

Larsson L-I, Sundler F & Håkanson R. Pancreatic polypeptide—a postulated new hormone: identification of its cellular storage site by light and electron microscopic immunocytochemistry. *Diabetologica* 12:211-26, 1976. [Departments of Histology and Pharmacology, University of Lund, Sweden]

The candidate hormone pancreatic polypeptide (PP) was localized to a fourth endocrine cell type of the islets of Langerhans by light and electron microscopical immunocytochemistry. Ultrastructural localization of PP to the secretory granules of the cells suggested that it was actively secreted to the blood like a classical peptide hormone. [The SCF® indicates that this paper has been cited in more than 345 publications.]

New Cell Type in the Islets of Langerhans

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This paper has its origins at the University Library in Lund, where we frequently went to read the latest literature. One day in 1973, we came across a paper by R.L. Hazelwood *et al.*¹ They described a biologically active peptide in the chicken pancreas (avian pancreatic polypeptide, APP) that could represent a new hormone. Through our close collaboration with Rolf Håkanson at the Department of Pharmacology, we had a strong interest in gastrointestinal and pancreatic endocrinology. It occurred to us that if APP really was a hormone then it should occur in distinct endocrine cells. Joe R. Kimmel graciously supplied us with good antibodies, and, by immuno-

cytochemistry, we localized APP to a new endocrine cell type of the chicken pancreas.²

Ron E. Chance, Tsung-Min Lin, and colleagues at the Eli Lilly Company in Indianapolis had isolated mammalian pancreatic polypeptides (PPs), which were closely homologous to APP.³ Ron kindly supplied us with good antisera to the PPs, and this enabled us to localize it to endocrine cells of the pancreas of man⁴ and several other mammals. By combining immunocytochemistry and electron microscopy, we could show that PP occurred in the secretory granules of a novel pancreatic islet cell type. In man, the PP cells contained characteristic small secretory granules and, although such cells had been described before, they had never been associated with a specific product. In fact, two distinct types of small granulate cells were detected, and only one of them contained PP. Thus, the human islets of Langerhans may still contain unknown endocrine or paracrine cell types.

The reason this paper has been frequently cited most certainly relates to the fact that a new endocrine cell type of the islets of Langerhans was described. Interest in the cellular composition of the islets comes from diabetologists, endocrinologists, clinicians, and pathologists working with islet cell tumors. Thus, the audience was set to devote its interest to PP cells. In terms of biological activities, however, PP turned out to be a disappointment. Today, interest is more focused on structurally related peptides, like neuropeptide Y.⁵ On a more personal side, the work resulted in longlasting friendships with Kimmel, Chance, and their associates.

Apart from availability of good antibodies produced by Chance, the development of the peroxidase-antiperoxidase (PAP) method for ultrastructural immunocytochemistry⁶ was a strong factor in bringing this work about.

1. Hazelwood R L, Turner S D, Kimmel J R & Pollock H G. Spectrum effects of a new polypeptide (third hormone?) isolate from chicken pancreas. *Gen. Comp. Endocrinol.* 21:485-97, 1973. (Cited 100 times.)
 2. Larsson L-I, Sundler F, Håkanson R, Pollock H G & Kimmel J R. Localization of APP, a postulated new hormone to a pancreatic endocrine cell type. *Histochemistry* 42:377-82, 1974. (Cited 110 times.)
 3. Lin T-M & Chance R E. Spectrum of gastrointestinal actions of a new bovine pancreatic polypeptide (BPP). *Gastroenterology* 62:852, 1972.
 4. Larsson L-I, Sundler F & Håkanson R. Immunohistochemical localization of human pancreatic polypeptide (HPP) to a population of islet cells. *Cell Tissue Res.* 156:167-71, 1975. (Cited 155 times.)
 5. Mutt V, Fuxe K, Hökfelt T & Lundberg J H, eds. *Neuropeptide Y*. New York: Raven Press, 1989. 353 p.
 6. Sternberger L A. *Immunocytochemistry*. New Jersey: Prentice-Hall, 1974. 246 p. (Cited 4,290 times.)
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