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Said S I & Mutt V. Polypeptide with broad biological activity: isolation from small intestine. *Science* 169:1217-8, 1970.
[Department of Medicine, Medical College of Virginia, Richmond, VA and Department of Chemistry, Karolinska Institute, Stockholm, Sweden]

This paper reported the discovery and isolation of the peptide we later called "vasoactive intestinal peptide" or "VIP." A 28-residue peptide chemically related to secretin and glucagon, it could increase organ blood flow, lower blood pressure, and augment cardiac output. [The *SCI*® indicates that this paper has been cited in over 695 publications.]

Sami I. Said
Department of Medicine
University of Illinois
College of Medicine
Chicago, IL 60612

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In the late 1960s my associates and I found that extracts of mammalian lungs were strongly vasoactive, causing systemic vasodilation and hypotension upon injection into other animals. We determined that this vasoactivity could not be explained solely by the histamine and prostaglandin content of lung tissue, and we concluded that we were dealing with one or more vasoactive peptides. A physician and physiologist by training, I decided to seek expert help with the isolation of these peptides.

On the advice of Sune Bergström, then rector of the Karolinska Institute, Stockholm, I went to Viktor Mutt's laboratory and was accepted for a sabbatical year. Together, we extracted and partially purified a vasodilator peptide from porcine lung. On the premise that the same peptide might occur in other organs—including, we hoped, the intestine—we then turned our search to intestinal extracts, which were more readily available to us. Using the same bioassay that had guided our work on the lung (measuring the increase in peripheral blood flow and the fall in arterial blood pressure of dogs), performed at the Thoracic Clinic Research Laboratory, we soon discovered that peptide fractions from porcine duodenum indeed contained a vasodilator component. (The presence of a vasodepressor principle in intestinal extracts had actually been noted by W.M. Bayliss and E.H. Starling almost 70 years earlier, during their experiments leading to the discovery of secretin.) We isolated a highly vasoactive peptide and named it vasoactive intestinal polypeptide (VIP).

This name was not included in the *Science* report, which accounts for its absence from a computer printout on this peptide! Two subsequent papers, describing the purification procedure and the amino-acid sequence, were published in the *European Journal of Biochemistry* on condition that we used the more proper-sounding term, "octacosapeptide"![1,2]

A few years after its isolation from the gut, VIP was rediscovered in the brain and in peripheral nerves.[3,4] Its new and correct identity as a neuropeptide quickly replaced its earlier label as a candidate hormone of the gastrointestinal tract. Since then, interest in VIP has continued to grow, owing to its widespread occurrence in the human body as well as in the animal kingdom, its potent and varied biologic activities, and its potential importance as a neurotransmitter or neuromodulator in many organ systems.[5,6]

Today VIP is widely viewed as a physiological regulator of major body functions, including brain metabolism and blood flow, gastrointestinal motility and secretion, cardiovascular and respiratory function, neuroendocrine secretion, immune responses, and sexual activity and reproduction. Hypersecretion of VIP by certain tumors results in a distinct clinical entity, and VIP has been linked to several other diseases, including bronchial asthma, cystic fibrosis, and the acquired immunodeficiency syndrome (AIDS).

The impact of the discovery of VIP is not yet fully realized, but it has already had an immense influence on my own career. The work leading up to this paper, and the continuing research since then, has introduced me to several exciting disciplines previously alien to me: peptide biochemistry and pharmacology, endocrinology, gastroenterology, neuroscience, and, most recently, molecular biology. With that came valued new acquaintances and friendships with colleagues around the world.

1. **Said S I & Mutt V.** Isolation from porcine intestinal wall of a vasoactive octacosapeptide related to secretin and to glucagon. *Eur. J. Biochem.* 28:199-204, 1972. (Cited 390 times.)
2. **Mutt V & Said S I.** Structure of the porcine vasoactive intestinal octacosapeptide: the amino acid sequence. Use of kallikrein in its determination. *Eur. J. Biochem.* 42:581-9, 1974. (Cited 270 times.)
3. **Said S I & Rosenberg R N.** Vasoactive intestinal polypeptide: abundant immunoreactivity in neural cell lines and normal nervous tissues. *Science* 192:907-8, 1976. (Cited 360 times.)
4. **Larsson L-I, Fahrenkrug J, Schaffalitzky de Muckadell O, Sundler F, Håkanson R & Rehfeld J F.** Localization of vasoactive intestinal polypeptide (VIP) to central and peripheral neurons. *Proc. Nat. Acad. Sci. USA* 73:3197-200, 1976. (Cited 365 times.)
5. **Lundberg J M, Änggård A, Fahrenkrug J, Hökfelt T & Mutt V.** Vasoactive intestinal polypeptide in cholinergic neurons of exocrine glands: functional significance of coexisting transmitters for vasodilation and secretion. *Proc. Nat. Acad. Sci. USA* 77:1651-5, 1980. (Cited 190 times.)
6. **Said S I & Mutt V, eds.** Vasoactive intestinal peptide and related peptides. *Ann. NY Acad. Sci.* (In press.)

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