicine Award, and the Creasy Award in part as a result of the impact of this Citation Classic.