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REVIEW

1998: The centenary of the discovery of the Golgi apparatus

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1998 is the year of the centenary of the discovery of the Golgi apparatus. This event is considered in its historical context: the first cell theory of 1838–1839, the first polemics in cytology and the research on the cell organelles at the turn of the century. The first approaches to clarify the physiological significance of the apparatus is traced from Golgi (1909) to Bowen (1929).

***Keywords*: Camillo Golgi, Golgi apparatus, black reaction**

Introduction

On 19 April, 1898, Camillo Golgi announced to the Medical–Surgical Society of Pavia the discovery of the "apparato reticolare interno" [1]. But the reaction from the scientific world was far from being enthusiastic. On the contrary, disregard and skepticism followed. Too many cell structures were being 'discovered' at the time. In addition, the apparatus showed great morphological variability and Golgi's technique (fixation in osmio-bichromate solution, followed by reaction with silver nitrate) was difficult to reproduce. But Golgi and his numerous students (Figure 1) stood steadfastly by the endocellular reticulum. Publishing more than sixty articles in various journals they prevented the discovery from being ignored. In Golgi's final research [2], one can even find the initial attempt to clarify the physiological significance of the Golgi apparatus.

Cell, nucleus, 'protoplasm': the first polemics in cytology

From 1838, the cell became an object of continually increasing study. Previously, attention had only been paid to tissue as a whole. Organisms were constructed of 'fibres' and 'humours'. The first cell theory, the 'Zellenlehre' of botanist Matthias Jacob Schleiden [3] and zoologist Theodor Schwann [4], proclaimed the cell as the elementary unit of both the plant *and* animal kingdoms. The first to accept the new theory were histologists and anatomists, later physiologists and pathologists and finally researchers of inheritance and developmental biology. But the path leading to the current conception of the cell was by no means straight. The first great cytological issue concerned the role and nature of the first visible cell structure, the nucleus. Schleiden and Schwann considered the nucleus to be the genetic center, whereas the cytoplasm was disregarded as 'grease'. Twenty years later the pathologist Rudolf Virchow went beyond Schwann's conception of the direct evolution of the nucleus out of amorphous material. He coined the aphorism "omnis cellula e cellula" with which he raised the process of cell division, by this time often observed, to the status of a paradigm of cell reproduction [5]. Beside this, there was another movement that overcame the 'Zellenlehre'. In the 1860s distinguished authorities like the zoologists Thomas Huxley and Ernst Haeckel and physiologist Ernst Wilhelm von Brücke were against the definition of the cell as "nucleus, membrane, and 'mucus'" and established the "theory of the protoplasm". The cell was defined as a small lump of protoplasm, in which the phenomena of life were to be searched.

Endocellular structures: hypothetical, artificial or real?

For a long time, there was no general accordance about the structure of the cytoplasm. In the second half of the 19th century there were two main conceptions. The first supposed a metastructure. The cell was not considered to be the minimal element and the main interest dealt with the search

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Figure 1. Camillo Golgi (first row, fourth from the right) with the students of his laboratory, about 1900. (By courtesy of the Istituto di Patologia generale 'C. Golgi' in Pavia.)

for subcellular 'vital units'. Herbert Spencer stated 'physiological units', Charles Darwin found the term 'gemmulae', Eduard Pflüger spoke of 'lebendes Eiweiss', Oskar Hertwig used 'Bioplasten', Hugo De Vries 'Pangene', August Weismann 'Biophoren', only to mention the most important scientists (see [6]). The quantity of terms should not hide that the existence of these subcellular units was more than hypothetical. The counterconception contemplated the protoplasm as a complex colloidal system and endocellular structures only as secondary, mostly temporary, formations.

In the meantime, microscopic resolution improved until, at the end of the 19th century, it had reached its limit. The hypothetical units seemed to be confirmed because numerous newly developed cytological techniques enabled the recognition of structures that had been invisible until then: mitochondria [7], (previously probably also Altmann [8], and Zoia and Zoia [9]) but also 'Pseudochromosomen' [10], 'Archoplasmaschleifen', 'Nebenkern' [12], 'Centralkapseln' [13], 'Trophospongien' [14, 15], 'Nissl-Körper' [16], 'amas vermiculaire' [17], 'spireme' etc. The cell seemed to become a field of unlimited discoveries. Only a few survived. This was the time when the Golgi apparatus was discovered. However, it was not preceeded by any hypothetical cytological conception, but was a by-product of neurological study. Golgi was still concerned to provide evidence for his theory of the brain as a continuous reticulum and experimented with variations of his 'reazione nera' (black reaction) developed 25 years before. But, instead of internervous connections he noticed in the Purkinje's cells of *Tyto alba* an endocellular reticulum [18] (Figure 2). In this historical context Golgi's discovery was not considered as a long desired revelation but increased the already existing confusion.

In the following years, when morphological and homological criteria were dominant, there were very different ideas about the morphology of the Golgi apparatus. For the Pavese School the 'apparato reticolare interno' was net-like, for the contemporary Madrid School around Santiago Ramòn y Cajal the 'conduits de Golgi-Holmgren' represented a canalicular system with osmiophilic borders and a silver-reducing content [19]. Cajal interpreted Golgi's discovery as a negative image of the 'Saftkanälchen' (sap canals) observed by the Swede Emil Holmgren using trichloroacetic acid [14, 15]. North American researchers held a similar view (e.g., [20, 21]). From 1910 the Lemberg School of Jòzef Nusbaum and Jan Hirschler was engaged with cytoplasmic inclusions, especially the 'Golgi apparatus', of invertebrate cells. They observed single lamellar rods or rings for which they adopted Perroncito's term 'dictyosomes'. Finally they described double structures consisting of a chromophile externum and a chromophobe

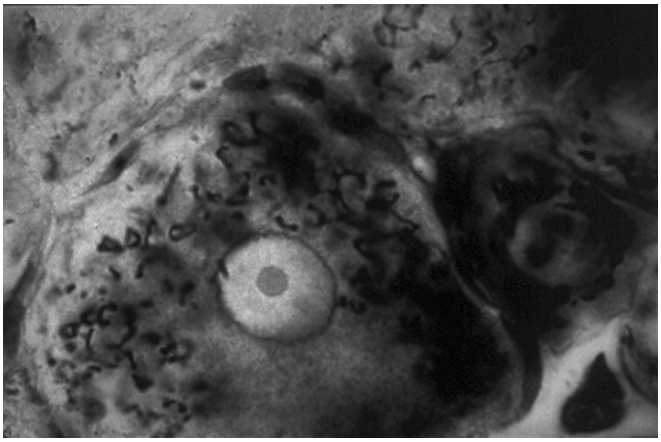

Figure 2. Golgi preparation. Spinal ganglion cells. Presumably Golgi's photographic method, stained with carmine. Author and date unknown. (Preparation in possession of the Istituto di Patologia generale 'C.Golgi' in Pavia.)

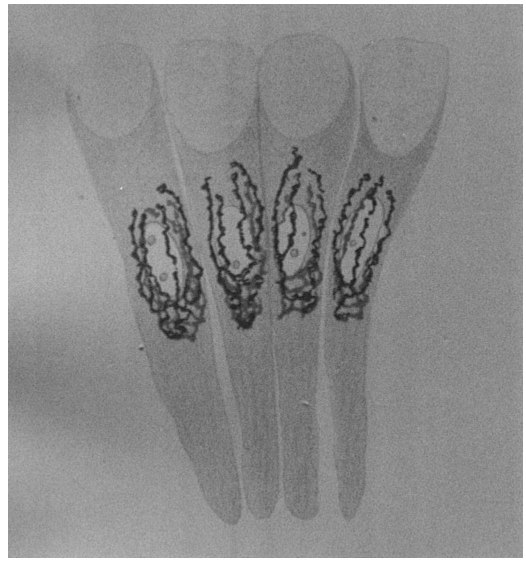

Figure 3. The 'apparato reticolare interno' in the mucous cells of the stomach of the frog. Golgi's photographic method. From Golgi [2].

internum [23]. The filamentous 'apparato' had become first a duplex canal and finally a vacuole with a scale-like rod on its surface.

The function of the Golgi apparatus: first approaches

In consideration of the general disagreement about the existence and the nature of the apparatus the question of its physiological significance was long considered as useless. In addition, Golgi, like most of his Italian colleagues, was very opposed to theory in general and instructed his disciples to refuse any opinion before irrefutable visual evidence could be given. Nevertheless, he must have had the right idea: for in his explicit task to investigate the physiological role of the apparatus he turned away from the nerve cells, his preferred object of study, and chose epithelial cells of the intestine and the stomach [2] (Figure 3).

Golgi and his students had already noticed the pleiomorphy of this organelle in different functional, developmental and morbid cell-stages (e.g., [24–27]). Adelchi Negri had examined the net in the cells of the pancreas but he claimed to have found no difference between hungry and fed animals [28]. Golgi however could detect a significant change in topography and morphology which could be associated with the functional stage of the cell. But he refused to make any general conclusion. His philosophical as well as his technical approach prevented him from having a more definite result.

Cajal can be said to have initialized the dynamic view of the Golgi apparatus. He had been Golgi's great opponent in the neurological controversy. Even the mutual Nobel Prize award in 1906 could not end the hostility between them. But Cajal, also being very familiar with the silver techniques, was one of the first non-Italians to confirm the existence of the Golgi apparatus. As it had happened before, Cajal adopted the initiative of Golgi and gave the research a new direction. He tried to overcome the debate of morphological variety bringing the different constitutions of the Golgi apparatus in the same cell type into a logical order and interpreting them as representatives of different phases of the secretion cycle. However, he did not make the apparatus the agent of secretion. From now on the static conception of the apparatus had become a dynamic one, culminating in the declaration that not the structure but the Golgi *substance* is of importance [29].

The phenomena of secretion were only readily investigated, when the purely morphological and topographical arguments were left aside and secretion was understood as a formation of secretory granules. Kolatchev [30] developed an osmium technique which enabled him to visualize them as well as the Golgi apparatus. His colleague at St. Petersburg was Dimitri Nassonov, who traced the formation of the primary granules and localized them in the meshes of the Golgi apparatus [31] (see Figure 4). Six years later Robert Bowen summarized, in a masterly work, the proof for the active role of the Golgi apparatus during secretion [32].

Based on this new conception, the first comprehensive paradigm of the Golgi apparatus research, an abundance of publications followed during the Thirties, however without bringing much progress and being overlapped in the Forties by the 'Golgi artifact theory'. Exceptions were e.g., Bowen's students Arthur Pollister, Aura E. Severinghaus and Hadley Kirkman. Maybe there was no leading spirit and the rise of the 'neutral-red-cytology' (Gatenby's [33] expression for the exaggerated use of neutral red in cytological research) probably led to incorrect conclusions or maybe there was no further development possible with light microscopic

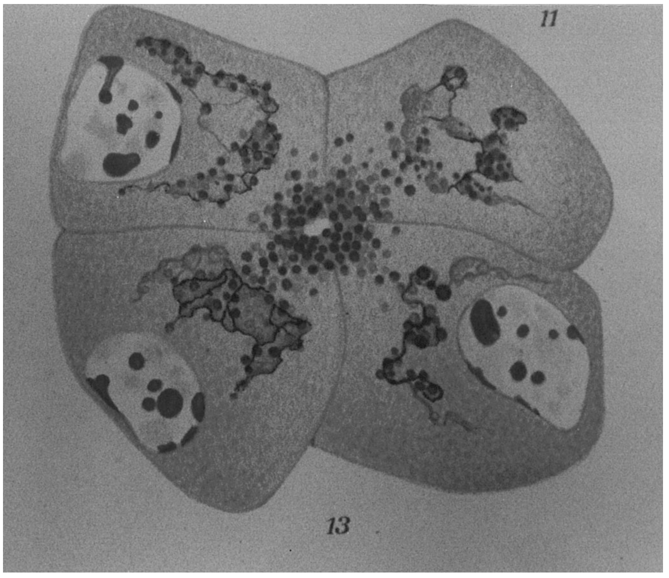

Figure 4. The relation of the Golgi apparatus to secretion in the cells of the pancreas of Axolotl. Champy, postosmicated. From Nassonov [31].

techniques. Obviously, electron microscopy of the Fifties and the cytochemistry of the Sixties were necessary to begin a new era of Golgi research.

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