The cell's components at the end of the 19th century

Let's jump back to the end of the 19th century: still mysterious and debated, the neuron has just been christened (by Wilhelm Waldeyer in 1891); it can at last be stained in its entirety (thanks to Camillo Golgi's "black reaction" developed in 1873); and it can therefore be seen under a microscope. More than anything else, however, the neuron is finally a cell, the protagonist of the "neuron doctrine", officially enunciated in 1891 (see Shepherd, 1991). The cellular dignity of the neuron is strenuously defended by several supporters and admirers, among whom stands Santiago Ramón y Cajal (see Cajal's biography by Javier DeFelipe on this web site).

The other cells, i.e. the elementary components of the body outside the nervous tissue, were much ahead of the neuron in terms of dignity as individual independent units. Since the formulation of the cell theory by the botanist Matthias Jakob Schleiden (1804-81) in 1838 and the zoologist Theodor Schwann (1810-82) in 1839, it had become clear that the cell was not an undifferentiated structure. In the second half of the 19th century, the basic constituents of the cell were considered to be represented by the cell wall, a viscous substance named "protoplasm", and by a differentiated element, the nucleus (described in epithelial cells by Abbot Felice Fontana in 1781 and officially identified in 1831 by the Scottish botanist Robert Brown in several vegetal cell types).

It soon became evident that the protoplasm was not homogeneous, but the identification and classification of structures in the cytoplasm (a term that progressively substituted that of protoplasm) turned out to be long and difficult (see Bentivoglio and Mazzarello, 1998). Supposedly, cellular components were actually misleading microscope images, represented by partially stained constituents of the cell organelles, which were subsequently identified as such, or artefacts due to the precipitation of cellular colloid complexes, due to the fixation and staining procedures. However, at the end of the 19th century the time was ripe to confer dignity on intracellular components. Thus, mitochondria were christened by Carl Benda in 1898, and the "ergastoplasm" (or endoplasmic reticulum) by Charles Garnier in 1897.

The Golgi apparatus or Golgi complex entered the scene in the same years, as a gift of neurons to the fragmented knowledge of the cell composition. The existence of structures equivalent to the Golgi apparatus or to components of this organelle had been reported more or less clearly a few years before Golgi's discovery in some cell types (such as germ cells and pancreatic cells), but they were not recognized as belonging to the same morphological entity, and were considered to be strictly related to cell division and to the nucleus.
Camillo Golgi's discovery of the "internal reticular apparatus"

After his studies on malaria and a long period of academic commitments as Rector of the University of Pavia (see Golgi's biography by Paolo Mazzarello on this web site), Camillo Golgi concentrated again on the investigation of the nervous system. Probably exasperated by the growing success of his rival Cajal, Golgi wished to obtain further insight into his "diffuse neural network", and decided to reduce the intensity of metallic precipitates, and therefore the blackening, of the nervous structures. He thus applied to small specimens of nervous tissue a rapid variant of his "black reaction", reducing the length of silver impregnation and using osmium dichromate solution as first step of the impregnation.

In tissue samples of the spinal ganglia stained with this technique, Golgi noticed in the cytoplasm a net-like structure (Figure 1).

**Figure 1:** First Golgi drawing of the impregnated "internal reticular apparatus" in the body of a Purkinje cell of the cerebellum in 1898.

The same impregnation of an intracellular reticulum was obtained in the Purkinje cells of the cerebellum of the barn owl (Figure 2), and Golgi felt certain that his observations were consistent. In April 1898 he officially reported this discovery at the Medico-Surgical Society of Pavia, describing the novel structure in the Purkinje cells of the cerebellum. In the same report, Golgi described an external covering of nerve cells, revived in recent years by interest in perineuronal nets.
Figure 2: Golgi's drawings of the impregnated "internal reticular apparatus" in spinal ganglion neurons.

Golgi thus reported the existence of what he correctly considered to be a novel intracellular structure, with a complex three-dimensional organization (see below, "Favourite sentence 1"), occupying a preferential perinuclear zone and detached from the cell membrane. Probably as a result of the observation that these multiple components were interconnected and seemed to belong to one and the same structural and functional entity, Golgi stated that "the most distinctive features of this apparatus lies in its overall appearance", and christened it as "internal reticular apparatus" (Golgi, 1898). Very reluctant to provide a functional interpretation of his findings, Golgi somewhat timidly forwarded the hypothesis that the apparatus could subserve a "nutritive" role in the cell.

Golgi immediately encouraged his disciples to search for the apparatus in non-neural cell types, and it soon became clear that this structure was probably ubiquitous in cells. It soon also became evident from several studies, including the investigations performed by Nussbaum (1913) and Cajal (1914), that the appearance and intracellular location of the structure were changing according the state of functional activity of the cell. In particular, the apparatus changed during secretion, thus suggesting that it could be involved in the secretory process. Golgi himself, in his last contribution focused on the internal reticular apparatus performed on mucous gastric cells, described that the structure was changing during the different phases of the secretory cycle (Golgi, 1909).

Golgi's discovery was criticized as possible artefact of metallic impregnation. The debate continued during the first decades of the 20th century, giving a great impulse to cytology and cell biology, and was finally solved in the mid-1950s by the advent of electron microscopy, when the cell constituents could be observed directly in ultrastructural studies (Dalton and Felix, 1954). Associated with the cell organelle of which he became the eponym ("the Golgi"; see Fabene and Bentivoglio, 1998 for terminological debates), Golgi's name is still a protagonist of cell biology and of the molecular biology of protein synthesis and targeting.

Cajal (1917) stated at the end of his autobiography: "For all those who are fascinated by the bewitchment of the infinitely small, there wait in the bosom of living being millions of palpitating cells which, for the surrender of their secret, and with it the halo of fame, demand only a clear and persistent intelligence to contemplate, admire, and understand them."

The palpitating neuron thus surrendered one of its secrets to the man who contemplated them with clear and persistent intelligence, but did not understand its connectivity. He did understand, however, the machinery essential for the cell, and neuron, factory.

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Bibliography


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Favourite sentences

1. Golgi defined the novel intracellular structure as:

"a fine and elegant reticulum hidden within the cell body and with such a characteristic aspect that even small fragments of it, when the reaction is partial, can be recognized with certainty as belonging to the same endocellular apparatus ... The characteristic aspect of this internal reticular apparatus may result from the mainly ribbon-like shape of its threads, from the manner of dividing, forming anastomoses and coursing of these threads ... from its presence in tenuous small plaques or small roundish disks transparent in the center, which serve as nodal points of the reticulum, and finally from the peculiar yellowish colour the threads assume due to the reaction."


2. Albert Kölliker, the father of histology, believed in Golgi's discovery, and in a letter to Golgi dated 4 May 1900 Kölliker wrote:

"Quant à votre apparato reticolare [in Italian in the text] je suis de l'avis qu'il faut le ... regarder comme un système de canalicules intérieurs, étant en rapport avec les procès chimiques, qui ont lieu dans les cellules nerveuses et peut être aussi avec les fonctions spéciales des cellules. [As for your reticular apparatus I believe that this should be ... regarded as a system of internal canals, being in relationship with the chemical processes which occur inside the nerve cells and perhaps also with the special functions of the cells]."


3. For once, Cajal and Golgi agreed, and Cajal stated:

"the reticular Golgi apparatus is an anatomical feature constant in the protoplasm of all living cells, both embryonic and adult."

Cajal (1914).

4. However, the debate on the Golgi apparatus as fact or artefact continued; as recently as the
mid-1950s John R. Baker, an Oxford scholar and fierce opponent to the existence of a Golgi apparatus, stated that this structure:

"takes the form of a network merely because it fills up the spaces between tightly-packed other objects in the cytoplas ... There are many unrelated objects in cells on which osmium or silver may be deposited by the 'Golgi techniques' ... if one is determined to have a net, one can have it ... The techniques commonly called 'Golgi techniques' have this in common, that when applied to certain nerve-cells of vertebrates, they produce a network ... When I look at the living cell of a vertebrate, I do not see a network ... The 'Golgi' methods, I believe, represent an unconscious attempt to get some sort of a view, in a paraffin section, of objects consisting partly or in some cases wholly of lipid. If Golgi had not devised his arbitrary method (while looking for something else), we should have missed the whole of this controversy, which has served only to retard progress in cytology."


5. But after a struggle of more than 50 years, the organelle receives recognition:

"Finally, probably to the surprise of many cytologists, the Golgi apparatus, which has always been the most controversial of all cell structures, is emerging from the clouds and appearing as a unique organelle, clearly recognizable structurally and probably with equally definite unique functions."