



## REVIEW

# Pancreatic neuroendocrine tumours. What do we know of their history?☆



Salvador Navarro<sup>1</sup>

*Servicio de Gastroenterología, Institut de Malalties Digestives i Metabòliques, Hospital Clínic Barcelona, Spain*

Received 22 July 2015; accepted 2 September 2015

Available online 20 March 2016

### KEYWORDS

Neuroendocrine  
pancreatic tumours;  
History;  
Hormones

### PALABRAS CLAVE

Tumores  
neuroendocrinos  
pancreáticos;  
Historia;  
Hormonas

**Abstract** Starting with Paul Langerhans, who first described pancreatic islets in 1869, this article reviews the various protagonists who, in the last century and a half, have contributed to the discovery of the main hormones originating in the pancreas, the analytical methods for their measurement, the imaging techniques for identifying tumoural location, and the various pancreatic neoplasms.

© 2015 Published by Elsevier España, S.L.U.

### Tumores neuroendocrinos pancreáticos. ¿Qué conocemos de su historia?

**Resumen** Tomando como punto de partida la descripción de los islotes pancreáticos realizada por Paul Langerhans en 1869 se efectúa una revisión histórica de los diferentes protagonistas que, aproximadamente, a lo largo de este último siglo y medio han contribuido a la identificación de las principales hormonas que tienen su origen en el páncreas, de los métodos analíticos que permiten cuantificarlas, de las técnicas de imagen que informan sobre la localización de los tumores y de los diferentes tipos de neoplasias que se originan en esta glándula.

© 2015 Publicado por Elsevier España, S.L.U.

## Introduction

Pancreatic neuroendocrine tumours (PNET) account for fewer than 3% of all pancreatic tumours, 1–2% of which

are familial syndromes (multiple endocrine neoplasia-type 1 [MEN-I], Von-Hippel Lindau disease, neurofibromatosis type I or tuberous sclerosis). No sex or age predilection has been observed, although they are most common between 20 and 60 years of age. Clinically, they may be functioning or non-functioning. The former are diagnosed as a result of the symptoms produced by the various hormones that they secrete, while the latter are usually diagnosed incidentally following an imaging study performed on the patient for symptoms unrelated with the tumour, or due to the onset of pain.

DOI of original article:

<http://dx.doi.org/10.1016/j.gastrohep.2015.09.001>

☆ Please cite this article as: Navarro S. Tumores neuroendocrinos pancreáticos. ¿Qué conocemos de su historia? Gastroenterol Hepatol. 2016;39:293–300.

E-mail address: [6119snc@comb.cat](mailto:6119snc@comb.cat)

<sup>1</sup> Senior Advisor Emeritus.

## The hormones

The importance of understanding of the microscopic structure of the pancreatic gland cannot be overlooked in the context of PNET. It was a Parisian student called D. Moysé who apparently first described the structure of the pancreatic acini in his thesis published in 1852.<sup>1</sup> Some years later, in 1869, Paul Langerhans (Berlin [Germany], 1847–1888), a student of Rudolph Virchow at the famous Berlin Pathological Institute, published his thesis *Beiträge zur mikroskopischen Anatomie der Bauchspeicheldrüse*<sup>2</sup> (Contribution to the microscopic anatomy of the pancreas) in which he described (by means of staining studies with glycerine and Berlin blue), 9 different types of pancreatic cells, defining the structure, but not the function, of what years later became known as the islets of Langerhans. It was not until 1893 that French histologist Gustave Édouard Láguesse (Dijon [France], 1861–1927), professor of histology at Lille, finally insisted that the pancreatic islet cells should receive the name of their discoverer, Langerhans, and postulated that they generated hormones, specifically a substance that affected carbohydrate metabolism.<sup>3</sup> This substance was first called *insulin* in 1909 by Belgian Jean de Meyer (1878–1934), although some attribute it to Scottish physiologist Edward Albert Sharpey-Shafer (Middlesex [United Kingdom], 1850–1935). Based on his findings, Láguesse coined the term “endocrine”, and paved the way for what is known as endocrinology; the term was later reiterated by Nicola Pende (Noicattaro [Italy], 1880–1970) in his treatise *Endocrinologia. Patologia e clinica degli organi a secrezione interna*, published in 1916.<sup>4</sup>

When talking about endocrinology, it is important to remember the concept of hormone. These are biochemical messengers secreted into the blood by the endocrine glands, and which act selectively on a target organ whose cells have specific surface receptors that enable the hormone to bind to them and produce its effect.

It is therefore helpful to bear in mind that in 1894, J.L. Dolinsky, a co-worker of Russian physiologist Ivan Petrovich Pavlov, observed that the introduction of acid into the duodenum caused pancreatic secretion, leading him to suspect that gastric acid stimulated this secretion, possibly by producing a substance that reached the pancreas through the circulation.<sup>5,6</sup> Ernest Henry Starling (London [United Kingdom], 1866–1927) and his brother-in-law William Maddock Bayliss (Wolverhampton [United Kingdom], 1860–1924) named this substance secretin in 1902.<sup>5,7</sup> In June 1905, Ernest Henry Starling gave a lecture to the Royal Society of Physicians entitled *The chemical correlation of the functions of the body*, in which he demonstrated how the cells of an organism communicated via chemical messengers that used the circulation to carry out their specific biological action at a distance. During a dinner at Gonville and Caius College, Cambridge, Starling is believed to have spoken with William Hardy, director of the college and renowned biologist, and suggested the convenience of finding a suitable word to designate that chemical messenger. Accordingly, they asked William Vesey, a colleague who was an expert in Greek, who suggested using the verb “ὀρμαῖο” (hormāō, which means to excite or stimulate), and so the term “hormone” was born.<sup>8</sup> This account appeared in an

essay by Joseph Needham (a biochemist at Cambridge who was present during the conversation) entitled *Order and life*, published in 1936. William Maddock Bayliss was also attributed with the discovery that trypsin originated in the form of a proferment, which he called trypsinogen.<sup>9</sup>

In 1905, John Sidney Edkins (London [United Kingdom], 1863–1940) discovered a substance obtained from extracts of pyloric mucosa in anaesthetised cats, which induced the secretion of gastric acid and pepsin, and which he called *gastrin*.<sup>7</sup> This finding was eclipsed, however, with the discovery of histamine in 1910, which had similar effects. Serious doubts were therefore raised with respect to Edkins’s hypothesis regarding the existence of gastrin.

Roderick Alfred Gregory (London [United Kingdom], 1913–1990), a professor of physiology at the University of Liverpool, worked on biochemical processes of carbohydrate metabolism and the circulation, especially the heart. In 1939, he obtained a grant from the Rockefeller Foundation and worked in Andrew Conway Ivy’s laboratory at Northwestern University (Illinois, USA), where he became interested in problems related to the gastrointestinal tract.<sup>10</sup> He later returned to the Chemistry Department at Liverpool University, where he made important contributions to the study of intestinal hormones. In 1964, together with his co-worker, Hilda J. Tracy, he defined the chemical structure of gastrin, and discovered that this hormone was produced in excess in the tumours of patients with Zollinger-Ellison syndrome (described in 1955).<sup>11,12</sup> These findings led to the acceptance of Edkins’s original hypothesis.<sup>13</sup>

In 1921, Frederick Grant Banting (Alliston, Ontario [Canada], 1891–1941) and Charles Herbert Best (Washington County [Maine, USA], 1899–1978), then a student, ligated the pancreatic ducts in a series of dogs, isolating a hormone that they initially called isletin, but later came to be called *insulin* (Fig. 1).

In 1923, Banting and John James Rickard MacLeod (Clunie [Scotland], 1876–1935), a professor of physiology in Toronto, received the Nobel Prize in Physiology or Medicine for this discovery. Best, the student who had helped Banting, was ignored. Upset by this, Banting shared the prize money with his young colleague.<sup>7,14</sup> Frederick Sanger (Gloucestershire [United Kingdom], 1918–2013), a biochemist who worked at Cambridge University, was one of only 4 people to have been awarded a Nobel prize twice, the others being Marie Curie, Linus Pauling and John Bardeen. He received the first award in 1958 after having identified the amino acid sequence of insulin in 1955. However, human insulin was not synthesised until 1974 by the Swiss P. Sieber.<sup>15</sup>

John Raymond Murlin (1874–1960), a professor of physiology at the University of Rochester between 1919 and 1945 and co-founder of the *American Institute of Nutrition* in 1928, researched diabetes, insulin and protein metabolism. In 1923, he discovered, together with Charles P. Kimball, *glucagon* in an extract of dog duodenal mucosa and pancreas,<sup>16</sup> although this discovery has also been attributed to Christian de Duve (Thames-Ditton [United Kingdom], 1917–2013); de Duve was a cytologist and biochemist who won the Nobel prize in Physiology or Medicine in 1974 (which he shared with Albert Claude and George Emil Palade) for having described the structure and functions of the different organelles inside the cells. Nevertheless, it was not until

Download English Version:

<https://daneshyari.com/en/article/3290053>

Download Persian Version:

<https://daneshyari.com/article/3290053>

[Daneshyari.com](https://daneshyari.com)