

## MINIREVIEW

# BIOCHEMISTRY AT THE EARLY 20<sup>TH</sup> CENTURY: THE MAIN CONTRIBUTORS

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### ABSTRACT

Biochemistry or biological chemistry is the science that studies all the chemical processes that take place in the living organism of humans, animals, protozoa and plants. In our article we reveal, the contribution of distinguished scientists to this field at the early 20th century tracing also the first steps of the scientific development of biochemistry.

**Keywords:** biochemistry, André Lwoff, Paul Berg, history of medicine.

### RÉSUMÉ

**La biochimie au début du 20-ème siècle : les principaux contributeurs**

La biochimie ou la chimie biologique est la science qui étudie tous les processus chimiques qui se déroulent dans l'organisme vivant de l'homme, des animaux, des protozoaires et des plantes. Dans notre article, nous révélons la contribution des scientifiques éminents à ce domaine au début du vingtième siècle, retraçant également les premières étapes du développement scientifique de la biochimie.

**Mots-clés:** biochimie, André Lwoff, Paul Berg, histoire de la médecine.

### INTRODUCTION

Biochemistry or biological chemistry is the science that studies all the chemical processes that take place in the living organism of humans, animals, protozoa and plants. When these processes concern the body in

a normal state, it is called "Physiological Chemistry". When the aforementioned research extends to disease states of the organism it is called „Pathological Chemistry“. The concept of Biochemistry encompasses Physiological and Pathological Chemistry as well as a particular branch of Phytochemistry that includes

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the same processes focusing on plant organism. Since the events that take place throughout the world are physical and chemical processes, biochemistry has undoubtedly provided with the invented, formulated and cultivated research methods, the means to infiltrate into the essence of animal phenomena<sup>1</sup>.

With the contribution of biochemistry, it has been proven that many organisms carry out a lot of chemical processes, thus are referred to as "perfect chemical laboratories". Till 19th century, the in vitro technical production of many of these substances was not possible, thereby debunking the theory of a new imaginary force of life, the so-called force vitale (vital force). To achieve the above processes the understanding of the chemical composition of various organs of the body, like the cells that compose the organism, is required. Biochemistry, from an insignificant branch of biology, evolved into a separate science and developed tremendously from the beginning of the 20th century with the discovery of the chemical composition and architectural structure of the fatty acids, carbohydrates, proteins, nucleoproteins, lipids, phosphatides, etc., which compose the protoplasm and the nucleus of cells<sup>1</sup>. Pioneers of biochemistry should be considered Antoine-Laurent de Lavoisier (1743-1794), Justus von Liebig (1803-1873), Michel-Eugène Chevreuil (1786-1889), Emil Fischer (1852-1919), Pierre-Eugène Berthelot (1827-1907), Hans Fischer (1881-1945), Émile Abderhalden (1877-1950), Friedrich-Karl-Johannes Thiele (1865-1918), Richard Willstätter (1872-1942), Karl-Martin-Leonhard-Albrecht Kossel (1853-1927), Arne-Wilhelm-Kaurin Tiselius (1902-1971), Axel-Hugo-Theodor Theorell (1903-1982), Jokichi Takamine (1854-1922), Rodney-Robert Porter (1917-1985), Otto-Fritz Meyerhof (1884-1951), Phoebus-Aaron-Theodor Levene (1869-1940), Sir Hans-Adolf Krebs (1900-1982), Edwin Krebs (1918-2009), Arthur Kornberg (1918-2007), David Keilin (1887-1963), Sir Frederick-Gowland Hopkins (1861-1947), Robert Hill (1899-1991), Sir Arthur Harden (1865-1940), Vincent Du Vigneaud (1901-1978), Louis Pasteur (1822-1895), Melvin Calvin (1911-1997), Olof Hammarsten (1841-1932), Otto von Fürth (1867-1938), Carl von Voit (1831-1908) and Max Rubner (1854-1932).

Biochemistry is not only limited to the research above, i.e. the identification of the chemical composition of the organ and tissue substances that compose the organisms and are found to the secretions and excretions but it also tries to solve the problem of the interstitial exchange of compounds taking place inside an organism, in order to further understand its regular functions<sup>1</sup>.

## THE FORERUNNERS OF BIOCHEMISTRY

### André Lwoff (1902-1994)

André Lwoff was born in 1902 in the French city Ainay-le-Château. In 1922 he received a bachelor in natural sciences. He studied in the laboratory of Professor Félix Mesnil (1868-1938) of the Pasteur Institute and then of the professor Édouard Chatton (1883-1947) who was specialized in protozoa. He received two PhDs; in medicine (1927) and in natural sciences (1932). After training in Heidelberg (1932), where he studied cell metabolism, he visited the Molteno Institute of Cambridge to continue his training in cellular biochemistry. In 1938 he was appointed head of the department of Microbial Physiology (Pasteur Institute), where he collaborated with Jacques Monod (1910-1976). In 1965 he was awarded the Nobel Prize in Physiology or Medicine<sup>2</sup>.

André Lwoff was a microbiologist, biochemist, geneticist, and virologist. He studied microbial nutrition, growth factors, vitamins, enzymes, and bacteriophages. His work aimed at basic research on the development of viruses and in particular the discovery of pre-phages or dormant viruses inside microbial cells, either of infectious etiology, or pre-existing, embedded inside the genetic material and replicated alongside with it, as well as releasing agent, such as ultraviolet rays that awaken the dormant viruses to give birth to an infectious virus. He also studied the problems of viral virulence, the inflammatory response in viral infections and intracellular relationships. From 1959 to 1968 he held the chair of Microbiology at the Paris School of Natural Sciences. From 1968 to 1972 he headed the Cancer Research Institute in Villejuif<sup>3</sup> (Figure 1).

### François Jacob (1920-2013)

François Jacob was born in 1920 in Nancy. He served with the Free French Forces led by Charles de Gaulle (1890-1970) in the Second World War and he was honored with several medals. He continued his studies and received a PhD in medicine in 1947 and a PhD in natural sciences in 1954. He initially worked in the laboratory of Microbial Physiology (Pasteur Institute) which was headed by the Nobel Laureate Dr. André Lwoff (1902-1994). Later he became director of the newly established Microbial Genetics Laboratory. His research focused on the biochemical genetics and the genetic mechanisms that exist in germs and bacteriophages. He has studied the relationships between bacteriophages and host bacteria (mainly on lysogeny). In collaboration with Élie Léo Wollman (1917-2008), he analyzed the mechanisms of genetic recombination of bacteria. In 1965 he was awarded the Nobel Prize in Physiology or Medicine for his discoveries concerning the genetic control of enzyme and virus synthesis. The



**Figure 1.** The Nobel Laureate microbiologist and forerunner of biochemistry, André Lwoff (1902-1994)



**Figure 2.** The Nobel Laureate biologist and biochemist François Jacob (1920-2013)

Prize was awarded jointly to François Jacob, André Lwoff and Jacques Monod<sup>4</sup> (Figure 2).

#### **François Gros (1925-)**

François Gros was born in Paris in 1925. He worked in the biochemistry department of the Pasteur Institute, under the guidance of Professor Michel Machebœuf (1900-1953). In 1953 he received his PhD regarding the mechanism action of antibiotics. After training in the United States at the laboratories of Professors Sol Spiegelman (1914-1983) and Rollin Hotchkins (1911-2004), he returned to the Pasteur Institute and worked in the laboratory of the Nobel laureate Professor Jacques Monod (1910-1976) until 1963. He was appointed head of the department of Microbial Physiology at the Institute of Physicochemical Biology of Paris. His research focused on RNA synthesis and its role in protein biogenesis. In 1960 he was awarded the Leopold Mayer Prize of the French Society of Biochemistry<sup>5</sup>.

#### **Paul Berg (1926-)**

Paul Berg was born in 1926 in New York. After working as a researcher at the American Cancer Society, at Professor Kalckar's Institute of

Cytophysiology in Copenhagen and at the University of Washington School of Medicine in St. Louis he became a Professor in the 1960s. His research focused on the study of DNA transfer. He became interested in bacteria that do not have a defined cell nucleus. It has been known since the 1960s that in the case of coliform bacteria, viruses that invade the cell could replace a portion of the microbial DNA with their own. As a result, the micro-organism begins to produce virulent protein. Berg in the 1970s succeeded in producing recombinant DNA using SV40 and lambda bacteriophages. As a result, he produced synthetic viruses with unpredictable properties. This outcome caused a lot of reactions and thus the investigation was suspended until 1974 when an international conference set out rules ensuring the proper use of the above new achievements. Berg was awarded the Nobel Prize in Chemistry for his research in 1980, which he shared with Walter Gilbert (1932-) and Frederick Sanger (1918-2013)<sup>6,7</sup>.

#### **James Dewey Watson (1928-)**

James Watson was born in Chicago in 1928. In 1947 he received a degree in zoology. He was educated in genetics at Indiana University Bloomington and he

was influenced by the work of geneticists Hermann Joseph Muller (1890-1967) and Tracy Morton Sonneborn (1905-1981) and by the Italian microbiologist Salvador Edward Luria (1912-1991). He worked in Copenhagen in the biochemical laboratories of Herman Kalckar (1908-1991) and Ole Maale on the DNA of viral particles (virion) that infect bacteria. In 1951 he met Maurice Hugh Frederick Wilkins (1916-2004) in Naples; this acquaintance changed his research interests towards the chemical structure of nucleic acids and proteins. His research was conducted at the Cavendish Laboratory in Cambridge in collaboration with Francis Harry Compton Crick (1916-2004). In March 1953 he proposed the double helix structure of the DNA molecule. At the same time, Watson devoted himself studying the structure of the subunits (sous-unités) of the tobacco mosaic virus using Roentgen diffraction techniques and proving that these subunits also contained the helical structure. In the following years, at the California Institute of Technology, he collaborated with Alexander Rich (1924-2015) in the diffraction of Roentgen rays with RNA. In 1956 he taught at the Harvard Biology Department where few years later he became a Professor (1961). In 1965 he returned to the Cavendish laboratory and re-collaborated with Crick. He accepted in his laboratory a number of prominent foreign biochemists, such as Swiss Alfred Tissières (1917-2003) and French François Gros (1925-). Since then he has been particularly interested in studying the role of RNA in protein biosynthesis. Watson was honored with the following scientific awards: John Collins Prize of the Massachusetts General Hospital (1959); Eli Lilly Award in Biochemistry (1959); Lasker Award (1960); Research Corporation Prize (1962); Nobel Prize in Biochemistry with Maurice Wilkins (1916-2004) and Francis Crick (1916-2004) in 1962<sup>8</sup>.

## CONCLUSIONS

Over the years, instrumentation advanced rapidly and novel physical techniques made possible the detailed analysis of structure. Biochemistry provided to science a new path of research, contributing

to every field of medicine, helping also to establish better therapies for several diseases. Currently biochemistry is considered the science of future and its applications to diagnoses, pharmacy, biotechnology and even agriculture promise a better world.

## Author contributions

S.N.M. and M.K. conceived the original draft preparation. S.N.M., G.T., K.L., M.K., G.A. were responsible for conception and design of the review. G.A., M.K., G.T. were responsible for the data acquisition. S.N.M., G.T., K.L., M.K., G.A. were responsible for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review. S.N.M., G.T., K.L., M.K., G.A. contributed equally to the present work. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

## Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article“

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