Review

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The Golgi Apparatus with the Historical Point of View

Tarihsel Bir Bakış Açisi ile Golgi Apparatusu

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ABSTRACT

Scientists were introduced to the Golgi apparatus (GA) in 1898, when it was discovered by Camillo Golgi in 1898 as a "cytoplasmic reticular network". Researchers heard Camillo Golgi's name not only because of the GA, but also because of many definitions such as Golgi silver impregnation techniques, Golgi type I and II cells, Golgi cells of the cerebellum, and Golgi tendon organ. In fact, although the GA beared the name of this scientist, many scientists did numerous studies on the morphological and functional properties of this unique organelle before him, simultaneously with him or after him. Despite the simple technical possibilities of the old times, the scientists, whom we gratefully commemorated, obtained magnificent findings about the GA and presented them to the world of science. In this short article, which was a review, the following historical developments, starting from the discovery of the GA, were summarized.

Keywords: Camillo Golgi, Golgi apparatus, discovery, historical narrative

ÖZ

Bilim insanları Golgi apparatusu (GA) ile Camillo Golgi tarafından 1898 yılında "sitoplazmik retiküler bir ağ" olarak keşfedildiği 1898 yılında tanıştılar. Araştırmacılar Camillo Golgi'nin ismini sadece GA'dan dolayı değil, Golgi gümüş impregnasyon teknikleri, Golgi tip 1 ve 2 hücreler, beyinciğin Golgi hücreleri, Golgi tendon organı gibi pek çok tanımlama ile duydular. Aslında GA bu bilim insanının ismini taşıyor olsa da kendisinden önce, eş zamanlı olarak veya sonra pek çok bilim insanı bu benzersiz organelin morfolojik ve fonksiyonel özellikleri ile ilgili sayısız çalışma yaptılar. Eski zamanların basit teknik olanaklarna rağmen minnetle andığımız bilim insanları, GA ile ilgili muhteşem bulgular elde ederek bilim dünyasına hediye ettiler. Bu derleme niteliğindeki kısa yazıda GA'nın keşfinden başlamak üzere takip eden tarihsel gelişmeler özetlenmiştir.

Anahtar Sözcükler: Camillo Golgi, Golgi apparatus, tarihsel gelişim

Discovery of Golgi Apparatus and Historical Developments

The Golgi apparatus (GA), defined as the "post office of the cell", was first described in history about 100 years ago by the Italian doctor and pathologist Camillo Golgi, who was known for his studies on the nervous system (1844-1926). Professor Golgi was working at the University of Pavia, the oldest and most respected university in Italy, founded in 1361. Camillo Golgi and Spanish Anatomist Ramón y Cajal (1852-1934) shared the Nobel Prize in Physiology and Medicine in 1906 for their separate studies on the anatomy of the nervous system (1). The first award in this field was given to the German physiologist Emil Adolf von Behring, who discovered serum therapy in the development of diphtheria and tetanus vaccines in 1901. Serum therapy was interpreted as opening a new path in the field of Medical Sciences. Emil Adolf von Behring went down in history with the sentence that "a

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victorious weapon was placed in the hands of the doctor against sickness and death" (2).

Camillo Golgi developed a new technique in 1873 that stained neurons and special cells in the nervous system, thus allowing them to be marked. This technique was called the 'black reaction' because it stained the cell bodies and extensions of the nervous system black. With his technique, Golgi determined that the axons he clearly saw formed an uninterrupted network carrying nerve impulses (1). Today, the scientific writings of Camillo Golgi, including original drawings, are exhibited in the History Museum of the University of Pavia. Golgi has studies on various parts of the brain. However, his studies on the cerebellum, olfactory bulb, hippocampus and cerebral cortex are particularly important. For example, Golgi cells, which were named after him, were identified in the cerebellum (3). While Camillo Golgi's work on the nervous system continued, his rival, Santiago Ramo'n y Cajal, was also on the rise in the scientific world. Cajal developed a theory that challenged Golgi. While this theory, known as the "neuron theory", was generally supported by scientists, Golgi's work was criticized (4). These criticisms did not deter Camillo Golgi. While examining the spinal ganglia in 1897, he noticed that there was a cytoplasmic network in their cell bodies, although not in every cell. Later, he detected the same reticulated structure in the cytoplasm of Purkinje cells of the genus Tyto alba owl (barn owl) (3). Yet this new and strange structure was not stained in every cell. Therefore, he shared his observation with his assistant Emilio Veratti (1872-1967). Emilio Veratti (5), who described the sarcoplasmic reticulum in 1902, confirmed its existence by showing this cytoplasmic network in the 4th cranial nerve. He made the first official presentation of this structure, which he described as the "internal reticulated structure", on 19 April 1898 at the Pavia Medical-Surgical Society (6,7). He stated that this newly discovered reticulated structure consisted of anastomosing ribbon-shaped filamentous elements, small plates with a clear center that served as the nodal points of the reticulum, and rounded discs (8). Antonio Pensa (1874-1970), working in the General Pathology and Histology laboratory of Golgi in 1899, detected this organelle in the cells of the adrenal medulla (9). A short time later, 5th year medical student Adelchi Negri (1876-1912) demonstrated the presence of a similar structure in thyroid, epididymis, salivary glands, and ovarian cells besides nerve cells (10). Negri incidentally detected intraneuronal inclusions while examining rabies-infected brains. These inclusions are known as "Negri bodies". (8). Meanwhile, Edoardo Gemelli (1878-1959), one of Golgi's students, showed that a similar structure was found in the cells of the pituitary gland (11). From these observations it became clear that this structure was probably ubiquitous in eukaryotic cell types. Camillo Golgi hypothesized that this cytoplasmic network might be related to secretory function, more broadly to cell nutrition (8). Camillo Golgi changed the technique defined by Ramón y Cajal in 1903 and developed a new technique (12). With the advantages of this new technique, he was able to observe the morphology and localization of the GA during the secretion process in the mucous glands of the frog stomach. Thus, he found that the GA was located in the apical cytoplasm above the nucleus (13). Camillo Golgi tried to explain the physiological role of the GA in gastric and intestinal mucous cells (14). Meanwhile, Giuseppe D'Agata (1927-2011) was investigating this reticular network in the gastric epithelium (15).

In fact, although the GA was defined by being inspired by the work of Camillo Golgi, between 1867 and 1887, various scientists talked about the reticular structures existing in the cell from time to time before or after Camillo Golgi introduced this organelle (3,4,16,17). Perhaps these researchers also observed the GA. Yet all these years the GA was considered almost entirely a specific subject of the University of Pavia. Camillo Golgi and his students published more than 70 articles on this organelle. In these articles, they reported the changes observed in the GA in various developmental, physiological and pathological conditions, as well as the wide variety of cell types they observed (18). Thus, the organelle was found to be highly unstable and variable. Despite all these studies, the authenticity of this organelle was questioned by many researchers in the following years. Scientists defined this structure as an unreal structure that occured due to fixation or metallic impregnation technique (3). For example, George Palade and Albert Claude, scientists of the Rockefeller Institute, who showed similar cytoplasmic structures 20 years later in various cells without applying special staining methods using 40-55% ethanol, suggested based on these observations that GA represented one or more myelin figures that emerged artificially during the preparation of cytological samples (19). These discussions continued even when the GA could not be demonstrated with the first electron microscopic examinations (20). Finally, the GA, which was observed electron microscopically in the mid-1950s, was accepted as a real organelle and gained the respect it deserved (3). Taking into account Palade's suggestion that phosphate-buffered osmium tetroxide should be used, Bethesda National Cancer Institute scientists Albert Dalton and Felix (21) soon demonstrated the detailed electron microscopic structure of the GA in epididymis cells. These researchers described the organelle as a structure in the cytoplasm consisting of folded, smooth-surfaced sacs and numerous vesicles and vacuoles with the staining technique developed by Camillo Golgi (21).

For many years, scientists focused on morphology rather than the function of the GA. It was known almost from the beginning by light microscopic observations that this organelle developed well in secreting cells. However, the role of this organelle in secretion and glycosylation was not elucidated until the 1960s (22). Palade suggested that the GA was associated with the vectorial transport of secretory proteins in exocrine pancreatic cells, and that vesicular transport also occured between the sacs of this organelle (23). Fleischer et al. (24), Morre et al. (25), and Neutra and Leblond (26) emphasized the important role of the GA in glycoprotein synthesis. The results of the autoradiographic studies of Godman and Lane showing the uptake of sulfate into the GA suggested that this organelle had an important role in sulfation and therefore in glycoprotein biosynthesis (27). Between 1967-1975, various researchers conducted numerous studies on the role of the GA in the secretory pathway and vesicular transport

(28-30). In the 1980s, studies were carried out emphasizing the importance of mannose-6 phosphate in the exiting of lysosomal enzymes from the GA and in targeting them (31-34). Between 1981 and 1984, Rothman et al. studied substance transport in the Golgi sacs (35-37). The COPII protein cover was determined by Duden et al., Seratini et al., and Waters et al. in 1991, and by Barlow et al. in 1994 (22).

In parallel with the technological developments, it was possible to reach detailed information about the location of the GA, its morphological, functional and pathological features. Extraordinary new information is being obtained about morphological and functional properties of the GA with the discovery of new genes, the development of advanced technology techniques such as green fluorescent protein based live cell imaging techniques, dynamic live cell imaging techniques, high resolution electron microscopy techniques that can create three-dimensional structure, and correlative microscopy techniques (CLEM) (38,39). In particular, CLEM provides great advantages for obtaining new findings about substance trafficking, targeting and signaling mechanisms in Golgi sacs.

Naming the Golgi Apparatus

The discovery of the detailed morphological features of the GA with the use of electron microscopes caused this organelle to be given various names such as "Golgi body", "Golgi zone", "Golgi substance", and "Golgi net". In 1910, Carlo Besta named this organelle "Golgi apparatus" (40), but this name was officially entered into the scientific literature in 1913, using it in Nusbaum's article (41). The definition of "Golgi complex" entered the scientific literature in 1956 with the study of Dalton and Felix (42). Today, both the names "Golgi apparatus" and "Golgi complex" are used, but the "Golgi apparatus" is mostly preferred. Scientists are accustomed to the word "Golgi" not only because of this organelle, but also because of Golgi's silver implantation techniques, Golgi type I and type II cells, Golgi cells in the cerebellum, and Golgi tendon organ. Especially in recent years, many new terms have entered the literature in parallel with the fact that techniques that provide detailed information and three-dimensional imaging provide new information about the features of this organelle and its region. These are definitions such as "Golgi receptor", "Golgi strip", "Golgi cluster", "Golgi skeleton", "Golgi sac", "Golgi tubule", "Golgi vesicle", and "Golgi vacuole" (43). Although Camillo Golgi's name was mentioned in these common uses, many researchers do not know who this scientist actually was, how, where and under what conditions he lived. This review article was written with respect to Camillo Golgi and the scientists in his team, who provided the recognition of the GA, despite the limited possibilities that could not be compared with today's technological facilities, and other scientists who played very important roles in the recognition of the GA with their research, although their names were not remembered.

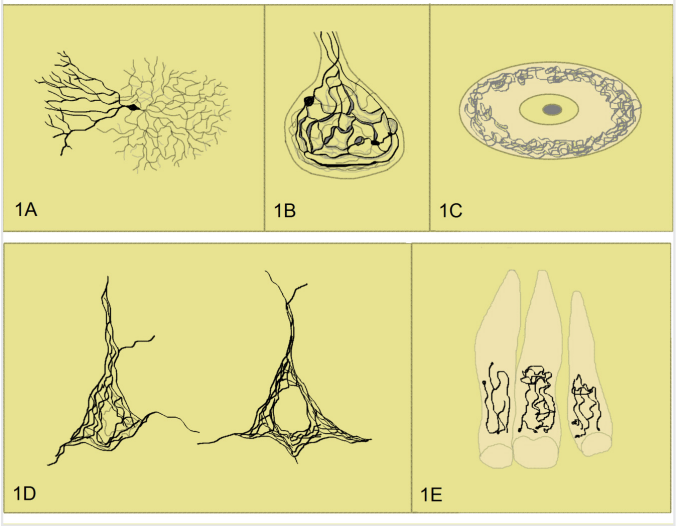

Figure 1. It was drawn by the author, inspired by Camillo Golgi's own drawings from the works of him on display at the University of Pavia Museum. 1 A. Nerve cell stained with black reaction by Camillo Golgi, 1B. First published figure showing the Golgi apparatus in the spinal ganglion cell, 1C. Golgi apparatus, defined as a reticular network in the cytoplasm of the spinal ganglion cell, 1D. Golgi apparatus in nerve cell in mouse cerebral cortex, 1E. Golgi apparatus in frog gastric mucosa cells (the original of this figure probably belongs to Emilio Veratti)

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