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Wilhelm Waldeyer (6 October 1836 to 23 January 1921) in 1896. (Photograph courtesy of the Bildarchiv Preussischer Kulturbesitz, West Berlin.)

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Centennial of Wilhelm Waldeyer's introduction of the term "chromosome" in 1888

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Wilhelm Waldeyer's celebrated paper "Über Karyokinese und ihre Beziehungen zu den Befruchtungsvorgängen" in which the term "chromosome" was introduced, was published in 1888. An English translation "On karyokinesis and its relation to the process of fertilization" appeared in 1889. In this extensive review with 210 references, Waldeyer summarized the experimental and theoretical work of his contemporaries such as Edouard-Gérard Balbiani (1823–1899), Edouard van Beneden (1846–1910), Theodor Boveri (1862–1915), Otto Bütschli (1848–1920), Jean Baptiste Carnoy (1836–1899), Walther Flemming (1843–1906), Hermann Fol (1845–1892), Oscar Hertwig (1849–1922), Carl Rabl (1853–1917), Wilhelm Roux (1850–1924), Anton Schneider (1831–1890), Eduard Strasburger (1844–1912), August Weismann (1834–1914), and many others.

In the first part Waldeyer gave an overview on what was known in 1888 of the mitotic process. Then he continued (Waldeyer 1889, p. 181): "I must beg leave to suppose a separate technical name 'chromosome' for those things which have been called by Boveri 'chromatic elements' in which there occurs one of the most important acts in karyokinesis, viz. the longitudinal splitting."

Waldeyer's term proved eventually to be more successful than all other competitive terms, such as "chromatic elements," "nuclear loops," "karyosomes," "nuclear segments," or "idants." It is now a universally accepted term in the life sciences. Due to the importance of the structure it designates, it has become an integral part of the vocabulary of all major languages.

Wilhelm Waldeyer (full name: Heinrich Wilhelm Gottfried von Waldeyer-Hartz; 1836–1921) was a famous anatomist of his time and head of the Institute of Anatomy at the University of Berlin from 1883 until his retirement in 1917 (cover illustration). Several of his numerous histological, anatomical, and pathoanatomical publications are still being quoted, and in standard anatomical textbooks his name has been preserved in technical terms such as Waldeyer's germinal epithelium of the ovary and Waldeyer's lymphatic ring of the pharynx. (For a review of Waldeyer's scientific work and his complete bibliography see Sobotta, 1922.) From his histological studies he derived a keen interest in the process of nuclear and cell division, although he did not publish any experimental investigation of his own on chromosomes.

In the context of this celebration it should be remembered that 19th century scientists had much more to offer than a generally accepted name for the "stainable bodies" which became distinctly visible at mitosis and meiosis, but whose structure and functional importance was not clarified before the 20th century. Virtually all cell biologists today hold the view that the cell, its membranes, organelles, and its information-containing molecules have come into existence in the course of some billion years of evolution. Hence for modern cell biologists and cytogeneticists the following paradigms seem to be almost self-evident, logically interdependent truths: Each cell is derived by cell division of a preexisting cell (*omnis cellula e cellula*), each cell nucleus is derived by (indirect) division of a preexisting nucleus (*omnis nucleus e nucleo*), and each individual chromosome is derived by replication and splitting of a preexisting chromosome (*omnis chromosoma e chromosoma*). In short, cells and their organelles are not generated spontaneously *de novo* in our days. However, only a hundred years ago, this was by no means a generally shared belief among cytologists. More important for these scientists, who thought within the limits of various theoretical frameworks completely different from the one generally shared by present day cell biologists and geneticists, acceptance of one paradigm (such as *omnis cellula e cellula*) did by no means create a "logically" compelling force to accept the others. A few examples may suffice to illustrate this point. For a more comprehensive presentation and references of the original literature see Cremer (1985).

Theodor Schwann (1810–1882) and Matthias Schleiden (1804–1881), the founders of the cell theory (1838/39), were firmly convinced that cells could form *de novo* from a "structureless substance" called the "cytoblastem." Still in 1845 Matthias Schleiden described in detail the spontaneous generation of yeast during the fermentation of currant-juice. The rejection of their theories on cell formation first by Robert Remak (1815–1865) and then by Rudolf Virchow (1821–1902) culminated in Virchow's famous statement *omnis cellula e cellula* (1855). This paradigm soon became accepted by a majority of cytologists. However, while some scientists such as Remak proposed a direct nuclear division (later called amitotic division), the very fact that nuclei were apparently no longer visible in dividing cells was considered by most of these

Dedicated to Professor Dr. H.G. Schwarzacher on the occasion of his 60th birthday.

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scientists as clear evidence that nuclei dissolved and disappeared completely at this stage of the cell cycle. In daughter cells new nuclei were—in a kind of intracellular *generatio spontanea*—independently formed *de novo*. The discovery (first in 1873 by Anton Schneider) and detailed description of an indirect mechanism of nuclear division, called karyokinesis, in the seventies and eighties of the 19th century, was therefore unexpected. In 1880 Walther Flemming, one of the main proponents of indirect nuclear division, stated: 'The reader of my article may have received the impression that I have pleaded for the principle "*omnis nucleus e nucleo*." However, I do so only by adding the proviso: as far as we know now. I do not doubt the possibility of a free generation of cells, of a free generation of nuclei, of *generatio spontanea* in general. I cannot even find this, as others do, a strange conception.' Flemming's tentative formulation of the new paradigm reminds us that *generatio spontanea* was taken seriously in the scientific community, even two decades after Louis Pasteur (1822–1895) had refuted the spontaneous generation of yeast in elegant and decisive experiments. Flemming and others still hoped that scientists might become able one day to define conditions in the laboratory suitable for the spontaneous generation of cells. The new paradigms would not explain, when and how cells and cell organelles had formed for the first time—a problem which in the opinion of contemporary scientists had already been solved in principle by the old theory.

Oscar Hertwig whose experimental investigations of fertilization in the sea urchin (1876–1878) became one of the cornerstones of the hypothesis that the nucleus and its chromosomes contained a hereditary substance, proudly claimed in 1917: "My teachings concerning the continuity of nuclear generations and my observations on which I have based these teachings have been generally accepted by science as the correct ones." However, the same Oscar Hertwig with many of his scientific contemporaries stubbornly rejected Carl Rabl's theory of the structural continuity of chromosomes in the interphase nucleus, as well as Theodor Boveri's more refined theory of chromosome individuality. Instead, Oscar Hertwig continued to believe that chromosomes would completely dissolve in the interphase nucleus ("Verschmelzungstheorie").

The great synthesis of a 19th century chromosome theory of heredity was published in 1892 by August Weismann. His book "Das Keimplasma. Eine Theorie der Vererbung" (The germ plasm. A theory of heredity) stands as an example of a great theory now fallacious in virtually all its details but immensely fruitful in its basic tenets. Weismann summarized all arguments in favor of the localization of a hereditary substance within the "chromatin granules" of the chromosomes. He rejected any reminescence of *generatio spontanea* and claimed that this substance (which he called "Keimpasma" or "Idioplasma") was the result of an immensely long selective evolutionary process and of both extreme complexity and stability. Weismann hypothesized "biophors" as the most minute hereditary particles within this idioplasma. These biophors "which migrate into the cell-body through the pores of the nuclear membrane" should effect a distinct state of cellular differentiation with regard to cell structure and function. Like all of his contemporaries Weismann had no grasp of the idea of information-containing molecules and he felt that biophors should materially contribute to all cytoplasmic structures. The chemical nature of the hereditary substance was a matter of speculation. Waldeyer (1888) already referred to Johann Friedrich Miescher's (1844–1895) discovery of "nuclein" and to Albrecht Kossel's (1853–1927) early papers on "histon" and "adenin."

Weismann's highly speculative theory was not compatible with Mendelian segregation. After Mendel's work achieved prominence in 1900 it was largely abandoned in favor of the new chromosome theory of heredity put forward in 1902/03 by Theodor Boveri and Walter S. Sutton (1877–1916). They, together with Thomas H. Morgan (1866–1945) and his school, soon became the acknowledged forefathers of modern cytogenetics, that is as the saga goes today. In fact, the chromosome theory of heredity was by no means generally accepted as quickly as we might now believe. Cyril D. Darlington (1902–1982) remembered in 1960: "Morgan's 'Theory of the gene' appeared in 1926. Its reception in England could scarcely have been more unfavorable. Seven men might have been willing to assert their belief in the chromosome theory and give their reasons for it. But against this view were several hundred who held a contrary opinion."

The 19th century advancement of biology from the cell theory to the concept of the decisive role of chromosomes in heredity may be regarded of great significance not only for the life sciences but for human knowledge in general. This historical process of methodological progress, new theoretical concepts, experimental observations, paradigms, and scientific "revolutions" testifies to the turning away from vitalistic theories of life which had dominated for thousands of years. It is certainly not less important than the recent developments in gene technology being derived from the elucidation of the physical structure of DNA.

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