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GASTON RAMON (TO CENTENARY OF THE DISCOVERY OF ANATOXINS)

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In the history of science, there are great scientists who, without being physicians, wrote golden pages in the History of Medicine. Such was Louis Pasteur, founder of scientific microbiology and immunology. Such was his follower Gaston Ramon (1886–1963), French veterinarian and immunologist who created 100 years ago first anatoxin for active prevention of diphtheria and later tetanus and thus opened era of anatoxins (toxoids) — vaccines based on toxin molecule devoid of toxic properties, but preserving immunogenicity and antigenic specificity. For many centuries, diphtheria (originally known as 'croup') was incurable contagious disease, especially among children. In XIX century, it affected in France up to 30,000 people per year and killed every second infected child. In 1888, at the Pasteur Institute (Paris), Emile Roux (1853–1933) and Alexandre Yersin (1863–1943) demonstrated for first time that symptoms of diphtheria are caused not by bacteria themselves, but by deadly toxin released by them. The long-term search for method of treatment and prevention of diphtheria did not bring the desired result. It will take many years, before Gaston Ramon in 1923 will be able to neutralize diphtheria toxin by acting on it with formalin at certain temperature and thus will receive "anatoxin", mean of vaccination against diphtheria. The article analyzes stages of these studies, which proved high effectiveness of anatoxin and proceeded with widespread implementation of vaccination against diphtheria and later tetanus in short time in France and in Russia (with active participation of Pavel F. Zdrodovsky, 1890–1976). The separate section of the article is devoted to life story of Gaston Ramon and his activities in the Pasteur Institute. The scientist who opened the era of anatoxins did not become Nobel Prize winner, despite the fact that various organizations and scientists from many countries of the world have nominated him 155 times for the Nobel Prize in Physiology or Medicine in different years. He received recognition in France, his Motherland: Gaston Ramon is holder of the Grand Cross of the Order of the Legion of Honor and streets, colleges, lyceums, schools are named after him.

K e y w o r d s : history of microbiology and vaccinology; Gaston Ramon; anatoxin (toxoid); diphtheria;, tetanus.

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Introduction

On November 14, 1888, in Paris (France), with funds raised by international subscription, the Institute of Microbiology was opened for struggle against rabies and other infectious diseases. Famous scientists (many of whom were from Russia), as well as ordinary people and heads of the Governments participated in this international subscription to raise funds for its creation (construction of the building and financing of its activities). The first director of the Institute was an outstanding French scientist, chemist, microbiologist, founder of scientific microbiology and immunology Louis Pasteur (1822–1895).

Sometime later, during Pasteur's lifetime, at the suggestion of the Academy of Sciences of France, the Institute was renamed in his honor and received the name known worldwide today — the Pasteur Institute (Fr. l'Institut Pasteur). Very soon it became the largest center of scientific thought in the field of microbiology at that time. Ten scientists of the Pasteur Institute have been awarded Nobel Prizes in Physiology or Medicine [1]. Among them is our outstanding Russian biologist, pathologist, immunologist and bacteriologist Ilya Ilyich Mechnikov (1845–1916), the creator of the phagocytic theory of immunity, one of the founders of evolutionary embryology [1, p.7; 2, p. 6–75].

Followers of Louis Pasteur's scientific ideas on combating infectious diseases are called 'Pasteurians' [3, p. 7]. Pasteur's fruitful ideas were took up by his outstanding disciples, among them Pierre Paul Émile Roux (1853–1933), who, in turn, became the teacher of the outstanding French scientist Gaston Ramon (Gaston Léon Ramon, 1886–1963).

It is well known, neither Pasteur nor Ramon were doctors. The first was a chemist, the second — a veterinarian. And yet, it is to them that medicine owes a number of outstanding discoveries. Both of them worked in cramped, poorly furnished rooms called laboratories. Both showed ingenuity in using simple tools, sometimes

[1] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire

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made with their own hands. Like Louis Pasteur, Gaston Ramon did not derive material benefits from his discoveries and donated them to the Pasteur Institute. And it was Gaston Ramon who was able to realize the idea of Pasteur, who dreamed of producing harmless and immunogenic chemical vaccines [4, p. 350–351].

Here is how the prominent Soviet immunologist and microbiologist Pavel Feliksovich Zdrodovsky (1890–1976), academician of the Academy of Medical Sciences of the USSR, who headed the Department of Experimental Pathology and Immunology of the N. F. Gamalei Institute of Epidemiology and Microbiology, writes about the beginning of Ramon's scientific activity: 'Having started his activity in a poor 'quasi-laboratory' (in Ramon's words) as a modest immunizer veterinarian at the suburban Branch of the Pasteur Institute in Garche, Ramon went through a long and difficult way as a humanist researcher, inspired by the ideas and faith of a true Pasteurian. Now he is a researcher with a worldwide reputation and authority, whose vaccine preparations and methods are widely used in all countries for the prevention of infectious diseases and the production of specific serums" [3, p. 8].

In the mid-1920s, the name of Gaston Ramon became known in the Soviet Union thanks to systematic studies of anatoxins and microbial vaccines conducted by the Russian scientists P. F. Zdrodovsky and K. T. Khalyapin [3, p. 49].

Discovery of anatoxins

For many centuries, diphtheria (known as 'croup') has been an incurable contagious disease, especially among children. In the 19th century in France, this serious bacterial sore throat affected up to 30,000 people a year and killed every second infected child [2].

The impetus for an intensive search for a solution to the problem was the death of Napoleon's nephew from croup in 1807. After that, the Emperor of France did his best to encourage doctors who studied this dangerous disease. To activate the research aimed at "discovering a method of treatment and prevention of croup", a prize of 12,000 francs was set up, but the results of these works did not bring the desired result [3, p. 72].

In 1826, Pierre-Fidèle Bretonneau (1778–1862), who devoted himself to the study of croup, compiled a classic description of this disease and for the first time gave it the name *diphtheria* (from the Greek *diphthera* — pellicle, skin), and his disciple Armand Trousseau (1801–1867) renamed diphtheria into the commonly accepted today name *diphtheria* [5, p. 404]. After numerous observations, Pierre Bretonneau (half a century before Pasteur's discoveries), with the foresight of a genius, established that diphtheria is a specific contagious disease caused by a special "virus" [3, p. 72].

As it turned out later, this "virus" subsequently proved to be a toxin. What is hidden behind this term?

The term "*toxin*" was first proposed in 1888 by Ludwig Brieger (1849–1919), Professor of Medicine at Humboldt University (Berlin), using it to describe various poisons secreted by bacteria [3].

In the same 1888, at the Pasteur Institute, Émile Roux (1853–1933) and Alexandre Yersin (1863–1943) showed for the first time that the symptoms of diphtheria are caused not by the bacteria themselves, but by a deadly *toxin* released by them.

In 1894, Roux proposed using serotherapy (serums containing antibodies against diphtheria toxin prepared by horse immunization [6, p. 220]) to create passive immunity in treatment of diphtheria. After conducting large-scale trials, this method has halved mortality and saved the lives of thousands of children with diphtheria [4].

The term "*anti-diphtheria serum*" was introduced by the German physician Emil von Behring (1854–1917), a follower of Robert Koch (1843–1910), who published a number of articles on the successful application of serotherapy in medical practice. On December 24, 1891, in one of the clinics in Berlin, he first used a serum to save a child with diphtheria. For his discoveries, Emil von Behring was awarded the first ever Nobel Prize in Physiology or Medicine in 1901 "for his work on serotherapy, and above all for its use in the struggle against diphtheria, with which he opened a new direction in the field of medical knowledge and thereby gave the physicians a victorious weapon against disease and death" [2, p. 29].

It will take many years before Gaston Ramon, a French veterinarian and immunologist, will be succeeded in finding how to weaken the diphtheria toxin by "adding dilute formalin (0.4%–0.5%) to the toxin filtrate and subsequently heating it for several weeks at low temperature (38–40°)", and thus in 1923 obtained *anatoxin* possible to develop immunity to diphtheria [7; 8]. "This modified toxin, — Ramon noted, — turned into a new substance and characterized by harmlessness, immunogenicity and the ability to flocculate, was designated with the consent of É. Roux as an *anatoxin*". At the same time, he explains that the term *anatoxin* goes from the Greek roots: *ana-* (backward) — something the opposite; and *toxikon* (poison); hence the term *anatoxin* means something that has ceased to be toxic, i.e. no longer a toxin — *anatoxic*, in contrast to the word '*atoxic'*, i.e. simply non-toxic *a priori* [3, p. 43; 9, p. 724].

After successful experiments on animals, Ramon proved the high effectiveness of *anatoxin*, and then he conducted an experiment on himself, which resulted in only temporary redness of the skin without a general reaction [10, p. 56].

Gaston Ramon tirelessly fought for the introduction of vaccination against diphtheria and tetanus in his country, despite the fact that in France the effectiveness of his discovery has long been disputed [10, p. 53].

An important milestone in the recognition of *anatoxin* as a vaccine against diphtheria was the day of December 10, 1923, when Director of the Pasteur Institute,

[2] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire/gaston-ramon-pro-humanitate

[3] https://www.pasteur.fr/fr/journal-recherche/actualites/poisons-bacteriens-aux-toxines-premiers-travaux-pasteuriens

[4] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire/gaston-ramon-pro-humanitate

Émile Roux, spoke at the Academy of Sciences of France (l'Académie des sciences de France) with the message '*Sur le pouvoir floculant et sur les propriétés immunisantes d'une toxine diphthérique rendu anatoxique (anatoxine)*' (approximate translation: '*On the ability of flocculation and immunizing properties of anatoxic toxin (anatoxin)*') [11, p. 19; 12, p. 268]. In his speech, Roux noted that "everything said about diphtheria toxin can be transferred to other toxins, in particular to tetanus toxin, which can also be converted into tetanus toxoid" [3, p. 43]. (The term '*toxoid*' instead of '*anatoxin*' was introduced by Paul Ehrlich).

The first experiments on immunization of children and adults with diphtheria anatoxin in Paris began in late 1923 — early 1924 [3, p. 76]. A little later, immunization against diphtheria with Ramon's anatoxin began to be carried out in other countries of different continents; and already in 1925, the effectiveness of this method was enthusiastically written about: "Diphtheria anatoxin is an ideal preparation for active immunization against diphtheria" [3, p. 81].

In 1930, anatoxin vaccination was introduced in the French army, and in 1936, combined vaccination against diphtheria, tetanus and typhus became obligatory in the army [3, p. 91–92]. In the same year, a law on obligatory tetanus vaccination in the French army had been adopted [10, p. 56], and in 1938, mandatory vaccination of children aged 1 to 14 years began in France.

In the USSR, according to P. F. Zdrodovsky and K. T. Khalyapina, in 1928 in Baku more than 4,000 children were vaccinated with diphtheria toxoid; subsequently, there was not a single diphtheria disease among them [3, p. 85, 123].

It is important to note that in 1931, at the suggestion of P. F. Zdrodovsky, mandatory vaccinations of preschool children against diphtheria with Ramon's anatoxin were introduced in Leningrad. Soon, in 1935, the widespread introduction of vaccinations of children against diphtheria began throughout the country, and in 1940 in the RSFSR vaccinations of all preschool children against diphtheria became mandatory [3, p. 92].

It is noteworthy that after Edward Jenner's epochal discovery of the smallpox vaccine at the end of the 18th century, the diphtheria vaccine remained the second used in the world on a massive scale.

Nowadays it's even hard to imagine that before the works and discoveries of Pasteur, Roux, Mechnikov, Ehrlich, Bereing, Ramon, the average lifetime in Europe was a little more than 30 years, and mortality from infectious diseases often exceeded losses on the battlefields [2, p. 32].

Gaston Ramon's life and work

Gaston Léon Ramon was born on September 30, 1886 in Belshome (Fr. Bellechaume), Yonne, France, in the family of a baker — 26-year-old Léon Ramon André and 19-year-old Ramon Clémence Léontine [13, p. 438]. It's interesting that, the Ramon family's pedigree also has Spanish roots that go back several centuries. The small village of Belshome (numbering about 500 inhabitants at that time) was located in the north-east of France, 156 km from Paris, and was (and is now) part of the Yonne Department of the Burgundy-Franche-Comté region. Even today, according to the 2019 census, this village has about the same number of inhabitants [12, p. 253].

Leon Ramon's family had many children. The eldest was Gaston. Very soon his abilities were noticed, and his parents decided to give young Gaston an education [14, p. 809].

At the age of four, he was sent to the municipal school of Sens, the nearest major city in the Department of Yonne (about 30 km from Belshome). Since childhood, Gaston was not distinguished by good health, he was prone to asthma, from which he suffered all his life, but he studied successfully, and one of the teachers achieved for the young talent the award of a scholarship to continue his studies at the Lycée de Sens. His family was not rich having a small bakery, which used only manual labor. They needed working hands, and Gaston's father initially refused a scholarship for his son, but then changed his mind, realizing that his son needed to continue his studies, and this scholarship gives him such a chance [10, p. 53].

Thus, having successfully graduated from school, Gaston continues his studies at the Lycée de Sens (now the Lyceum named after Stefan Mallarmé). From 1904 to 1905, he served in an artillery regiment as a reserve assistant veterinarian.

In 1906, he passed the competition in three veterinary schools, being in the top ten he chose the prestigious National Veterinary School Alfort (founded in 1765) of the city of Maison-Alfort. While studying there, Ramon was fond of chemistry, and his supervisor of practical classes, Monvoisin, taught him how to work with formalin to prevent milk souring in experiments. This small detail will be crucial for his further discoveries. It should be noted that by conducting these experiments, Ramon developed observation and a taste for experiment — the qualities of a scientist so necessary for his future research in immunology or bacteriology [10, p. 54]. At the Veterinary School, he passed two internships: at the Department of Chemistry and the Department of Infectious Diseases. His diligence, sharp mind, discipline and conscientiousness distinguished him from other students [13, p. 439].

After graduating from the Veterinary School of Alfort in 1910, with the degree of Doctor of Veterinary Medicine, Gaston Ramon in 1911, at the age of 25, began working at the Branch of the Pasteur Institute in Garche (near Paris), where he met the famous bacteriologist Émile Roux, friendship and collaboration with whom lasted all his life. Roux appointed a young specialist to the serum production laboratory, where Ramon worked until 1920, immunizing horses and collecting a huge number of doses of anti-tetanus, anti-diphtheria and anti-gangrenous serums. During the First World War (1914–1918), when a large number of anti-tetanus and anti-gangrenous serums were required, Ramon remained at his post, despite his great desire to go to the front. With his participation, 10,000,000 doses of serums were produced for France, 1,000,000 for Italy,

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500,000 for the US Army, 10,000 for Serbia. In 1918 alone, 20,000 ampoules of tetanus serum were produced daily [10, p. 54]. This work has enriched him with useful knowledge and skills so necessary for future discoveries.

In 1915, Émile Roux (then director of the Pasteur Institute) offered Ramon to find an antiseptic suitable for the preservation of serum from microbial contamination. After many laboratory studies, the talented assistant brilliantly coped with the task, offering formalin, familiar to him from his studies at the Veterinary School of Alfor, as an antiseptic. "We have proved, — Ramon wrote, — that formalin is an excellent antiseptic for preserving the sterility of biological preparations, in particular, therapeutic serums" [3, p. 45].

In 1917, Gaston Ramon married Marie Marthe Momont, the great-niece of É. Roux [12, p. 256]. The couple had three children: two sons — both doctors, and a daughter — a pharmacist. Gaston's wife was a faithful companion in all the trials of her husband's life, sharing all his worries, his glory and preserving the family hearth [13, p. 439].

In 1920, Ramon received permission from É. Roux to create a small laboratory near his residence in the Branch of the Pasteur Institute in Garche. It is interesting to note that this laboratory consisted of one person — Gaston Ramon, without a single technical assistant. He had to do everything himself, and later Ramon admitted that if he had assistants, he would not have seen what the eyes of a natural scientist see. In his work, he always followed the motto of a genuine Pasterian, for whom "difficulties stimulate the activity of the researcher" [3, p. 6; 10].

Working in the laboratory, Ramon studies the works of Louis Pasteur, Émile Roux, and well-known French veterinarians: Jean-Batiste Chauveau 1827–1917), Pierre-Victor Galtier 1846–1908), Jean Joseph Henri Toussaint (1847–1890), Henry Bouley (1814–1885), Edmond Nocard (1850–1903) [10, p. 54].

Thus, gradually mastering the knowledge and skills in the field of veterinary vaccination, Gaston Ramon in the period from 1922 to 1926 came to his famous discoveries on the successful immunization of humans and animals, which indicates a close scientific interaction of veterinary science and medicine.

Here is what Gaston Ramon himself writes about his discoveries: "In less than 4 years — we emphasize this — the following were discovered: the principle of flocculation (1922); the principle of anatoxins (1923); the principle of vaccination with anatoxins against diphtheria, tetanus, etc. (1923–1924); the principle of auxiliary and stimulating immunity ('adjuvant') substances (1925) and the principle of associated deposited vaccines (1926) [3, p. 17].

His contribution to the science of vaccines, achieved as a result of painstaking and hard work, was significant and fundamental. "For ten years, I did not take any vacation or rest, I did not waste time on empty entertainment...", wrote Ramon in 1936. He entered science as one enters religion, paying true homage to Dr. Roux. At the Pasteur Institute, he held various positions, up to the director of the Institute (1940). The main milestones of his life and activities are presented in the table below.

The main events of Gaston Ramon's life and work

Years	Events
30 September, 1886	Date of birth of Gaston Ramon (in the village-commune Belshom (Fr. Bellechaume), Yonne (156 km from Paris), France
1890–1904	Studying at the municipal school of Sans
1904–1905	Service in an artillery regiment as a reserve assistant veterinarian
1906–1910	Studies at the Alfort National Veterinary School (L'École national vétérinaire d'Alfort) of the city of Maisons-Alfort (academic degree — Doctor of Veterinary Medicine, 1910)
1911–1920	Work at the Branch of the Pasteur Institute in Garches (Annexe de Garches de l'Institut Pasteur, in the Laboratory for the production of serums
1915	The use of formalin as an antiseptic for the preservation of serum from microbial infection
1917	Marriage to Marie Marthe Momont
1920	Creation of a small laboratory in the Branch of the Pasteur Institute in Garche, consisting of one person — Gaston Ramon
1922	Discovery of the flocculation principle
1923	Discovery of the principle of anatoxins
1923	Obtaining anatoxin for vaccination against diphtheria, tetanus, etc.
10 December 1923	Emile Roux presented a report by Gaston Ramon on the flocculation ability and immunizing properties of diphtheria anatoxin (toxoid) at the Academy of Sciences of France
1923–1924	Discovery of the principle of vaccination with anatoxins for prevention diphtheria and tetanus
1923–1924	The first experiments on immunization of children and adults with diphtheria anatoxin in Paris
1925	The principle of auxiliary and stimulating immunity ('adjuvant') substances
1926	The principle of associated vaccines
1926–1944	Director of the Branch of the Pasteur Institute in Garche
1933	Honorary Member of the All-Union Institute of Experimental Medicine (VIEM), the USSR
1934	Member of the Academy of Medicine of France (Académie de médecine de France)
1934	Deputy Director of the Pasteur Institute
1935	Member of the Veterinary Academy of France (Académie Vétérinaire de France)
1940	Director of the Pasteur Institute
1940	Member of the Surgical Academy of France (Académie de Chirurgie de France)
1941–1948	Honorary Director of the Pasteur Institute
1943	Member of the Academy of Sciences of France (Académie des sciences de France)
1947	Director of the National Institute of Hygiene (Institut national d'hygiène)
1948	Head of the International Epizootic Bureau (Office international des epizooties — OIE) in Paris
1956	Knight of the Grand Cross of the Legion of Honor (Chevalier de Grand-Croix de la Légion d'honneur)
1957	Publication of the Gaston Ramon's fundamental work '*Quarante années de recherches et de travaux*' (Forty Years of Research and Achievement)
1958	Grand Gold Medal of the National Center for Scientific Research of France (La grande médaille d'or du Centre national de la recherche scientifique — CNRS)
1962	The publication of the Russian translation of Gaston Ramon's fundamental work '*Сорок лет исследовательской работы*' (Fr.: '*Quarante années de recherches et de travaux*')
1963	The death of Gaston Ramon at the age of 76

Gaston Ramon, who worked all his life to save lives, protested against the war and the atomic bomb: "Fabulous sums are being spent on the discovery and production of increasingly deadly machines... — he wrote in 1957, — Despite so many delusions of the human spirit and disgusting evil deed... the servants of the laws of peace, health, labor, salvation continue to relentlessly follow the path drawn by Pasteur" [5].

In the same 1957, Ramon's fundamental work '*Quarante années de recherches et de travaux*' (Forty years of

research work) was published, which became a kind of hymn for the history of vaccination and immunology of the first half of the 20th century. In 1962 it was translated into Russian with a preface by the author [3].

Like Pasteur in his anniversary speech at the Sorbonne, so Ramon in the conclusion of his work devoted to his forty years of research, was able to say: "I did everything I could." Just like Pasteur, Gaston Ramon believed that the sole purpose of all his research and work "was to protect human from certain diseases that directly threaten him, and from diseases that, affecting domestic animals, threaten human well-being" [3, p. 451].

It is no coincidence that a bronze palm is installed on his grave in his native Belshom, on which only two words in Latin are inscribed: "*PRO HUMANITATE*" (For humanity) [6].

Recognition and memory

Gaston Ramon's discoveries have made his name famous all over the world. He was elected an Honorary Doctor of many foreign universities, and in 1933 — an honorary member of the All-Union Institute of Experimental Medicine (VIEM) USSR [15, p. 515].

In his homeland, Gaston Ramon is a member of the Academy of Medicine (Académie de médecine de France, 1934), the Academy of Surgery (Académie de Chirurgie de France, 1940) and the Academy of Sciences of France (Académie des sciences de France, 1943).

From 1926 to 1944 he was the head of the suburban Branch of the Pasteur Institute in Garche; and at the same time — deputy director of the Pasteur Institute in Paris (1934–1940), director (1940), and then honorary director of the Pasteur Institute (1941), director of the National Institute of Hygiene (Institut national d'hygiène, 1947). From 1935 to 1945 he published the journal '*Revue d'immunologie*' (Review of Immunology)[16, p. 334, 338].

In 1948, Gaston Ramon left the Pasteur Institute and headed the International Epizootic Bureau (Office international des epizooties — OIE) in Paris (since 2003 — the World Organization for Animal Health) [7].

There he is actively working to combat foot-and-mouth disease and tuberculosis of cattle, as well as rabies and myxomatosis. Until the last days of his life, he, according to him, will strive to "make himself useful" — to serve veterinary medicine, of which he is proud to be involved [8].

The French government highly appreciated the merits of Gaston Ramon — in 1956 he became a Knight of the Grand Cross of the Legion of Honor [9], and in 1954 he was awarded the Grand Gold medal of the National center for scientific research of France (La grande médaille d'or du Centre national de la recherche scientifique — CNRS), which has been awarded since 1954 to an outstanding scientists for a significant contribution to the development of science.

The streets of many cities of France bear the name of Gaston Ramon, colleges, lyceums, schools are named after him.

In his native Belshome, where there are streets bearing the names of Louis Pasteur (Pasteur Street), Emile Roux (Dr. Roux Street) and Pierre Curie, on July 5, 1964, the "Professor Ramon Street" appeared — the central street of the commune, where the Belshome City Hall is located (Mairie de Bellechaume, 50 Rue Professeur Ramon) [10].

On the same day, a commemorative plaque was installed on the house where Gaston Ramon was born, with the inscription: "*Inventeur des anatoxines diphtérique et tétanique, Directeur honoraire de l'Institut Pasteur*" (To the creator of diphtheria and tetanus anatoxins, Honorary Director of the Pasteur Institute) [12, p. 253].

In May 1967, a bust of Gaston Ramon was unveiled at the Alfort Veterinary School (where Ramon studied), and a postage stamp with his image was issued the same year.

In May 1969, a medallion in honor of Gaston Ramon was opened in the Gallery of the Pasteur Institute in Paris, and in 1983, in the city of Sens, where Gaston studied at the municipal school, and then at the lyceum, a plaque was installed on the building of a new hospital complex that bears his name — the Gaston Ramon Hospital Center [10, p. 59].

However, Gaston Ramon never won the Nobel Prize. In November 2020, the magazine "*Le Point*" published an article by journalist Frederic Levine "*Vaccination pioneers: Gaston Ramon, diphtheria and tetanus*". It emphasizes that various organizations and scientists from many countries of the world have nominated Gaston Ramon 155 times over the years for the Nobel Prize in Physiology or Medicine, but he never became its laureate — such an outstanding scientist as Gaston Ramon, who saved humanity from diphtheria and tetanus, remained in the shadow of the history of the most prestigious scientific award [11].

Indeed, it is possible to find confirmation on the official website of the Nobel Prizes '*The Nobel prize*' that Gaston Ramon was nominated 155 times for the Nobel Prize for the discovery of anatoxin, setting a kind of record. In 1934 alone, he was nominated for the Nobel Prize 24 times. The nominees were scientists and public figures from Algeria, Denmark, France, Yugoslavia and other countries [12]. The second "record holder" in terms of the number of nominations for the Nobel Prize in

[5] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire/gaston-ramon-pro-humanitate

[6] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire/gaston-ramon-pro-humanitate

[7] https://www.pasteur.fr/fr/institut-pasteur/notre-histoire/gaston-ramon-pro-humanitate

[8] https://data.bnf.fr/fr/11964945/gaston_ramon/

[9] https://www.leonore.archives-nationales.culture.gouv.fr/ui/notice/312983

[10] https://www.societe.com/entreprises/_rue%20du%20professeur%20ramon/89210_BELLECHAUME.html

[11] https://www.lepoint.fr/sciences-nature/les-pionniers-de-la-vaccination-gaston-ramon-la-diphterie-et-le-tetanos-02-11-2020-2399121_1924.php

[12] https://www.nobelprize.org/nomination/archive/show_people.php?id=7545

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Physiology or Medicine is Gaston Ramon's teacher Émile Roux, he was nominated 115 times. For many years he was close to it, but he never got it [13].

It is well known that there are no borders for infectious diseases (the COVID-19 pandemic is proof of this), but scientists who have discovered a life-saving medicine or vaccine in their country simultaneously save the population of other countries and continents of the Globe from misfortunes. And how can we not recall the words of Louis Pasteur, said at the International Congress of Physicians in Copenhagen in 1884, but relevant today:

"Science has no Homeland, or rather, the whole of humanity is its homeland. But if science does not have a Homeland, then the first concern of a scientist should be work for the glory of his Homeland ... Humanity uses the works of researchers from different countries. It compares, it chooses, it takes pride in the successes and glory of a particular people. You, who contribute your work to the universal world heritage, you, whose names form part of your Motherland, you can be proud of the fact that working for the good of your Homeland, you deserve the gratitude of the entire human race" [3, p. 12; 17, p. 375].

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