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Phage Therapy: Insights from the Past, the Great Need of the Present, and Glimpses into the Future

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THIS YEAR WE CELEBRATE the 130th birthday of Giorgi Eliava, who founded the iconic, influential, and inspirational Eliava Bacteriophage Institute in what is now known as the Republic of Georgia. Having brought knowledge of phages from Felix D’Herelle of France to Georgia, Giorgi Eliava was very much ahead of his in time, and he founded the Institute exactly 100 years ago. These two pleasingly round numbers, coupled with an increasing amount of interest in bacteriophages, seemed like an opportune moment to bring together both historical, current, and future aspects of phage therapy in a series of seminal articles for the Phage Community. To celebrate and honor him and all the work leading to where phage therapy is today, our *PHAGE: Therapy, Applications, and Research* Editorial Board decided to assemble a series of articles that reflect the different aspects of bacteriophage therapy.

To give readers an overview of the history of phage therapy, we are delighted that Peder Worning from the Hvidovre Hospital, Denmark has written a special *inPhocus* article appropriately named “Once upon a time ...”. As our regular readers know, this series usually gives a voice to phage work within a specific geography—but here, we go back in time to introduce our readers to the colorful twists and turns and events of the history of phage therapy.

Our editorial board member Nina Chanishvili, from the Eliava Institute in Georgia, has a deep-rooted knowledge of the history of her institute, having spent much of her career pioneering phage therapy there, and also by having family connections to the Institute that date her relationship back to when she was a young child. She was therefore perfectly poised to lead this beautifully penned article outlining the history of the Eliava Institute, showcasing the life and work of Giorgi Eliava.

Dr. Chanishvili’s knowledge was bolstered by her work within the archives of the Pasteur Institute, Paris, to uncover forgotten and buried information about Giorgi Eliava. Although phages were discovered and recognized as biological entities both by Frederick Twort (1915) and Felix D’Herelle,

it was Giorgi Eliava who actually facilitated their translation into useful products to target bacterial infections. His vision to translate phages was remarkable in scope, and he left behind a legacy in the form of the Institute itself, which remains at the forefront of bacteriophage biology today. In addition, he motivated and enabled the training of talented individuals who were able to maintain and grow the facility and who have subsequently trained further generations of phage scientists and clinical partners. Today, many researchers have and continue to work closely with clinical and scientific collaborators from all over the world, sharing their hands-on knowledge of how to isolate, manipulate, and use phage products.

Continuing with our historical theme, we are pleased to bring you what is arguably the oldest scientific article ever published about phages. The article, by Gamaylaya, was published (*Énzymes destroying bacteria*; Society of Russian Physician, November 20, 1898) before phages were known about and thus does not refer to them as such, but it is clear from his descriptions that bacteriophages could be transferred from one bacterial culture to another and cause lysis. This Gamalaya article is often cited, as an early observation of pre-phage history, but has, up to today, only been available in Russian. We are happy to present here an English version, sympathetically translated by our editorial board member Andrey Letarov, a phage biologist from the Winogradsky Institute in Moscow. With this read, *PHAGE* readers will be transported back to the 19th century to enjoy what was being experienced by this scientist.

Moving from the historical aspects of bacteriophages to the modern-day, it is really important to examine the phage literature with close and fresh eyes and to learn from it, improve our practices, and to better understand the steps needed to take phage products to a modern market. Like any scientific discipline, bacteriophage biologists often follow procedures from within the phage literature, but translating phages into applied products requires a broader knowledge of developing standard pharmaceuticals. Who better to point out some inconsistencies between the phage literature

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and the antibiotic development literature and suggest how to solve such issues than Prof. Steve Abedon from the University of Ohio? Prof. Abedon has worked in this area for several decades and is an avid contributor to bacteriophage literature. For this issue, he contributed two articles: one aimed at the phage researcher, unpicking the frailties and inconsistencies of phage therapy development, and a shorter article aimed at a more general reader to highlight what to do and what to avoid when developing a therapeutic product.

Another country with a fascinating historical and current relationship with bacteriophage research, and in particular bacteriophage therapy, is Israel. The large pool of clinical and microbiology talent associated with displaced scientists and doctors after the chaos of the Second World War resulted in the necessary skill sets coming together such that various early phage treatments could be pioneered. Israel remains at the forefront of bacteriophage therapy development and both the historical and current aspects of phage therapy have been beautifully assembled by our editorial board member Prof. Ronen Hazan, a phage biologist from Hebrew University, Jerusalem, Israel.

In terms of review and opinion articles, we aimed to highlight interesting ways in which bacteriophage therapy is moving forward, with readers learning and being inspired by different models. One particularly exciting initiative is currently being undertaken by a consortium of doctors and phage researchers in Australia under the banner of the Phage Australia-Phage Directory who are applying a large-scale personalized approach to target AMR infections. The details of this consortia and scope have been outlined by the team themselves; Jessica Sacher and Jan Zheng from Phage Directory, in Atlanta, GA, USA, and Ruby Lin from Westmead Institute for Medical Research, in Sydney, Australia. They show that many of the perceived blockages to developing bacteriophage therapy can be removed if there is an appetite to make a change. This article also highlights the momentum that can be garnished from a single powerful case—in this case, a young child who was spared an amputation by treatment with bacteriophages.

Finally, a vital part of the *PHAGE* journal is to present Genome Introductions to showcase novel phages. Here we present the discovery of the first *Staphylococcus pseudintermedius*/*S. aureus* polyvalent lytic bacteriophages, showing that you do not have to go so far to find new phages, as these were isolated from a dog! This suggests that dog hair could be a useful novel phage reservoir for skin-associated bacteria. In contrast to the previous articles from 100 years ago, where it was difficult to get much information of how phages may work, we are now in a world where, often, the sequencing of a phage is accessible and affordable. To interpret the genomes, however, standard phenotypic assays should be carried out as outlined in our guidelines. This talks to the point that data is only relevant if it is accessible, and this forum, by providing a close linkage between new genomes and their behavior, will make it easier for downstream analyses. We very much encourage you to publish your new phages in this collated standardized way.

I wish you a great summer and hope to see many phage researchers at the Viruses of Microbes meeting in Portugal, which we are so pleased can happen in person! *Phage; Therapy, Applications, and Research* is an official sponsor, and myself and any of our editorial board members will be very happy to talk with you about anything *PHAGE* journal related!

As is the case for any new journal, we are keen to get indexed on key databases and our Mary Ann Liebert team have been working hard to achieve this based on the great content our authors are submitting. We are delighted to share the news that *PHAGE* has now been accepted for indexing on Scopus making our journal an even more attractive place to publish your work and be enjoyed by a wide receptive readership.

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