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### Professor Giorgi Eliava and the Eliava Institute of Bacteriophage

Nina Chanishvili, PhD, Dmitriy Myelnikov, PhD, and Timothy K. Blauvelt, PhD<sup>3</sup>

### **Abstract**

In the history of medicine little is known about Prof. Giorgi (George) Eliava, who must be recognized as one of the central figures in the story of bacteriophages. Today it may be said without any exaggeration that without the support that Eliava provided to Felix d'Herelle, much of our knowledge about phage therapy would never have been acquired. Eliava played a central role in developing and promoting therapeutic uses of bacteriophages in the Union of Soviet Socialist Republics and beyond, and it was largely due to his efforts—and the institute that he established—that phage therapy survived in Soviet Georgia during the Cold War when it was largely abandoned in the West. Because of his progressive thinking, tireless activities, and close collaborations with many foreign scientists, including d'Herelle, Eliava became a victim of Stalin's regime in 1937, declared an "Enemy of the People" and executed. Most photographs and documents belonging to Eliava were destroyed by the Committee for State Security (*Komitet gosudarstvennoi bezopasnosti*), so it is difficult to ascertain many of the details of his life, and his scientific activities are largely unknown. His memory was restored only after the reassessment of the outcomes of the Great Terror and Stalin's regime in later periods. In this article, we bring the remarkable but little-known story of Giorgi Eliava to a wide readership and thus pay tribute to his talent and his dedication to science, and celebrate his contributions to phage research and phage therapy.

Keywords: George Eliava, biography, research, Eliava Institute, history, current status

Gaccording to the old style\*), 1892 in the village of Sachkhere in western Georgia to the family of a well-known doctor Grigol Eliava and his wife Mariam Nakashidze. Grigol Eliava was well educated and an excellent doctor, always ready to help people, especially the most vulnerable. He had a very active social life and published many articles on contemporary issues. From 1908 he was a member of the Society for Literacy among Georgians, over which he undisputedly presided during 1909–1921.

He was also the chairman of the Batumi Doctors' Society.<sup>2</sup> Between 1894 and 1916 Grigol Eliava was elected five times as a delegate to the Batumi City Council.<sup>3</sup> Grigol was a widower with one daughter, Nino, when he married Giorgi's mother Mariam Nakashidze. She was a very kind and educated woman, a perfect mother. Until her 16th birthday, her stepdaughter Nino did not know that Mariam was not her birth mother. Nino and Giorgi had a young sister, Elizabeth (Ezochka), who was in poor health and died at a young age.

From his early childhood, Giorgi was interested in literature, music, and sports; in particular, he was very fond of boxing. In 1907, he graduated from the Batumi gymnasium with honors. His father wanted him to become a doctor and to take over his medical practice, but Giorgi reportedly said, "I cannot earn money by taking it from patients." In 1909, he

<sup>\*</sup>Russian Empire had followed the Julian ("old style") calendar until its collapse; by 1917, the gap between dates according to the Julian and Gregorian ("new style") calendar comprised 13 days. Georgia moved to the Gregorian calendar in 1918.

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FIG. 1. The University of Geneva was founded in 1559 as the Academy of Geneva (Académie de Genève) by John Calvin (available from public domain).

entered the Imperial Novorossiysk University in Odessa,<sup>†</sup> initially intending to study literature. During his first years at the university, he joined the student revolutionary movement, because of which he was expelled in 1910 and deprived of the right to enter any other university in Russia.

He spent 3 months in Odesa prison, after which he was sent back to Georgia. In 1912, Grigol Eliava sent Giorgi and his sisters to Switzerland, perhaps to improve Ezochka's health. Giorgi attended lectures at the University of Geneva (Figs. 1 and 2) as an auditing student, where a lecture by Prof. Hector Cristiani inspired him to changed direction of his studies, as he decided to dedicate himself to bacteriology. By the beginning of the 20th century, it was generally accepted that most diseases are caused by microorganisms, that all diseases are accompanied by local disturbances in the structure of organs and tissues, and that the symptoms of diseases are a consequence of these disturbances.

Giorgi entered the Faculty of Medicine at the University of Geneva in the summer of 1912 and continued his studies until July 1914.<sup>4-7</sup>

During the summer of 1914, Eliava came back to Georgia for vacation, but with the start of the First World War he could not return to Geneva. Through the efforts of his relatives, he gained permission to continue his studies at the Faculty of Medicine at the Moscow University. On July 20 (old style), 1914, Nicholas II announced to his subjects that Russia had entered the war with Germany. The event took place at the height of the summer holidays; therefore, it was decided to delay the start of classes until October 1. In September 1914, an infirmary for wounded soldiers was opened in the university dormitory, and the students worked there as medics and orderlies, as well as resident doctors and paramedics. 8

This is likely when Eliava gained his first significant clinical experience. He graduated from the university in 1916, and in the same year he was appointed as head of the Caucasian Front Bacteriology Laboratory in Trabzon.\*\* In 1917, he became head of the Tbilisi Bacteriology Laboratory, which was under the auspices of the Caucasian Union of Cities. The government of the newly independent Democratic Republic of Georgia, founded in the aftermath of the 1917 revolutions in the Russian Empire, sent Eliava to the Pasteur Institute in Paris to advance his knowledge on bacteriology. At the same time, his mission included the procurement of bacteriological instruments, therapeutic sera, and medicines required for the needs of Georgian municipalities. 4-6

In 1919–1921, Eliava worked at the Pasteur Institute in Paris with famous bacteriologists, including Émile Roux,

<sup>&</sup>lt;sup>†</sup>There were no Universities in Georgia or anywhere in the Caucasus at this time, as part of Russian imperial suppression of higher education in many territories, in part aimed at preventing student uprisings.

<sup>&</sup>lt;sup>‡</sup>The University of Geneva (initially created as an Academy) was founded in 1559 by John Calvin (1509–1564) and his follower Theodore Beza (1519–1605). The University of Geneva, being a modest and low-prestige educational institution, benefited from the presence of the so-called "eastern students." They were highly qualified and carried out significant scientific work at the university, especially at the Faculty of Natural Sciences. Between 1810 and 1878, the majority of Russian students (matriculated students and auditors) were often casual travelers who made up less than 4% of the total student body of the Academy. In 1907–1913, 42% of the University of Geneva students originated from Russia" (https://nashagazeta.ch/news/la-vie-en-suisse/nashi-lyudi-v-zhenevskoy-akademii-1559-1878).

<sup>§</sup>A student studying outside the university at which he has matriculated and from which he expects to receive a degree.

<sup>\*\*</sup>From March 1916, Trabzon was controlled by the Russian Army.

# UNIVERSITÉ DE GENÈVE

SCHOLA GENEVENSIS MDLIX



## LISTE

AUTORITĖS, PROFESSEURS, **ÉTUDIANTS ET AUDITEURS** 

SEMESTRE D'ÊTÉ 1914

(Avril - Juillet)



GENÈVE

IMPRIMERIE CENTRALE, BOULEVARD JAMES-FAZY, 17 1914

NOM ET PRENOM	Date d'imma- triculat,	PAYS D'ORIGINB	ADRESSE A GENEVE
170 Devegney, Camille	Н 12	Genève	Quai des Bergues, 25
171. Dias Silveira, Irmael		Uruguay	Avenue de Lancy, 3
172. Dieker, Naoum	H 13	Russie	Bd du Pont-d'Arve, 22
178*Dimitrova, Marie	H 10	Bulgarie (Dobritcha)	Rue Leschot, 6
174*Dinaburg, Rachel	80 н	Russie (Gadiatch)	Rue de Carouge, 69
175. Djévad Réfik, Ismael		Turquie (Stamboul)	Rue Lombard, 4
176. Djevdet, Mehmet	E 11	Turquie (Smyrne)	Roseraie, 2
177*Djurachkovitch, Milena		Monténégro	Rae de l'Université, 5
178. Dobreff, Lubomir G.	E 14	Bulgarie (Varna)	Pl. de la Synagogue, 2
179. Dobrovitsky, Sacharie	H 13	Russie (Krioukoff)	Boulev. Pont-d'Arve, 21
180. Dolder, Walter	H 13	Genève	Collex-Bosey
18t. Domeratzky, Felix	H 08	Russie	Rue de Caronge, 75
182. Donnet, Victor	H 07	Genève	Rue du Pré-Jérôme, 9
183. Doubinsky, Boris	60 H	Russie (St-Pôtersbourg)	Grands-Philosophes, 24
184. Douchanoff, Liouben	H 13	Bulgarie	Rue du Grand-Bureau, 2
185*Doudoumoff, Kitza	H 13	Bulgarie (Haskovo)	Boulev. Philosophes, 24
186*Doukarskaja, Esther	H 11	Russie (Odessa)	Rue du Stand, 51
187. Dognaevsky, Zelman	H 13	Russie (Poltava)	R. Ecole-de-Médecine,12
188. Doundoua, Léon	00 H	Russie (Géorgie)	Rue Caroline, 9
189. Doutcheff, P. Dimitre	H 12	Bulgarie	Avenue de Lancy, 2
190*Dragouleva, Marie	H 13	Bulgarie	R. Ecole-de-Médecine, 47
191. Dreyer, Serge	H 08	Russie (Toula)	Chemin de la Tour, 4
192*Drenovska, Elena	H 43	Bulgarie (T. Seimene)	Boul. Georges-Favon, 37
193. Drouian, David	H 13	Russie	Boulev. Carl-Vogt, 45
194. Dupuis, Cesar	H 13	Vaud (Greesy)	Av. des Petits-Délices, A
195. Dvoretzky, Joseph	H 13	Russie (Pologne)	R. Ecolo-de-Médecine, 1
196. Dvofris, Gdalia	H 13	Russie (Kamenetz-Pod)	Grands-Philosophes, 5
197. Ebine, Leiser	E 13	Russie (Pologne)	R. du Prò-Jerôme, 13 bis
198*Edelschein, Sophie	H 08	Russie (Pologne)	Rue John-Grasset, 7
199*Efros, Freida	E 11	Russie	R. Vieux-Grenadiers, 3
200 Ehrat, François	H 10	_	Boul. Georges-Favon, 1
201. Eichenberger, Riebard	H 13	Argovie (Fahrwangen)	Rue dn Centre, 22
202. Eidelson, Avroum Jakob	E 14	Russie (Jitomir)	Chemin de la Tour, 4
203 El Dib, Osman Ibrahim	H 09		Glacis de Rive, 21
204. El Falaki, Moustapha	H 13		Rue des Maralchers, 42
205. Elgawaly, Mahmoud		Egrpte	Boul. Georges-Favon, 35
206. Eliava, Georges	E 12	Russie (Koutais)	Avenue du Mail, 25
207. El Kalaoui, MobSelim	H 12	Egypte	Boul. de la Cluse, 37
208*Elsner, Zina	H 07	Russie (Stavropol)	Rue Bergalonne, 10
209 Ensinger, Erwin	H 10		Place E. Claparède, 5
210. Epstein, Isokhor-Hirch	H 13		Quai du Cheval-Blanc, 16
211. Epsteine, Meer	H 13	_	_
212. Erb, Max			

FIG. 2. List of administrators, professors, students, and auditors of the summer semester 1914 (April–July). Giorgi Eliava is listed here under number 206. (Available from: https://www.unige.ch/archives/adm/documents-en-ligne/listes-des-autorites-professeurs-etudiants-auditeurs-et-laboratoires/).



FIG. 3. One of the first "Phage hunters"—Giorgi Eliava (Photo by Felix d'Herelle, 1933–1935, Archives of the Pasteur Institute).

Charles Nicolle (a 1903 Nobel Prize winner in Medicine), Albert Calmette, and Gaston Ramon. He became very close friends with Eugene and Elizabeth Wollman (Eli Wolman; unpublished data), who went on to become the founding figures in the field now known as Molecular Genetics. Eliava was a talented, energetic, joyful, charming, and cheerful person, who loved jokes, music, playing the piano and dancing. A raconteur with a good sense of humor, he was always the heart of any company and easily gained people's trust. In addition, he was fond of horse-riding and hunting, which are popular Georgian sports (Fig. 3).<sup>5</sup>

In the beginning of the 1920s, Eliava learned about Felix d'Herelle's discovery of bacteriophages at the Pasteur Institute, and heard rumors about his personality. At that time, d'Herelle's colleagues at the Pasteur Institute did not accept his ideas about the living nature of bacteriophages and for the most part they ignored him. Eliava, on the contrary, took these ideas seriously, since he had made similar observations working on Vibrio cholera, whereby the bacteria spontaneously disappeared after he had left a culture at his desk for some time. Eliava was especially interested in this phenomenon, and he volunteered to repeat d'Herelle's experiments and successfully replicated them. <sup>6,9</sup> After this, d'Herelle and Eliava finally became acquainted, laying the basis for their further collaboration and friendship.

Eliava visited the Pasteur Institute several times between 1925 and 1927, and in 1930-1931 where he stayed for an extended period to immerse himself in research. 6,10 Although Eliava published relatively few articles, all of them touched on very significant topics that remain relevant today. 11-19 It is noteworthy that practically all of them were published during periods coinciding with his stays at the Pasteur Institute. Some of them were published in Georgian and Russian on phages and others on important medical topics. One of them, for example, from 1934, discussed the negative aspects of treating patients with syphilis with medications containing heavy metals.<sup>20</sup> These publications point to Eliava's wide range of professional interests. Together with d'Herelle, Eliava discovered lysins, which are by-products of bacteriophages<sup>11</sup>; in collaboration with E. Pozerski<sup>14</sup> he found that quinine, widely used as treatment against malaria across the globe,<sup>21</sup> also affected bacteriophages.

Eliava was among the first scientist, together with Pozerski, 15 to elaborate the hypothesis that bacteriophages may change the nature of the host bacteria. In particular, according to the authors' observations the bacteria (B. Shiga<sup>††</sup>) cultured in presence of the corresponding active bacteriophage acquired resistance to the latter. This trait was persistent during at least 15 generations of the strain treated with the phage. Moreover, the phage treatment also affected the morphological and agglutinating (serological) properties of the bacterial strain.

He was already studying the immune response to phage therapy in 1921, <sup>12</sup> and the adsorption of bacteriophages on leukocytes. <sup>18</sup> In his article "Au sujet de l'adsorption du bacteriophage par les leucocytes" ("About bacteriophage adsorption by leukocytes"), 18 which was publicly presented by Pozerski, ‡‡ he wrote "in practice, there is considerable discrepancy between the action of the lytic agent in vitro and its activity in vivo, especially when it comes to studying the behavior of Bactreiuphagum Intestinale outside its normal habitat—the intestinal contents—and to introduce it, for example, into the circulatory stream." He performed several experiments "to determine which of the constituents of the blood can prevent the free exercise of lytic power."

Based on the results of his experiments, he put forward a hypothesis according to which the insufficient action of bacteriophages after their introduction into the bloodstream was due to the fact that leukocytes effectively fixed bacteriophage corpuscles, which destroy the bacteriophage, that is, performing an action usually applied against foreign bodies.18

To determine the dimensions of phages the researchers ultrafiltered phage lysates through increasingly and tighter membranes to ascertain the limit of the passage of the bacteriophage "corpuscles" and assign them defined dimensions. However, the estimates ranged considerably from 1 to  $30 \,\mu\text{m}$ . Eliava and Suarez<sup>16,17</sup> also attempted to perform phage measurements, for which they used albumin, hemoglobin, and tournezol protein as controls. To avoid clotting they filtered phage lysates and proteins with known molecular weights under a rotating electric charge. §§ As a result of these experiments, they concluded that the phage corpuscula are smaller than  $5 \, \mu m$ . <sup>16</sup> Of course, any of these measurements are far removed from current understanding, but the experimental design was innovative for the time.

In 1931, Eliava, in collaboration with Nattan-Larrier and Richard, 19 conducted experiments to test the assumption of Blair and Reeves<sup>22</sup> that phages against Escherichia coli, Shigella flexneri, and Salmonella typhi can pass through the placenta even when administered through cutaneous or interparental routes, but not through oral administration. These conclusions contradicted the results of Grasset, 23 who injected E. coli and Staphylococcus phages directly into the veins and heart of pregnant female rabbits and Guinea pigs, but had never observed that phages could cross the placenta.

Eliava and his coauthors<sup>19</sup> performed intracardiac inocu-

lation of an E. coli bacteriophage into five 5-week pregnant

<sup>††</sup>Shigella dysenteriae serotype 1.

<sup>‡‡</sup>Eliava arrived in Georgia in November 2021, thus he was unable to present this work himself in December.

Similar to the alternating voltage gradient used in the Pulse Field Electrophoresis method.

females, which were then sacrificed 3, 5, 5½, 8, and 24 h after inoculation. The blood of scarified female animals was collected and tested for presence of phages. The abdominal cavity of the females was opened, their uterus removed and incised, and the fetuses were removed, taking care that they were not contaminated with maternal blood. To search for bacteriophages in fetal blood, the researchers followed the same technique used to detecting it in maternal blood. In none of these cases did the bacteriophage pass into the blood of the fetuses.

Thus, the authors concluded that is unlikely that their bacteriophages passed through the placenta. Moreover, the placenta stops the bacteriophage that crosses the collodion ultrafilters. Eliava suggested that the placental "plasmodium" behaves similar to a living membrane, whose permeability certainly depends on numerous and complex conditions. It is not enough for a molecule to be very small for the placenta to allow it to pass from maternal blood into fetal blood; other factors besides mechanical ones are also certainly important and preponderant. Although there are several publications indicating that phages can pass through placenta, this issue still remains under discussion and warrants additional research even today.

In November 1921, Eliava returned to Georgia, bringing with him scientific equipment worth ~100,000 French francs,\*\*\* a gift from the Pasteur Institute to his Georgian colleagues.<sup>6</sup> 1921 was a very dark year in Georgian history, when following 3 years of independence the Georgian Democratic Republic was reoccupied by Russia under the Bolsheviks. Georgia was invaded simultaneously from the South, North, and East. This treacherous invasion took place, without any declaration of war, in the first half of February 1921. The Georgian government fled to France on March 17, 1921.<sup>8</sup> This news was publicized widely in European newspapers, so it is impossible to imagine that Eliava did not know about the mess that was happening in his country.<sup>26,27</sup>

Nevertheless, Eliava chose to return and set about his activities in bacteriology with great enthusiasm. In 1923, Eliava initiated the foundation of the Institute of Bacteriology, the antecedent of the present Eliava Institute of Bacteriophage, Microbiology and Virology (EIBMV), which was initially located in downtown Tbilisi. The first preparation manufactured by this new institute was a vaccine against diphtheria. The institute was responsible for dealing with epidemics in Georgia, and for the whole of the Caucasian region.

Considering this importance of the institute's activities, based on a decision of the Georgian Council of People's Commissars 1924 the institute was given space to expand, and a large 17-hectare plot land on the right bank of the river Mtkvari was allocated for the institute's vaccine department, and the building of a former match factory was converted for its use. In 1931, besides, it was decided to build an additional two floors above the original building of the institute in the city center. <sup>28</sup> In 1935–1936, the institution was renamed as the Institute of Microbiology and Epidemiology. By this time, the staff of the institute numbered >300 people.

Wishing to expand into phage technology, in 1935 Eliava appealed to the Georgian Party boss Lavrenty Beria. †††

In his letter to Beria, Eliava emphasized d'Herelle's reputation and the practical uses to which phages were being put, both in Georgia and globally. He stressed the geographically wide and biologically diverse application of phages against bacillary dysentery (caused by Shigella spp.) in the Union of Soviet Socialist Republics (USSR) and in Brazil; that plague (caused by Yersinia pestis) targeting phages similar to the ones he and d'Herelle had isolated were being tested in Egypt and Madagascar; the great potential of phages against the socalled "war diseases"—typhoid and paratyphoid (caused by different Salmonella serotypes)—that took more lives than the actual fighting; and the new developments on phage treatments for wounds, again with clear military relevance.<sup>29</sup> Through his personal connections, Eliava managed to obtain investment of about 200,000 out of 940,000 rubles required to establish the manufacturing plant for d'Herelle, but the remainder still had to be found.<sup>30</sup> However, his goal was much more ambitious than this initial plan to simply build a manufacturing base.

From the early 1930s, Eliava set about bringing to life his long-term objective of establishing a Bacteriophage Institute. After receiving a categorical refusal from Beria, with the help of his friend Budu Mdivani (with whom he had probably become friends during the time that they both worked in France), Eliava appealed to Moscow to another party boss, Sergo Ordzhonikidze. This time his appeal was successful, and it was decided to build a bacteriophage complex on the land in Saburtalo that had previously been allocated for a vaccine department (Fig. 4).

The plan included the construction of research laboratories, manufacturing plants, a diagnostic center, a clinic for about 400-500 patients, an administrative building, a staff hostel, a garage, a laboratory animal facility, and many small workshops. Eliava and d'Herelle's dream was even grander: to create a World Center for Bacteriophage Research in Tbilisi. It is difficult to imagine the grandiose scale of the work that was conceived by these two scientists. Eliava dedicated all of his energy, and even his life, to the realization of this plan. He would become the first director of this institution. He was a good manager and organizer, and was fully dedicated to the institute and its goals. In 1936, Council of People's Commissars issued an order to allocate about 13 million rubles\*\*\*\* for construction of the bacteriophage complex. The building started in 1934 and was finished in 1938. When completed, the Institute of Microbiology and

<sup>\*\*\*</sup>Corresponds to  $\sim$ 7,500 USD in 1921, an equivalent in purchasing power to about \$120,462.57 today.

<sup>†††</sup>Beria held the position of First Secretary of the Central Committee of the Georgian Communist Party (Bolsheviks) between 1931 and 1938. At the same time, he was also the first secretary of the Tbilisi City Committee of the Georgian Communist Party (Bolsheviks. During this period, from May 1937 to August 31, 1938, Lavrenty Beria was also the first secretary of the Tbilisi City Committee of the Georgian Communist Party (Bolsheviks).

<sup>\*\*\*</sup>Polikarpe (Budu) Mdivani served as the Soviet trade representative to France from 1924 until being excluded in February 1937. Between 1931 and 1936, he served as a People's Commissar of Light Industry and first deputy chairman of the Georgian Council of People's Commissars.

<sup>§§§</sup> In 1932–1937 Ordzhonikidze headed the People's Commissariat of Heavy Industry (NKTP).

<sup>\*\*\*\*</sup>This corresponds to  $\sim 2.5$  million USD according to the 1936 exchange rate, which nowadays would exceed the purchasing power of 50 million USD.





FIG. 4. The Vaccine Department. The first building of the Bacteriophage Institute (outside and inside views, 1934) (Archives of the Eliava Institute of Bacteriophages, Microbiology and Virology).

Epidemiology and the Bacteriophage Institute merged and formed the Institute of Microbiology, Epidemiology and Bacteriophage.<sup>6</sup>

Eliava was fascinated by d'Herelle's ideas to use bacteriophages for therapeutic purposes. He invited d'Herelle to Georgia, who then spent 18 months between 1933 and 1935 collaborating with Eliava and other Georgian colleagues. C'h††† D'Herelle intended to move to Tbilisi permanently and to live in the French cottage that was specifically built near the institute and that would be shared by his family and that of Eliava. D'Herelle was grateful to the Soviet government for providing him with ideal conditions and an environment for the realization of his ideas related to phage therapy.

While in Georgia, d'Herelle completed his survey work, *Bacteriophage and the Phenomenon of Recovery*,<sup>32</sup> which was translated to Russian by Eliava and published by Tbilisi University Press in 1935.<sup>6</sup> Naturally, it opened with a dedication to Stalin, who was described as one who "driven by the unconquerable and merciless logic of history, builds human society on completely new principles." "... I have written [this book] for the scientists of the USSR, this wonderful country which, for the first time in history, did not choose irrational mysticism as its guide, but sober science." <sup>30,‡‡‡</sup> For this book, d'Herelle was appointed as honorary professor of Tbilisi University.<sup>6</sup>

Eliava and d'Herelle travelled a great deal within the main cities of the USSR, attending microbiology conferences in Leningrad (1934), Moscow (1935), and Baku (1936)<sup>6</sup> (Fig. 5). On February 13, 1936, d'Herelle and Eliava presented their reports at the Plenary Session of the First Congress of the Azerbaijani Medical Society in Baku. Eliava presented his report entitled "The Nature of Bacteriophage," which was published in the proceedings of the congress<sup>33</sup> (Fig. 6).

Together with his institution building and administrative activities in 1927–1937, Eliava also lectured at the Tbilisi State University, where he headed the Department of Hygiene (1927) and later the Department of Microbiology

(1929). In 1934, Eliava undertook the establishment of an Anti-Plague Station in Tbilisi (the present National Center for Disease Control).<sup>6</sup>

Then suddenly in early 1937, Eliava was arrested by Stalin's People's Commissariat for Internal Affairs (Narodnyi komissariat vnutrennykh del) (the predecessor of the Committee for State Security [Komitet gosudarstvennoi bezopasnosti]) and declared an "Enemy of the People." His wife Amelia Wohl-Lewicka, an opera singer, was also arrested, and his stepdaughter Hanna was exiled. In 1937-1938, the time of the Great Terror, 29,051 citizens of Georgia became its victims, 14,372 of whom were executed and 14,679 were exiled (out of a Georgian population at that time of about 2 million).<sup>34</sup> Among the victims were Eliava's close friends, including the poets Paolo Iashvili and Titsian Tabidze, the composer Evgeni Mikeladze, the theater director Sandro Akhmeteli, and the engineer Vladimir Jikia, all of whom comprised the elites of Georgian society.<sup>35</sup> The majority of them, similar to Eliava, had been educated abroad in Europe.

In summer 1937, a special session of the Supreme Court of the Georgian Soviet Socialistic Republic announced its verdict on Prof. Giorgi Eliava, the director of the Bacteriophage Institute. The case files alleged the following about Eliava: in 1918, he had supposedly been recruited by the French Intelligence services to collect and convey information on sentiments among the Georgian people about French influence on Georgia's state and public life. In 1924, Eliava reportedly recruited a Georgian colonel to assist him to infiltrate the Red Army for the purposes of espionage and to supply him with intelligence on the structure and strength of the Red Army, for which he was to be paid 500–600 rubles per report.

Upon returning to Georgia, acting in the interests of British Intelligence, Eliava was alleged to have established contact with a number of state officials, from whom he systematically received information about the activities of the Georgian National Center, and performed and planned various acts of sabotage using bacteriological agents. He supposedly conspired with Budu Mdivani to use such bacteriological means for possible attacks on the Soviet Army in case of war. Eliava "confessed" to all the aforementioned on June 7–9, 1937, for which the Supreme Court of the Georgian Soviet Socialist Republic sentenced him to death. The verdict was carried out on July 9, 1937, at the height of Stalin's purges. Frustrated and disillusioned, d'Herelle never returned to Georgia.

<sup>††††</sup>From October 1933 through April 1934, and from November 1934 through May 1935.

‡‡‡‡\*To what extent the dedication was sincere remains uncertain.

D'Herelle certainly enjoyed his time in Soviet Georgia and was at least sympathetic to Communism, having experienced the Great Depression in the United States during his time at Yale; yet such dedications were common formal elements at this time. See Summers WC. Felix d'Herelle and the Origins of Molecular Biology. New Haven: Yale University Press, 1999.

<sup>§§§§</sup>During Stalin's Great Terror, more than a million people were shot or sent to the Gulag labor camps.



**FIG. 5.** Giorgi Eliava and Felix d'Herelle (c. 1933–1935) (available from public domain).

After 1937, Eliava's name was expunged from the public record for many years (Fig. 7). Photographs were destroyed, and mentions of his work omitted from official publications. Although Eliava's reputation was formally rehabilitated in 1957, alongside most victims of Stalin's Great Terror, his name remained absent from most sources. Cautious references began to appear in the 1960s and 1970s, notably in the institute's publications, but it was not until Perestroika and Georgian independence in 1991 that his contribution was fully recognized. His memory, however, was kept alive informally and in secret, and even more so the scientific institutions that he initiated and developed, and that continued to live on.

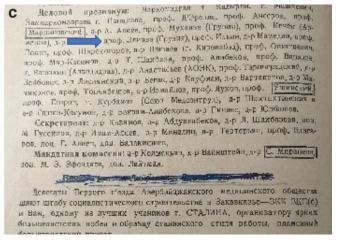
Despite the death of Eliava, the institute survived, and later in the Soviet period it became one of the largest microbiology facilities in the USSR. The main role in the development of its traditions was played by Eliava's right-hand person, Elene Makashvili, and many other dedicated largely female scientists and technicians who worked at the institute, comprising >90% of the staff. Makashvili joined the institute in 1924 immediately after graduating from medical university, and assisted d'Herelle during his stays in Tbilisi. Her contribution to developing and continuing phage research cannot be overestimated. She was the ghost author of an important publication that described the story of d'Herelle's visit to Georgia and his collaboration with Eliava.<sup>6</sup>

Another crucial factor for the development of phage research and manufacturing methods was the urgent demand for therapeutic treatments for military use during the "Winter War" with Finland in 1939–1940 and in the Second World War. The institute was a major supplier of phages to treat lacerations, gangrene, and intestinal infections at frontline hospitals. After the war, the Red Army remained the main consumer of phage products produced by the institute, which were mainly used for prophylactic purposes to decrease the incidence of dysentery and salmonellosis among soldiers. The service of the servic

During its peak period, when the institute belonged to the Soviet Ministry of Health, its research staff numbered about 100-120 people, including technicians, whereas the industrial part employed  $\sim 500-600$  people, including specialists and support personnel. They produced vast amounts of phage preparations (often several tons a day) against around a dozen bacterial pathogens, including Staphylococci, Pseudomonas, Proteus, and many enteric pathogens. Most of the Soviet studies reviewed in this article involved phages developed and produced at the EIBMV.







**FIG. 6.** The book "Proceedings of the 1st Congress of the Azerbaijani Medical Society" (1936)<sup>33</sup> (a). Here Eliava's name has been excised by a librarian (b). An interesting detail is that Eliava's name was erased only on the title page where it was very prominent, whereas in the table of contents and list of participants it was left unchanged. At that time usually conferences began with welcoming speeches addressed to the party leaders, and this session was no exception. It started with an expression of gratitude to comrade Lavrenty Beria, whose name was also erased by the same diligent librarian. It seems that this was done sometime after the arrest and execution of Beria in 1953. Just above Beria's deleted name Eliava is listed among the organizers (see an array) (c), a haphazard fact that takes on symbolic significance given the historical and social background of the situation (Library of the Eliava Institute of Bacteriophages, Microbiology and Virology).



FIG. 7. Scientific Council of the Institute of Microbiology and Epidemiology in 1935–1936. From left to right (sitting): M.G. Beridze (head of the anerobic laboratory), V.D. Gurgenidze (deputy scientific director), N.G. Egiazarova (head of the serology laboratory), E.M. Semenskaya (head of the hematology laboratory), L.I. Dadunashvili (director), V.S. Varazi (consultant), V.V. Voronov (consultant), I.L. Gvelesiani (head of protozoology laboratory), and S.S. Markovskaya (head of the serology department). Standing: I.I. Gamburger (head of the biocontrol laboratory), V.P. Katsitadze (head of the epidemiology department), and A.C. Matusis-Gavasheli (deputy head of the epidemiology department). Somebody is missing in the second row, only the shadow of a person who has been purposely expunged from this photo is visible. This could be Giorgi Eliava or somebody else who, similar to Eliava, became a victim of Stalin's purges, whose bust oversees the scene in the background (from a photo album of the Institute of Microbiology and Epidemiology, 1937?) (Archives of the Eliava Institute of Bacteriophages, Microbiology and Virology).

In 1991, Georgia declared its independence, after which its economic ties with Russia and the rest of the former Soviet Union republics were cut off. Independent Georgia lacked the resources to take such a huge organization under its patronage and to sufficiently subsidize it. Therefore, in the beginning of 1990s the Georgian government decided to undertake economic reforms and privatize all industries, including the manufacturing part of the Bacteriophage Institute. Ten small private manufacturing companies were formed on the basis of former industrial plants. The owners (the former staff of these plants) had few business skills, and many of these companies soon ceased to exist or were taken over by other more successful companies.

The research part of the EIBMV remained under governmental control, and after long discussions in 1995 it was decided that it should be transferred to become under the umbrella of the Georgian Academy of Sciences. The next reform of 2005, according to which research institutes were to become part of universities, almost ended the existence of the Bacteriophage Institute. Only thanks to the international reputation of the institute and the support of the international scientific community, who signed a petition to "Save Eliava," was it possible to restore the independent status of this institution.

Today the Eliava Institute retains its leading position within the field of phage therapy. In 2008, the institute founded a nonprofit organization, the Eliava Foundation, which in its turn formed several companies: Eliava Phage Therapy Center, Diagnostic Center, Pharmacy, and Eliava

BioPreparations, the last of which currently produces a number of commercial multicomponent preparations, such as Pyo-phage, Intesti-phage, Enco-phage, Fersisi-phage, SES-phage and a monoclonal preparation against Staphylococcus. The Eliava Phage Therapy Center is an outpatient day clinic, which due to foreign publications and documentaries has gradually become very well known outside Georgia. Hundreds of desperate patients with chronic infections, incurable with antibiotics, visit the clinic every year. Thus, Eliava's magnificent ideas finally were realized ... but in miniature!

The primary support for the Eliava Institute comes from the government, whereas its scientific research is funded by various local and foreign organizations, such as the EU Horizon2020 program, Civilian Research Development Fund, Defense Thread Reduction Agency, and Swiss National Science Foundation. The research topics cover various areas, from the application of phages as disinfectants for farming to the conducting of phage therapy clinical trials. The institute actively collaborates with numerous local and foreign universities and research centers. These contacts allow us to convey to a large audience the story of the bright and talented person, Giorgi Eliava, who devoted his entire life to science and to the study of bacteriophage and its use for the benefit of mankind.

This remarkable person would have turned 130 years old this year, and the institute that he was able to establish despite the huge obstacles from the circumstances of the Soviet Union at that time, is now 100 years old. We will celebrate these dates together with our collaborators and scientists

interested in bacteriophages in July 2023 by organizing a major conference entitled "Viruses of Microbes—2023" in Tbilisi, Georgia. We hope that this interaction and exchange of knowledge will serve for the future progress of phage therapy, which is so important nowadays amid the rising threat of antibiotic resistance.

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The authors confirm contribution to the article as follows: study conception and design by N.C.; data collection and article writing by N.C., D.M., and T.K.B.; review and editing by T.K.B. and D.M.

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