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REVIEW ARTICLE

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From the “apparato reticolare interno” to “the Golgi”: 100 years of Golgi apparatus research

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Abstract The year 1998 is the centenary of the Golgi apparatus. It is an occasion to pay tribute to Camillo Golgi and the other pioneers of Golgi apparatus research. From the very beginning, the discussion of the Golgi apparatus was characterized by a great variety of theories and innovative terminology, with signs of keen interest already evident during the era of light microscopy.

Key words Camillo Golgi · Golgi apparatus · History of cytology

Introduction

The Italian pathologist Camillo Golgi (1843–1926) the man who discovered what is now known as the Golgi apparatus, would have never thought that his would become one of the most cited names of today’s biomedical research. The discovery of the Golgi apparatus can be considered to be a by-product of Golgi’s neurohistological research. Golgi, who won the Nobel Prize in Medicin in 1906 for his contributions to neurohistology, has become a synonym for the organelle, to the point that the connection with the person of Camillo Golgi has been lost.

Camillo Golgi and the discovery of the “internal reticular apparatus”

The discovery of the Golgi apparatus is only one of the numerous discoveries made by Camillo Golgi and his pupils by applying modifications of a quite “miraculous” and still somewhat mysterious procedure, the “black reaction”. This technique signalled a turning-point in the history of neuroscience, enabling neurons and the structural organization of the nervous system to be observed with great clarity. Golgi’s technique helped to clarify the morphology of astrocytes and their relationship to blood vessels, identified the secretory canaliculi of the parietal cells of the gastric glands, the sarcoplasmic reticulum, as well as other structures [35]. Even the “perineuronal net”, described by Golgi [20] together with the “internal reticulum” and which was subsequently contested and forgotten, is recognized today [10].

Golgi was born in Corteno, a small town near Brescia in northern Italy, on 7 July 1843. He was a typical representative of Italian medicine of the second half of the nineteenth century [12], a follower of the positivistic philosophy that dominated his time. He opposed any type of general theoretical abstraction and sought scientific truth in descriptive morphology. He was trained in microscopy by Giulio Bizzozero (1846–1902), known as the “Italian Virchow” [9], and himself soon became a master of fine anatomical investigation. His scientific work is characterized by great technical skill, an astonishingly accurate morphological description, and numerous discoveries, but also by the harsh controversy with the followers of the theory of the neuron [31].

The “black reaction” (*reazione nera*) was created in the kitchen of Golgi’s private residence during the less eminent period of his scientific career as a physician at the Pie case degli Incurabili (Home for Incurables) in Abbiategrasso, a small town near Pavia. It was for this technique, published in 1873 [19], although fully recognized only after 1888, and for his subsequent series of fundamental descriptions of the anatomy of the nervous system he was awarded the Nobel Prize in 1906. In 1876 he received a professorship in histology, then in general pathology at the ancient University of Pavia. However, Golgi’s international reputation was contested. His (false) idea of the brain as a continuous reticulum was strongly criticized. Other scientists, in particular Golgi’s

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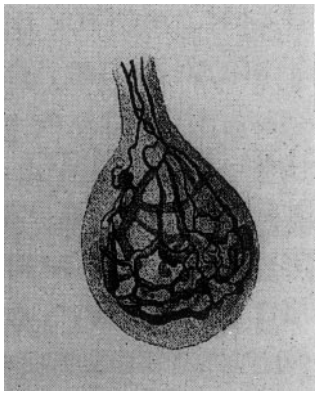

Fig. 1 Golgi's historical image of the "apparato reticolare interno" of a Purkinjie cell of Tyto alba. Fixation with 3% potassium dichromate and 1% osmic acid, impregnation with 0.75–1% silver nitrate. From [20]

great opponent the Spanish neurologist Santiago Ramón y Cajal (1852–1934), considered nerves to be single cells without direct contact.

In 1897, after a long period of administrative and political tasks, Golgi, then aged 55, returned to his laboratory in order to search for the supposed nerve cell connections. He still maintained his belief in the net-like structure of the brain and the validity of his technique. He continued to fix his preparations with osmic acid and potassium bichromate and to treat the pieces afterwards with silver nitrate. By modifying times of treatment, he obtained incompletely blackened nerve cells. In the Purkinje cells of an owl he became aware of a fine internal net (Fig. 1). Remaining incredulous, Golgi hesitated to publish his discovery until it was confirmed by his assistant Emilio Veratti (1872–1967).

On 19 April 1898, at the meeting of the Medical-Surgical Society of Pavia Golgi [20] announced his observation, named *"apparato reticolare interno"*. He described his new finding as a fine and elegant net within the cell lumen. Between the juxtanuclear apparatus and the cell surface there always remained free space. The strands of the net divided, anastomized, and showed fine plates or disks resembling knots. The whole structure was tridimensional and was adapted to the form of the cell. In subsequent communications, Golgi reported his studies of the apparatus in the spinal ganglion (Fig. 2) and cortical cells of various mammals, applying Veratti's [44] suggestion to add 0.1% of platinum chloride to the fixative [21–23]. He noted the increase in complexity and the decrease in impregnability of the internal net in older animals. He was fully aware that he had discovered something new, although initially it was thought to be a peculiarity of nerve cells.

Maybe the apparatus has already been observed and almost certainly it would have been discovered without him [13], but Golgi and his collaborators (Fig. 3) attracted general attention since they were clearly the first to give a detailed description and define the status of an independent cell organelle. Golgi himself was puzzled about the significance of this cell structure. By publishing more than 70 articles, he and his students produced all the information obtainable using this purely morphological approach; this included, apart from the technique and the first morphological criteria for identification, proof of its general presence in all mammalian cells (see the review of Riquier [40]), its division by dictyokinesis [38, 39], the first attempt to elucidate its physiological significance in secretory cells [14, 24], and, remembering pathology, various studies of the apparatus in altered cells (e.g. [30, 32, 41, 42] (Figs. 4, 5)). About 1915, the Pavesian school abbandoned Golgi apparatus research, and other scientists introduced new ideas, methods and approaches.

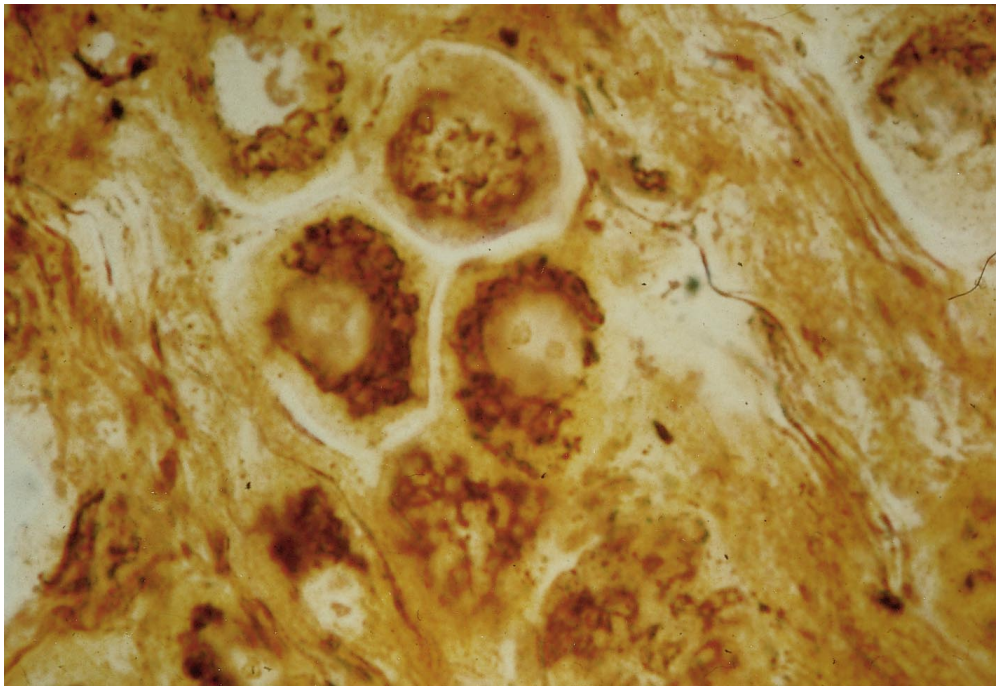

Fig. 2 Historical preparation of the Golgi apparatus in spinal ganglion cells of a chicken. Photographic method. (Preparation in possesion of Prof.R.Bortolami, Istituto di Medicina Veterinaria, Bologna)

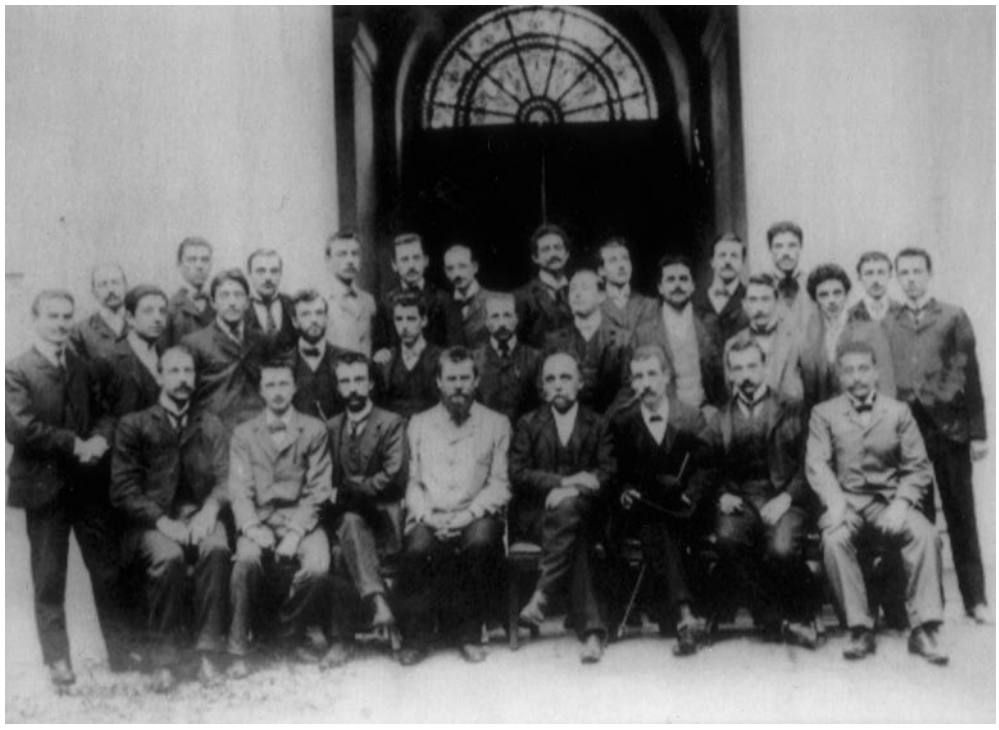

Fig. 3 Camillo Golgi (first line, fourth from the right) with the students of his laboratory, about 1900. (Courtesy of the Istituto di Patologia generale "C.Golgi" in Pavia)

The Golgi apparatus: canals, rods, a special substance, or only burst vacuoles?

At the turn of the century cell biology was characterized by great technical advances and, subsequently, a multitude of cytological discoveries. Some of these proved to be real such as mitochondria or the endoplasmic reticulum (called "ergastoplasm" by Garnier [17]), but mostly they were artefacts. In this light, it is not surprising that Golgi's announcement did not provoke great enthusiasm. The first reactions were attempts to homologize the internal reticulum with other structures, such as neurofibrils, mitochondria, "sap canals" [29], *Pseudochromosomen* [25], *Archoplasmaschleifen* [26] and many others. Overcoming initial problems of reproducibility and scepticism, Golgi apparatus research soon became an attractive field for cytological investigation.

One of the main problems of classical Golgi apparatus research was the inability to produce generally valid data. Topography, volume and shape varied among different species and cell types and in developmental, physiological and pathological stages. Furthermore, even using slightly different procedures, researchers obtained different results which were interpreted in different scientific contexts. The pleiomorphism of the organelle caused a pleiomorphism of ideas.

The first great advancement of non-Pavesian research was the withdrawal from a static conception. Golgi's eternal opponent Cajal was intent on surpassing him in the field of Golgi apparatus research. Cajal [8] tried to bring a logical order to the different constitutions of the Golgi apparatus, interpreting them as representatives of different phases of physiological and pathological phe-

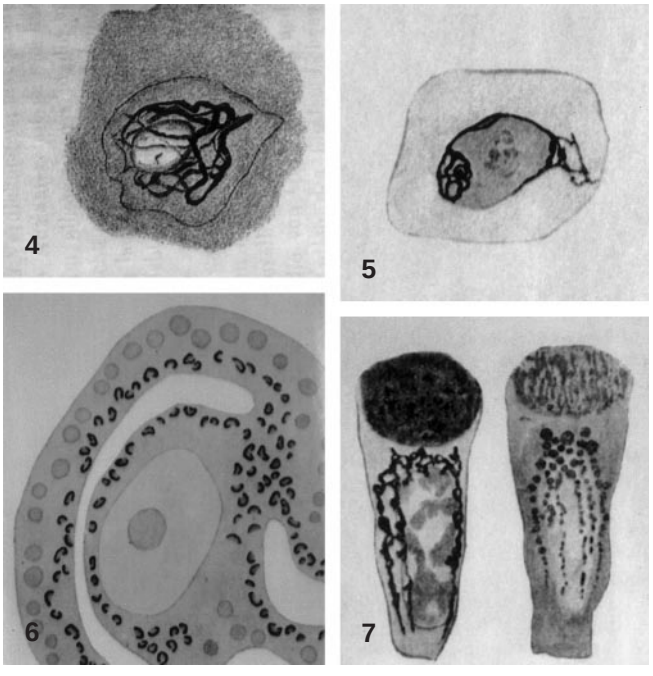

Fig. 4 The "apparato" in a tumour cell. Silver impregnation (Golgi-Veratti method). From [41]

Fig. 5 The endocellular reticulum in a breast carcinoma cell (Golgi-Veratti method). From [32]

Fig. 6 Hirschler's "membranous-lamellar" Golgi apparatus in the larva of *Limnaea stagnalis L.*. Fixation with sublimate and osmic acid, postosmication. From [28]

Fig. 7 Topographical identity of the Golgi apparatus (*left*) and the "vacuome" (*right*) according to Parat. Epitelial cells of the gastric mucosa of Triton. Silver impregnation (Da Fano method) (*left*), neutral red (*right*). From [36]

nomena. The Golgi apparatus had become transformable and part of a dynamic process. Finally, Robert H. Bowen [6] (1892–1929) considered the apparatus to be "a specialized cytoplasmic substance which may be moulded into any shape demanded by particular cellular conditions". The criteria for its identification now became its specific response to osmium and silver and its physiological role as a "great intracellular centre of chemical synthesis or enzyme formation" [5].

This conception facilitated investigation, although the basic problem was not resolved: "what is the Golgi apparatus and what was it made for?" Golgi declined formulating any hypothesis. Maybe he intended to avoid further controversy. Cajal [7] interpreted the net-like images as the silver-reducing content of Holmgren's "sap canals", identified using trichlorolactic acid (see [15]). The concept of the apparatus as a canalicular system also became popular in the United States. Robert Bensley [3] (1867–1956) and his students obtained a "canalicular apparatus" using a acetic-osmium-bichromate solution.

Counter-proof came from the Zoological Institute of Lemberg (Lwów). The Polish group of Józef Nusbaum [33] observed that the Golgi apparatus of invertebrate cells was not reticular but made of many single rods. Thus, the idea of a continuous system seemed improbable. Confirmation came from London and New York. J. Brontë Gatenby [18] (1892–1960) and Bowen [4] worked with male germinal cells where the "banana-shaped" Golgi apparatus, once identified, could be observed in vivo.

The Lemberg school marked another important step in Golgi apparatus research. Jan Hirschler [28] gave the description of a membranous-lamellar organelle of duplex constitution: a chromophile envelope ("Externum") and a chromophobe content ("Internum") (Fig. 6). After the decline of the canalicular theory this conception opened up another way of understanding how the Golgi apparatus elaborated its products.

After Italian, Spanish, Russian and Polish, and the first American and British contributions, the 1930s saw a real "boom" in Golgi apparatus research all around the world. However, in spite of all this progress, the accusation of being considered an artefact was an ever-present companion. The most serious criticism arose during the 1920s and early 1930s by French histologists at the Sorbonne and in the 1940s by Anglo-American scientists (see [1, 34, 45]). They suspected that the fixatives of the classical Golgi techniques caused distortions which were subsequently blackened by the metallic impregnations. For Maurice Parat [37] small vacuoles were the living representatives of the dicytosomes of fixed cells (Fig. 7). John Baker [2] thought silver and osmium deposited on parts of the vacuoles and between them. Today all this seems curious; however in the era of light microscopy there were good reasons to mistrust techniques which still elude explanation and are somewhat obscure.

Finally, in 1954 the first clear electron micrographs, made in Bethesda [11] and Stockholm [43], gradually convinced the predominantly hostile scientific comunity of the real existence of the Golgi apparatus, but its conception had to be changed again. The micrographs showed "a horseshoe-shaped group" made of large vacuoles, small granules and lamellae [11] (Fig. 8).

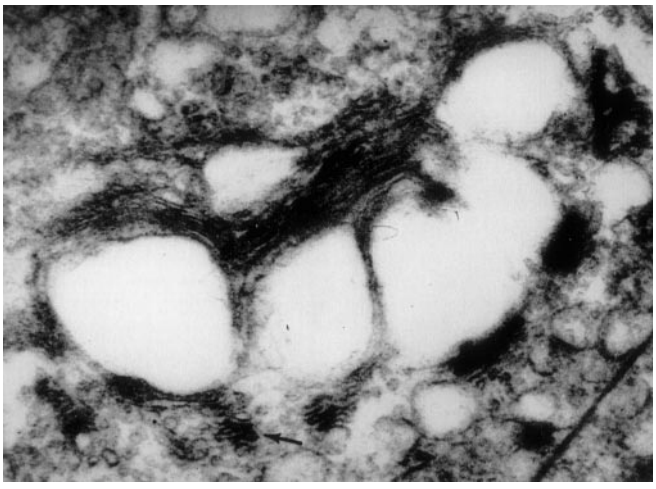

Fig. 8 Electron micrograph of the "Golgi substance" of 1954. Epididymis of a mouse. Fixation with buffered osmium. From [11]; reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

All these ideas are not curiosities of the history of Golgi apparatus research, but only some of the guiding conceptions. More than 100 names circulated in 1939 [27] and "terminological clones" are made today [16]. This is great fortune for Camillo Golgi. His name has became the terminological mark for this quite indescribable organelle.

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