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An historical note on the cell theory

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ABSTRACT

The development of the microscope was a precondition for the discovery of cells. This instrument magnifies objects too small to be seen by the naked eye. In 1673, the Dutch botanist, Anton van Leeuwenhoek, made a more advanced microscope and reported seeing a myriad of microscopic "animalcules" in water. He also made further studies of red blood cells and sperm cells. Most studies that followed were done on the easily studied plant tissues. Plant cells, rigidly encased in their cell walls, were ideal to study in situ. The cell theory proposes that nucleated cells are the basic structure of plants and animals. This concept was observed and published separately, first by the botanist, Matthias Schleiden, in 1838, and then by the zoologist, Theodor Schwann, in 1839. Their work demonstrated that cells form the basic unit of life of plants and animals. Rudolf Virchow concluded that all living organisms are the sum of single cellular units and that cells multiply.

1. Background

In 1665, an English botanist, Robert Hooke (1635–1702), at that time first secretary of the Royal Society in London, in his book "Micrographia Or Some Physiological Descriptions of Miniature Bodies by Magnifying Glass" [1] coined the term 'cell' to indicate the microscopic units in cork. With only thirty-times magnification, he saw a pattern of tiny rectangular holes in a thin slice of cork from the bark of an oak tree, and then saw a similar pattern in bones and plants. Hooke examined very thin slices of cork and saw a multitude of tiny pore that he remarked looked like the walled compartment of a honeycomb. Because of this association, Hooke called them "cells" or "pores". Further, Hooke had observed that these "little boxes" contained a liquid, which might possible go from one cell into the other and thus circulate. However, because Hooke's observations were limited by the magnifying power of his microscope, it was difficult for him to learn much about the internal structure and organization of cells.

Anton van Leeuwenhoek (1632–1723) was a Dutch scientist, known for his work on the development and improvement of the microscope. Leeuwenhoek used double-convex lenses mounted between brass plates and held close to the eye. He viewed objects on pinheads, magnifying them up to 300 times this a lot better than any earlier compound microscopes. He made a powerful single-lens microscope with which he observed many types of cells and tissues and even drew bacteria.

From investigating and experimenting with his microscope, Leeuwenhoek became one of the first scientists to refer to living cells when he observed an abundant number of single-celled organisms, which he called animalcules (plants and animals), swimming in a drop of pond water [2]. In 1674, van Leeuwenhoek saw for the first time red blood cells, and spermatozoa. However, Leeuwenhoek's discoveries of bacteria and spermatozoa were more or less ignored for many years.

Marcello Malpighi (1628–1694) and Hook's colleague Nehemiah Grew (1641–1712) made detailed studies of plant cells and established the presence of cellular structures throughout the plant body. Malpighi in his paper "Anatome plantarum" published in 1671 [3], called cells 'utriculi' and 'sacculi'. Grew in his book on "The Anatomy of Plants" [4] used the words "bladders", "cells" and "pores" indiscriminately, and provided a number of illustrations of plant material which indicate that he noticed the cellular structure.

2. The cell theory and their founders

Theodore Schwann (1810–1882) (Fig. 1) and Mattias Jacob Schleiden (1804–1881) (Fig. 2) are considered the founders of the "cell theory". Schleiden, professor of Botany at Jena, formulated the theory for plant cells, while Schwann generalized it to all living organisms, animals as well as plants. Schleiden influenced the young Carl Zeiss (1816–1888) to form his subsequently very important optical firm, the fruits of which were much improved microscopes.

In 1833, Schleiden joined the laboratory of Johannes Peter Müller (1801–1858) in Berlin. He sustained that organisms are made up of a society of cells and focused his attention on their origin, using embryonic plant tissue. He concluded that the cells developed de novo from a mass of minute granules within the cell which form a nucleus

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Fig. 1. A port trait of Theodore Schwann. (From Wilkipidia).

Fig. 2. A port trait of Mattias Jacob Schleiden. (From Wilkipidia).

called "cytoblast" around the nucleolus, with subsequent progressive enlargement of such condensed material to become a new cell [5].

Schleiden was wrong in regard to his notions concerning cellular replication. His main theory in this regard was that new cells were formed inside old ones from the nucleus. This interpretation which Schleiden deduced from his preparations is the same as that of the followers of the "endocytogenesis" theory postulating the formation of a cell within another.

In 1831, Robert Brown (1773–1858), a Scotch botanist and physician discovered under a primitive compound microscope the cell nucleus as an essential constituent of living cells. Brown was a naturalist who visited the "colonies of Australia" from 1801 through 1805, where he cataloged and described over 1700 new species of plants. Brown observed that: "a single circular areola, generally somewhat more opaque than the membrane of the cell (…) This areola, or nucleus of the cell as perhaps it might be termed, is not confined to the epidermis, being also found not only in the pubescence of the surface, but in many cases in the parenchyma or internal cells of the tissue." [6]

At that time, also Schwann was in Müller's laboratory as a medical student. He reported that in October 1837, he was dining with dr. Schleiden, who pointed out the important role that the nucleus plays in the development of plant cells. Schwann recalled him to have a similar organ in the cells of the notochord playing the same role as does the nucleus of plants in the development of plant cells. Schwann described nucleated cells of notochord and cartilage, in the larvae of toads, as well as in the kidney, liver, pancreas, salivary glands, and connective tissue of pig embryos. He published the results of these observations in three articles in the January, February, and April 1838 issues of the Neue Notizen aus dem Gebiete der Natur und Heilkunde [7]. In 1839, Schwann became professor at the Catholic University of Louvain, and in 1848 at the University of Liege, Belgium.

While studying more closely peripheral nerves, Schwann first described the membranous wrapping, produced by a specialized type of cell, which envelops the prolongation of nerve cell. Schwann's name has been associated with both the supporting cell and this membranous sheath. Today, the term Schwann sheath has become obsolete, whereas

Fig. 3. A port trait of Robert Remak. (From Wilkipidia).

the name of Schwann cell, remains universally used.

Schwann considered that new cells originate in a structure less substance which he called the *Cytoblastema* or *Cytoblastem*. He supposed that this substance sometimes existed within the pre-existing cells, but in animals it was usually extracellular. It was often fluid, but might also be solid: the matrix of cartilage was an example of it. According to Schwann: "The entire process of the formation of a cell consists of precipitation, around an initially arising small body (nucleolus), of first one (nucleus), and then, around it, a second layer (cell substance). The different layers grow by intake of new molecules among those already present, by intussusception, and this according to the law that the precipitation is more pronounced in the outer parts of every layer … Because of this law, only the outer part of every layer condensates into a membrane (of the nucleus and of the cell)." [8]

Robert Remak (1815–1865) (Fig. 3) like Schwann and Virchow, trained in Müller's laboratory at the University in Berlin. In 1852, Remak summarized his early work on cell generation: "Since the publication of the cell-theory, it has seemed to me that the extracellular creation of animal cells is as unlikely as the generation "aequivoca" (spontaneous generation). These doubts have led to my observations on the multiplication of blood cells by division in bird and mammalian embryos (…) and the division of muscle bundles in frog larvae; then finally in the spring of 1851, I succeeded in finding that all embryonic cells multiply by division." [9] He concluded: "These results are just as closely related to pathology as they are to physiology (…) I venture to suggest that pathological tissues are, like normal ones, formed not in an extracellular cytoblastem but are the descendants or products of normal tissues of the organism."[9] According to Remak: "The division of the cleavage cells starts from the nucleus and, when at the end of cleavage, the nucleolus can be recognized from the latter … At the lower, white half of the uninjured egg, one can observe by use of a magnifier, in the last stages of cleavage, how the light spot representing the nucleus divides into two spots, how those spots move away from one another, and how the cleavage cell divides in a way that each half is furnished with a light spot (nucleus) … Following cleavage, the cells begin to form an embryo by separating themselves into three layers (a sensory, a motoric, and a trophic one) and by proliferating within those layers through division, thus creating the cells that serve as the basis of tissues." [9].

3. The epigones

Rudolf Virchow (1821–1902) (Fig. 4) received his medical degree in 1843. Although six years Remak's junior, the two were appointed to the faculty in Berlin in the same year, 1847. In 1849, Virchow was appointed professor at Würzburg. He returned to Berlin seven years later, again the victor in a competition with Remak, this time for the coveted appointment to a new professorship of pathology. Virchow was not only the most famous pathologist of the nineteenth century but also throughout his working life a prominent left wing politician. He was at the barricades in Berlin during the revolution of March 1848.

In 1849, Virchow wrote that: "The cell, as the simplest form of life-