# THE HISTORY OF BIOCHEMISTRY

https://doi.org/10.15407/ubj88.06.098

#### NOBEL LAUREATE ILYA I. METCHNIKOFF (1845-1916). LIFE STORY AND SCIENTIFIC HERITAGE

Yu. V. EZEPCHUK<sup>1,2</sup>, D. V. KOLYBO<sup>3</sup>

<sup>1</sup>National Jewish Medical and Research Center, Denver, Colorado, USA; <sup>2</sup>The Gamaleya Institute for Epidemiology and Microbiology, Moscow, Russia; <sup>3</sup>Palladin Institute of Biochemistry, National Academy of Sciences of Ukraine, Kyiv; e-mail: kolibo@biochem.kiev.ua

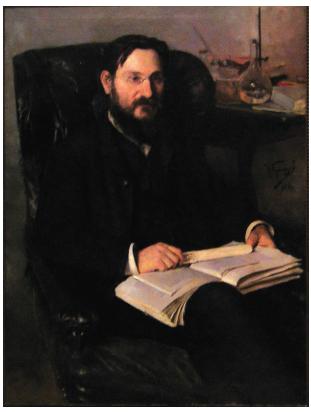
A century of science after I. Metchnikoff's death demonstrated the truth in many of his views and judgments in the field of immunology, pathology, bacteriology, zoology and comparative embryology. Today Metchnikoff is deservedly called the father of the theory of cellular immunity, and also a harbinger of the theory of natural immunity. His work in the field of lactic acid bacteria formed the basis for an entire industry of probiotics. Metchnikoff's doctrine of the possibility of extending human life is still relevant. This publication is one more attempt to tie the biography of the scientist with his creative legacy and his contribution in the world treasury of biological science.

Key words: biography, immunologist, bacteriologist, comparative embryologist, zoologist, pathologist.

In 2016 we mark 100 years since the death of outstanding scientist of the late XIX – early XX centuries – zoologist, microbiologist, and immunologist – Professor Ilya Ilyich Metchnikoff. For a fundamental discovery, regarding phagocytosis as a protection reaction of the organism, Metchnikoff was awarded the 1908 Nobel Prize in Physiology or Medicine (jointly with the German Professor Paul Ehrlich). The history of biological science has appreciated Metchnikoff contribution to the knowledge of the nature of the immune system and has put his name on a par with the greatest names of his contemporaries – Einstein, Darwin, Pasteur, Mendeleyev and Pavlov.

I. I. Metchnikoff was born on 3(15) May, 1845 in the village of Ivanovka, Kharkov province, now the territory of modern Ukraine. Soon after his birth, the family moved to the village Panasovka, which also belonged to the estate of his father [1-3].

His mother Emilia L. (nee Nevakhovich) (1814-1879) came from a noble family of Jewish origin. Her father – a philosopher, essayist and educator Yehuda Leib ben Noach, or, as he was called in the Russian manner Leo Nikolaevich Nevakhovich (1776-1831), wrote books, the most famous of which is "The



Portrait of Professor I. I. Metchnikoff by N. D. Kuznetsov, 1886



Nobel Laureate's Mother Emilie L. Mechnikova [7]

wailing of the Daughter of Judaea" (Vopl' Dshcheri Iudeiskoi). After the adoption of Christianity (Lutheran or Greek Orthodox) in 1806 (or 1809) Metchnikoff's grandfather was granted nobility. One of his sons Michael Lvovich was a cartoonist, publisher of

the first comic magazine in Russia "Eralash" (the Jumble). The second son – Alexander Lvovich – a playwright, was in charge of the repertoire of the Imperial Theatres [4-6].

Ilya Ilyich's father – Ilya Ivanovich (1810-1878) – a retired officer, a colonel, Ukrainian landowner. Father's family came from the old Moldavian boyar family Milescu-Spataru. Family name Metchnikoff, apparently, is a translation of the Moldovan title Spataru, or "spadăare", which means the squire, the sword carrier (swordsman or Chancellor).

Ilya Ilyich was the youngest child in a large family [7]. All the children were well educated and highly trained, but each of them met different fate. For example, one of the brothers, Ivan Ilyich, served as a provincial prosecutor in Tula and became a prototype of the main character of Leo Tolstoy's novel "The Death of Ivan Ilyich" (Smert' Ivána Ilyichá). (Tolstoy changed neither the real name nor the real middle name in the story) [8]. The main theme of the novel is the urge to find the meaning of life by the dying man. "This story is the brightest, most sophisticated and most complex work of Tolstoy" - considered, for example, the writer Vladimir Nabokov [9]. In Ilya Metchnikoff's opinion, Tolstoy was a writer, who "gave the best description of the fear of death". But the theme of "fear of death" is visibly



Visiting Leo Tolstoy in Yasnaya Polyana, 1908

or invisibly present in all the works of Metchnikoff: in his scientific work, journalistic and philosophical assays. "The fear of death — one of the main characteristics that distinguish man from the animals, even the most developed", — the scientist wrote: "All animals instinctively avoid death — but do not realize it" [10].

Fear of disease, famine, fire, death – all of these factors contributed to the pessimistic perception of reality characteristic of early Metchnikoff. However, he argued that "every pessimist at the end of life necessarily becomes an optimist". In his "Etudes of optimism" Metchnikoff quipped: "Tolstoy, who was, of course, a great connoisseur of human souls, did not know that the instinct of life, the need to live – not the same at different ages. ... Having reached the rape old age, a person begins to feel life satisfaction, a kind of satiety of it" [10]. The same happened with the scientist himself. At one of the turning points of his life, after a long illness caused by the agent of relapsing fever which, incidentally, the scientist infected himself, being on the verge of life and death, Metchnikoff unexpectedly defeated the fear of death, and along with the fear of death all doubts, frustrations and discouragement left him. From the deep pessimist the scientist transformed to consummate optimist, and remained so until his death.

But let us back to the scientist's childhood. Ilya Ilyich spent his childhood and adolescence in his father's estate in the village Panasovka, Kharkov province, now the village Metchnikovo. Ilya was the youngest son in the family, and therefore, most dearly loved by all, especially by mother. Probably, it was the mother, who decided that her son would be a scientist, and she did everything possible to support and develop interest in art, music and natural sciences in him.

Ilya began to show his talents in the early child-hood. Contemporaries said that he loved to sit with a beautiful picture book about animals, to catch bugs and butterflies, to observe nature and think about the mysteries of the universe. He eagerly desired to share the joy of contemplation of the world with everyone who was nearby. He even collected his own audience of peasant children and told them about the nature, the world and all that he knew or saw. He just could not be without listeners, therefore, inspired by the attention he gave coins and goodies to peasant children who came to listen to him [3]. There is a story how one professor (or ever student) from Odessa University was invited in the Metch-



Leo Ilyich Metchnikoff (1838-1888)

nikoff's house as a tutor to his elder brother Leo, and once unwittingly witnessed "a lecture on the nature of frogs", given by a seven-year old master to his peasants. Professor was impressed by what he had heard, and, of course, told his colleagues about the young talent from the village Panasovka. Thus, the fame of Metchnikoff-lecturer spread in the walls of the Odessa University long before Metchnikoff-docent joined to the University department.

Probably, of all the brothers Ilya loved his brother Leo, who determined his penchant for science, the most Leo Metchnikoff was a multi-talented personality, easily accepting any teaching. During his life, he tried his hand as a translator knowing a lot of oriental languages, and as a geographer and ethnographer, philosopher and writer. He was one of the members of the Orthodox Mission of General Mansurov in Jerusalem, commanded one of the Garibaldi batteries, even tried to gather Slavic regiment in his support, he studied medicine and painted excellently, led the faculty at universities in Japan and Europe. He was one of the founders of political economics and geo-political geography [11, 12], however, he could not return to his homeland, because he was suspected of being an anarchist and rebel.

In 1850 the whole family moved from Panasovka to Kharkov. Ilya entered at once the second class of the gymnasium, where he studied with a great pleasure and amazed teachers and companions by his abilities. Metchnikoff wrote his first scientific work at the age of 16 while studying at the gymnasium. The work was dedicated to slipper animalcule (infusoria) and was exepted for accepted publication in the journal "Vestnik Estestvennykh Nauk" in 1862. However, due to journal's financial problems, the article was published only three years later, in 1865 [13].

After graduating from high school Ilya decided to pursue higher education in Europe, but having faced with the cold reception of alien Germany, he returned to Kharkov. From Germany Metchnikoff brought the book which undoubtedly influenced all his subsequent work – a Darwin's landmark work "Origin of Species", published also in Russian in 1864 [14]. "By combining human with the animal world by a common origin, Darwin thus strengthened the hope to solve the problem of human existence with the help of the laws that govern living beings" – recalled Metchnikoff [15]. After becoming acquainted with the Darwin's work Metchnikoff became ever since a staunch evolutionist, and saw his calling in the further development of this theory. The issues that troubled the young scientist were the origin of multicellular organisms from unicellular and origin of chordates from invertebrates. The study of invertebrate larvae could give answers to these questions. Therefore, Metchnikoff dreamed to graduate from University as soon as possible and moved from the theoretical science to practical research.

Metchnikoff completed a four-year course at the University of Kharkov in two years, at the age of 19, and then continued to study in Germany and Italy, working on a master's thesis. By this time, Metchnikoff became convinced evolutionist-Darwinist considering invertebrates as the ancestors of more advanced forms of life. The objects of his research were planarian - flatworms, and cephalopods. Metchnikoff explored the features of the development of these animals, trying to answer the questions about the origin of multicellular organisms and the mechanisms of tissue differentiation. Thus, Metchnikoff developed a new field of natural science – comparative embryology. Ilya Ilyich expounded his findings on the Folia embryonalia cephalopods in his master's thesis [16], which he successfully completed at the age of 22 in the Odessa University; he immediately became a lecturer of this university. The young teacher often had to lecture to students who were much older than he. Of course, it was very difficult, but the opportunity to be realized, doing what he liked, inspired him very much.

In 1867 Metchnikoff and his friend Alexander Kovalevsky (1840-1901) went to St. Petersburg to



Student Ilya Metchnikoff, 1862 [7]

present their research at Russian Congress of Naturalists, after which Metchnikoff was invited to work in the St. Petersburg University. In 1868, Metchnikoff defended his doctoral thesis [17] at the University of St. Petersburg, and in the same year began to work as an assistant professor at the University.



Yang scientist Ilya Metchnikoff [18]

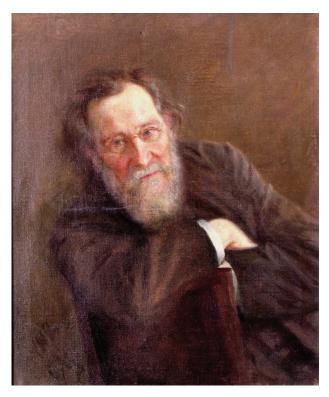
In St. Petersburg Ilya Ilyich met his future wife - Lyudmila Vasilyevna Fedorovich. "I wandered around and felt an incredible need to be loved, the need for various forms of affection ... but most of all thought of Liu (Lyudmila - niece of Professor Andrey Nikolayevich Beketov)" [19], whom he married in 1869. The bride was too weak because of tuberculosis, thus she was brought on a stretcher to church where the wedding took place. Metchnikoff hoped to heal his beloved wife, using all his strength as a scientist and as a loving husband. He moved from cold Petersburg to Odessa, then left teaching in Odessa and took his wife to Madeira, but Metchnikoff could not save her, Lyudmila died four years after the wedding. In desperation Metchnikoff took a huge dose of morphine, but miraculously survived [20]. It was early spring in cold Switzerland. After the first suicide attempt Metchnikoff poured over himself cold water and went out into the street in the hope of getting a deadly chill, but suddenly his attention was absorbed by insects, beating on the night lights. It was the thought of these insects, their evolution and the country way of life that returned the scientist to reality, reminding him about his work and calling. So, after a failed suicide attempt, Ilya Ilyich again immersed in the work, returning to the Odessa University.

In 1875 Metchnikoff decided to remarry, this time to his student Olga Nikolaevna Belokopytova, who was 13 years younger than him. The scientist all his life called her "my dear child, my dear girl", but in old age there was also a touching appeal to her in Ukrainian "my mom".

For Metchnikoff young Olga became not only a caring friend and helper, but also inspiration, muse, light and life itself. Even if the fate separated them for a while, there was no a single day when they did not write letters to each other. The daughter of the Marshal of the Odessa nobility, Olga was one of the most gifted Metchnikoff's students and a beautiful girl. Her admiration for her husband and teacher made Metchnikoff a real hero, able to turn the scientific world. Olga did not only help Metchnikoff in science, but also successfully ran a business in his estate Popovka. She built a school for peasant children for the money earned by her husband (by the way, the school is working to the present day), painted pictures, organized exhibitions, treated the peasants, and after the death of the scientist kept all his records and published the memories of her husband [3]. Needless to say, that it is Olga gave her husband all the things required to make Metchnikoff



Olga Belokopytova, 1873 [7]



Portrait of Ilya Metchnikoff by Olga Mechnikova, 1912 [7]

great optimist and life-loving man from a convinced pessimist.

While working on a master's thesis in Naples, Metchnikoff met Dr. Sechenov, who was on vacation there. A few years later Sechenov recommended Metchnikoff for the position of Professor of the St. Petersburg Medical Academy. However, Scientific Council, consisting mainly of doctors, who had contempt for biological science, rejected candidature of Ilya Metchnikoff. Professor Sechenov left the academy in protest, remaining practically destitute. Therefore, returning to Odessa, Metchnikoff immediately invited Sechenov to Odessa University as a professor at the Faculty of Natural Science. Sechenov gladly accepted the Metchnikoff's offer and two eminent friends were working together in Odessa for the long five years. Needless to say, what time it was, both for the Odessa University, and the entire city! Two Stars of universal scale shone in the walls of the Odessa Alma Mater, the power of their talents awakened fervent love for biology in young minds.

Ilya Ilyich repeatedly recalled with pleasure this period of their lives in Odessa. "Sechenov distinguished for exceptionally kind and soft heart" [19]. Apparently, all that can be said about Metchnikoff. Two professors became great friends, and Sechenov affectionately called Metchnikoff "mom" for the care that Metchnikoff showed to his Russian colleague.

Who else than Sechenov and Metchnikoff, embodied a secular elite of Odessa, were so in demand in all the events of life in the city. Even in a city court, the two professors became elder jury. However, as Metchnikoff recalled: "We have mostly ... pronounce sentences, which increasingly have been exculpatory". This state of affairs is really no surprise. For example, "one assistant prosecutor ... a long time to dwell on the fact that among the jury are those who on the basis of the doctrine of the brain reflexes believe every transgression untouchable". However, the professor simply felt that "it was impossible to take on his conscience convict the accused without sufficient reason" [19].

For students and professors, "as far as possible treated leniently in the exams and the discussion of their misdemeanors, considering the severity of harmful and unnecessary" [19].

However, life at the university was not always sweet for Metchnikoff. More than anything, the scientist appreciated the opportunity to quietly do



Metchnikoff and Sechenov with other professors at the Odessa University, 1873 [7]

things he loved – science. University gossip, political games and other irrelevant fuss, irritated the great scientist. Being away from any policy, he worried very much about the students who participated in the student unrest, and thus risked expulsion from the University. He was particularly annoyed by provocateurs professor pushing students to rash actions.

After March 1, 1881 the position of the university was particularly aggravated. Terrorists of the "Narodnaya Volya" killed Alexander II, one of the most progressive tsars of his era, educator and liberator, who abolished serfdom in Russia, carried out judicial and educational reforms. Universities wave of reaction began. Metchnikoff was always out of politics; however, the reaction pressure touched him as well. Unable to put up with the status quo Metchnikoff left the University.

After retirement, Ilya Ilyich went to Messina, where he worked for some time in his youth. At this time, stay in Messina was a turning point in his academic life. Metchnikoff recalled this period: "My main stay in Messina related to 1882 and 1883. There I went to "rest" after the retired out of the University of Odessa". It is here, in Messina, Metchnikoff made the most important discovery of his life. But give the floor to the scientist in the description of these events: "One day, when the whole family went to the circus to watch some amazing trained monkeys, and I was alone on my microscope, observing the life of motile cells in transparent larvae of sea stars, I was immediately struck by the new think. It occurred to me that such cells must be in the body against deleterious figures. Feeling that there lies something particularly interesting, I was so excited that began to walk around the room and even went to the beach to collect my thoughts. I told myself that if my assumption is correct, then a thorn inserted in the larvae of the starfish body, which has no vascular or nervous system, must be in a short time surrounded by adhesive on her mobile cell, just as is the case in humans, splinter his finger. No sooner said than done. In the tiny garden at our house, where a few days before on a tangerine tree was set up for children Christmas "tree", I picked some pink spikes and immediately put them under the skin of gorgeous, clear as water, starfish larvae. Of course, I was worried all night waiting for the result and the next day, early in the morning, happily stated luck experience. The latter formed the basis of the "theory of phagocytes", development of which the next 25 years of my life have been devoted to" [21].

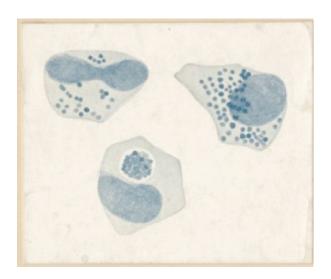
Thus Metchnikoff discovered phagocytosis. Of course, phagocytosis could be observed before him. As it was interestingly noted by British Professor Siamon Gordon [22] twenty years before Metchnikoff, this process was described in ... Ivan Turgenev's novel "Fathers and Sons". Here is an interesting excerpt from the novel: "But he (Pavel Petrovich) sometimes asked permission to be present at the tests of Bazarov, and once even brought his perfumed and washed excellent drug face of the microscope in order to see how a transparent infusoria swallowed a green speck and busily chewed it some very nimble jaws, is with her in the throat" [23]. However, phagocytosis was seen by contemporary scientists as a way to supply the cells, but not as a way to protect the body. Metchnikoff's merit consists in the fact that he saw in this process a powerful factor in the immunity of multicellular animals [24, 25]. His further work was devoted to the proof of the role of phagocytosis in protecting the body from infections.

Next, Metchnikoff conducted experiments with Daphnia – tiny planktonic crustaceans. The scientist entered into the daphnia body fungal spores and observed that some cells came to the spore and enveloped it, as they were devouring and destroying it, while daphnia continued to live as it nothing had happened. Metchnikoff introduced a lot of spores in Daphnia body and saw that cells could not cope with the abundance of foreign particles, and daphnia died [26].

Metchnikoff called these cells, protecting the body from foreign particles and tiny organisms, phagocytes, i.e., in a free translation, cell-eaters. They protect any living organism, including humans, from both living uninvited guests – bacteria, viruses, spores, fungi, and non-living – caught, for example, in wound mineral cuttings. Enveloping them on all sides, the phagocytes neutralize unwanted for organism alien creatures and blotches. Metchnikoff described two types of phagocytes in humans and other higher animals – macrophages (as they are called up to this day), and microphages (now – neutrophils) [27, 28].

Discovery of phagocytosis allowed understanding the body's defense system and developing the theory of cellular immunity – the immunity to infectious diseases. However, the theory met with great resistance among the luminaries of contemporary biological science.

What prevented contemporaries from perceiving this seemingly very elegant and logical theory



Phagocytes from Metchnikoff's drown [7]

of phagocytosis? Besides the usual envy it can be identified and some objective reasons. Firstly, phagocytosis had long been known in scientific circles as a way of eating rather than a way to protect organisms. Thus, performed by Metchnikoff in Messina experiment with a rose thorn, surrounded by phagocytes starfish, tended to be interpreted by most researchers as a reaction of the starfish hit with the "big piece of food" in the form of the rose thorn. Secondly, there are certain pathogens, which can parasitize in macrophages, thus remain alive within these cells. For example, the Koch bacillus – causative agent of tuberculosis, a part of their life cycle holds within macrophages, and the macrophages do not harm them, and it was also well known. Thus, the bactericidal function of macrophages had been questioned by nature itself. And most importantly, at a time it had got stronger humoral immunity theory, developed in the first place, by the German School of Immunology. According to this theory the protective factors are in blood serum, called antibodies, which can protect the body against infection, and protection of the organism directly depends on the number of antibodies in the serum. Using serum, immunity could be transferred from the immune animal to non-immune and even from animals to humans. Such experiments were practiced not only in Germany but also in the Pasteur Institute, where Metchnikoff started to work in 1887. For example, Deputy Director of the Institute Emile Roux, singled diphtheria toxin, proposed the use of a horse antitoxic serum as a therapy against diphtheria [29]. By the way, bringing this practice to perfection, Emil

von Behring in 1901 received the world's first Nobel Prize in Physiology or Medicine.

Metchnikoff continued to make the amazing experiments, confirming the validity of his theory, and was supported by the famous Louis Pasteur, who organized in his Institute a whole scientific department for Metchnikoff. Thus, in 1887, at the age of 42, Metchnikoff left his homeland forever. He settled in Paris, where he would live the rest of his life. First, Metchnikoff headed the Department of Comparative Morphology of Microorganisms in the Pasteur's Institute, and in 1905, several years after Pasteur's death, when Emile Roux was elected as a third director of the Institute; Metchnikoff became the deputy director of this Institute.

As mentioned by many authors, Metchnikoff would have done much more if he had not been so intolerant for the humoral theory of immunity. However, as we know, history does not know the subjunctive mood. Besides, it was a time of the birth



Emile Roux defeats Diphtheria (contemporary painting) (portrait signed by Meyer, 1895, reproduction from Pasteur museum [30])



Friends and colleagues: Ilya Metchnikoff and Emile Roux, 1905 [7]

of a new science, in which there was no place for scientific compromises. As a result, both scientists Metchnikoff and Erlich were right and the awarding of the Nobel Prize finally put an end to their contradictions. Ilya Ilyich began his Nobel speech with the words: "I have had the great honour of receiving, together with my excellent friend, Professor Ehrlich, the Nobel Prize for Medicine..." [31].

The wording of the merits for which Ilya Metchnikoff and Paul Ehrlich received the Nobel Prize, sounded very simple: "For the assessment of their work in the field of immunity" [32].

Metchnikoff is one of the founders not only of Immunology, but also Microbiology of Infectious Diseases. Back in 1886, after returning to Ukraine, Metchnikoff with Dr. Gamaleya opened in Odessa the first Russian private bacteriological laboratory, the purpose of which – the fight against infectious diseases [33]. Many of his works were devoted to the study of such dangerous diseases as cholera, tuberculosis, syphilis, typhoid fever. It is interesting that Metchnikoff was also nominated for the Nobel Prize for his work on the study of syphilis.

Ilya Ilyich was also interested in the aging process. The scientist believed that old age and death come from self-poisoning – every living organism accumulates microbial poisons. Especially in this respect, microbes living in large numbers in the

colon were considered to be harmful. To combat these germs Metchnikoff offered a lactic acid bacteria *Lactobacillus delbrueckii* (*bulgaricus*) – the microorganism contained in sour milk. The scientist began to promote the sour milk products and he himself included them in his diet on a daily basis for many years until the end of his life. Incidentally, the product prepared using receipt of Metchnikoff, still exists, and is called "Prostokavasha Metchnikoffskaya" (State Standard 31661-2012).

Through his work on the development and changes in the body, Metchnikoff is considered as the founder of gerontology – the science of aging. Metchnikoff himself called his doctrine of "rational Macrobiotics". In accordance with his teachings, retirement can come much later than it usually comes, and with a happy old age overcomes the fear of death. The correct the cycle of human development, the natural ending with a happy departure from life after completed all life missions, was named by Metchnikoff "orthobiosis". This teaching was the reason for the optimism of the scientist, set out in his work "Optimistic Studies" [34].

"Today, I finally turned 70 years old. I reached the limit of a normal life, determined yet by King David ..." [19], said the scientist at the end of life. It seems, it is about 89 Psalm of David according Synodal translation (or 90 Psalm according King James Version), which has a line: "The days of our years are threescore years and ten; and if by reason of strength they be fourscore years, yet is their strength labour and sorrow; for it is soon cut off, and we fly away" [35].

2(15) July 1916 scientist's heart stopped beating. He passed away at the age of 71, having lived a bright, good and productive life, left a huge scientific heritage, adopted and confirmed by the age-old history of science.

The widow of the scientist said: "Wrapped in a white shroud, framing his handsome face, he all white, he looked like a biblical prophet ... Now, it is all expressed complete peace of mind, radiant kindness and gentleness lit it" [3].

Metchnikoff also bequeathed his body to science for medical research — with the proviso that then the remains would be burned and buried in the territory of the Pasteur Institute, where Ilya Ilyich worked for almost 30 years, and where he performed many of his discoveries. All the conditions of the will were executed precisely. On July 18 his body was cremated at the cemetery Père Lachaise in Paris. The marble urn containing the ashes of the great



Ilya I. Metchnikoff in seventieth birthday

scientist was installed in the library of the Pasteur Institute, where he rests today.

A week after the death of the Nobel Prize winner, the magazine "Sparks of the Sunday" ("Iskry Voskresenia") wrote (abridged): "Ilya Metchnikoff, the great scientist, whose name is known all over the world, has died. The homeland is proud of its great son. This is the greatest scientist, physician, teacher and author of many scientific papers, the creator of the theory, which made a revolution in many fields of medicine and bacteriology. Metchnikoff set the task of his life to fight against the death, or at least, for its remoteness. With brilliant insight, he foresaw the emergence of a new man with a perfect physical body. Mourning the loss of a man painfully resounds in every heart..." [36].

Metchnikoff's scientific heritage is extensive [7, 37]. He was the first who gave experimental rationale for the phenomenon of phagocytosis and its role as a protective reaction of the organism; described two types of phagocytes (macrophages and neutrophils) and established the role of macrophages in the body's healing of injuries and the elimination of dead cells; so he laid the scientific foundations of the cellular theory of immunity [38, 39]. He has made a great contribution to the development of the science of infectious pathology showing the difference between the infectious process, asymptomatic carriage of infection and resistance to infection. In

the field of comparative embryology he proposed a model of evolutionary transition from unicellular to multicellular organisms [40]. The foundations of theoretical gerontology were laid by Metchnikoff. He proposed a theory of aging, which sees this phenomenon as the result of self-poisoning of an organism by waste products and microbial toxins [41]. Lactic acid products containing the bacteria *Lactobacillus bulgaricus* were recommended by him as healthy food supplements, that was the first introduction of the concept of probiotics [42]. He also expressed the idea of biological plant protection [43].

Thus, Ilya Ilyich Metchnikoff planted seedlings of scientific optimism and faith in the inevitable victory of science over threats. The entire history of modern biology and medicine reinforces this belief and cultivates seedlings into powerful trees growing on the basis of theoretical and practical knowledge.

## НОБЕЛІВСЬКИЙ ЛАУРЕАТ ІЛЛЯ ІЛЛІЧ МЕЧНИКОВ (1845–1916). ІСТОРІЯ ЖИТТЯ ТА НАУКОВА СПАДЩИНА

Ю. В. Сзепчук<sup>1,2</sup>, Д. В. Колибо<sup>3</sup>

<sup>1</sup>Національний єврейський медичний та дослідний центр, Денвер, штат Колорадо, США;
 <sup>2</sup>Науково-дослідний інститут епідеміології та мікробіології ім. Н. Ф. Гамалії, Москва, Росія;
 <sup>3</sup>Інститут біохімії ім. О. В. Палладіна, НАН України, Київ

Століття науки після смерті І. І. Мечникова продемонструвало істинність багатьох його поглядів і суджень із галузей імунології, патології, бактеріології, зоології та порівняльної ембріології. Сьогодні його справедливо називають батьком теорії клітинного імунітету, а також передвісником теорії природного імунітету. Його роботи, присвячені молочнокислим бактеріям, стали основою цілої індустрії пробіотиків. Вчення І. І. Мечникова про можливість продовження життя людини актуально і в наші часи. Ця публікація є ще однією спробою зв'язати біографію вченого з його творчою спадщиною і його внесок у скарбницю світової біологічної науки.

Ключові слова: біографія Іллі Мечникова, імунолог, бактеріолог, ембріолог, зоолог, патолог.

### НОБЕЛЕВСКИЙ ЛАУРЕАТ ИЛЬЯ ИЛЬИЧ МЕЧНИКОВ (184–1916). ИСТОРИЯ ЖИЗНИ И НАУЧНОЕ НАСЛЕДИЕ

Ю. В. Езепчук<sup>1,2</sup>, Д. В. Колибо<sup>3</sup>

<sup>1</sup>Национальный еврейский медицинский и исследовательский центр, Денвер, штат Колорадо, США; 
<sup>2</sup>Научно-исследовательский институт эпидемиологии и микробиологии им. Н. Ф. Гамалеи, Москва, Россия; 
<sup>3</sup>Институт биохимии им. А. В. Палладина, НАН Украины, Киев

Столетие науки после смерти И. И. Мечникова продемонстрировало истинность многих его взглядов и суждений в области иммунологии, патологии, бактериологии, зоологии и сравнительной эмбриологии. Сегодня его справедливо называют отцом теории клеточного иммунитета, а также предвестником теории естественного иммунитета. Его работы, посвященные молочнокислым бактериям, легли в основу целой индустрии пробиотиков. Учение И. И. Мечникова о возможности продления человеческой жизни по-прежнему актуально. Данная публикация является еще одной попыткой связать биографию ученого с его творческим наследием и его вклад в сокровищницу мировой биологической науки.

Ключевые слова: биография Ильи Мечникова, иммунолог, бактериолог, эмбриолог, зоолог, патолог.

#### References

- 1. Élie Metchnikoff. [Electronic resource]. Regime of access: https://en.wikipedia.org/wiki/Élie\_Metchnikoff.
- 2. Ilya Mechnikov Biographical. Regime of access: http://www.nobelprize.org/nobel\_prizes/medicine/laureates/1908/mechnikov-bio.html.
- 3. Metchnikoff O. Vie d'Elie Metchnikoff. Paris: Hachette, 1920.272 p.
- Rosenthal H, Lipman JG. Nevakhovich Löb. Regime of access: http://www. jewishencyclopedia.com/articles/11486nevakhovich-lob.
- 5. Berdnikov L. The Russian life of Leib Nevakhovich. Slovo\Word. 2009, 64. Regime of access: http://magazines.russ.ru/slovo/2009/64/be32.html.

- 6. Beizer M, Gilbert M. The Jews of St. Petersburg: excursions through a noble past. Philadelphia: The Jewish Publication Society, 1989. 277 p.
- 7. Ulyankina TI. Russian Nobel Laureats: Ilya I. Metchnikoff. Archive of the Russian Academy of Sciences. Regime of access: http://www.arran.ru/?q=ru/node/578.
- 8. Tolstoy L. The Death of Ivan Ilyich (1886). The Story and Its Writer. Ed. A. Charters. NY.: Bedford / St. Martin's, 2011. P. 794-833.
- 9. Nabokov VV. Lectures On Russian Literature. NY.: Harcourt Brace Jovanovich / Bruccoli Clark, 1981. 324 p.
- 10. Metchnikoff E. Études sur La Nature Humaine. Paris: Masson & Cie, 1903. 433 p.
- 11. Kartasheva KS. The roads of Leo Metchnikoff. Outstanding travelers and geographers. M.:Mysl', 1981. 56 p. (In Russian).
- 12. White JD. Despotism and Anarchy: The Sociological Thought of L. I. Mechnikov. *Slavonic East Eur Rev.* 1976; 54(3): 395-411.
- 13. Metchnikoff II. Some facts from the life of infusorium. *Vestnik Estestv. Nauk.* 1865; VII(47-52): 1564-1569. (In Russian).
- 14. Darwin Ch. The origin of species by means of natural selection, or the preservation of favored races in the struggle for life. Translated by Rachinsky SA. St.Pt., Glasunov AI. 1864; XIV: 399 p. (In Russian).
- 15. Metchnikoff II. Essay on questions about the origin of species (1876). Krasand, 2010. 256 p. (In Russian).
- 16. Metchnikoff II. The history of embryonic development of Sepiola. Thesis of Master degree in zoology. St.Pt.: Kukol-Yasnopolsii. 1867: 72 p.
- 17. Metchnikoff II. History of Nebalida development: A comparative embryological essay. *Notes Academy of Sciences*. 1868; 13(1, app. 1): 1-48.
- 18. Photo from site of Zoology museum of Saint Petersburg State University. Regime of access: http://zoology.museums.spbu.ru/.
- 19. Metchnikoff II. The pages of memory. A collection of autobiographical essays. Ed. by Koshtoyants KhC. M.: publ. AN USSR. 1946. 279 p. (In Russian).
- 20. Petryuk PT, Kuchma IYu, Reznik VI. Ilya Ilyich Mechnikov: biographical, scientific and psychiatric aspects (on the 165<sup>th</sup> anniversary). *Annals Mechnikov Institute*. 2010; (2): 53-62.
- 21. Metchnikoff E. My stay in Messina (Memories of the past). *Russkie Vedomosti*, 1908, N 302.

- 22. Gordon S. Elie Metchnikoff, the Man and the Myth. *J Innate Immun*. 2016; 8(3): 223-227.
- 23. Turgenev I. Fathers and Sons. 1862.
- 24. Herrlinger R. Historical development of the concept of phagocytosis. *Ergeb Anat Entwicklungsgesch*. 1956; 35: 334-357.
- 25. Gordon S. Phagocytosis: The Legacy of Metchnikoff. *Cell.* 2016; 166(5): 1065-1068.
- Metchnikoff II. Infection of Daphnia by bicuspidatus monospores and their phagocytosis. 1884.
- 27. Ulyankina TI. The origin of Immunology. M.: Nauka, 1994. 319 p.
- Zilber LA. I. I. Mechnikoff and the doctrine of immunity. *Scientific Legacy*. M.-L.: publ. AN SSSR. 1948; 1: 482-519.
- 29. Opinel A. The Pasteur Hospital as an element of Emile Roux's anti-diphtheria apparatus (1890-1914). *Dynamis*. 2007; 27: 83-106.
- 30. Portrait signed by Meyer, 1895, reproduction from Pasteur museum. Regime of access: http://phototheque.pasteur.fr.
- 31. Mechnikoff E. On the Present State of the Question of Immunity in Infectious Diseases. *Nobel Lecture*. December 11, 1908
- 32. The Nobel Prize in Physiology or Medicine 1908. Regime of access: http://www.nobelprize.org/nobel\_prizes/medicine/laureates/1908/.
- Zabolotny DK. The founders of the Odessa bacteriological station. Coll. of the Odessa sanitary-bacteriological institute. 25<sup>th</sup> anniversary of the Odessa bacteriological station. Odessa, 1927.
- 34. Metchnikoff E. The Prolongation of Life. Optimistic Studies / By edit. P.C. Mitchell. NY.: G P Putnam's Sons, 1910. 96 p.
- 35. Psalm 90:10 KJV.

- 36. Illust J Sparks Sunday, on July 10, 1916, N 27.
- 37. Underhill DM, Gordon S, Imhof BA, Núñez G, Bousso P. Élie Metchnikoff (1845–1916): celebrating 100 years of cellular immunology and beyond. *Nat Rev Immunol*. 2016; 16(10): 651-656.
- 38. Kaufmann SHE. Immunology's foundation: the 100-year anniversary of the Nobel Prize to Paul Ehrlich and Elie Metchnikoff. *Nat Immunol*. 2008; 9(7): 705-712.
- 39. Gordon S. Elie Metchnikoff: Father of natural immunity. *Eur J Immunol*. 2008; 38(12): 3257-3264.
- 40. Novikov PA. Mechnikov as a zoologist. The scientific heritage. / Ed. Acad. SI Vavilov, Acad. AM Deborin, Acad. VA Komarov. M.-L.: AN USSR, 1948; (1):427-519.
- 41. Podolsky SH. Metchnikoff and the microbiome. *Lancet*. 2012; 380(9856): 1810-1811.
- 42. Gasbarrini G, Bonvicini F, Gramenzi A. Probiotics History. *J Clin Gastroenterol*. 2016; 50(Suppl 2), Proceedings from the 8th Probiotics, Prebiotics & New Foods for Microbiota and Human Health meeting held in Rome, Italy on September 13-15, 2015: S116-S119.
- 43. Lord JC. From Metchnikoff to Monsanto and beyond: the path of microbial control. J Invertebr Pathol. 2005; 89(1): 19-29.

Received 14.11.2016