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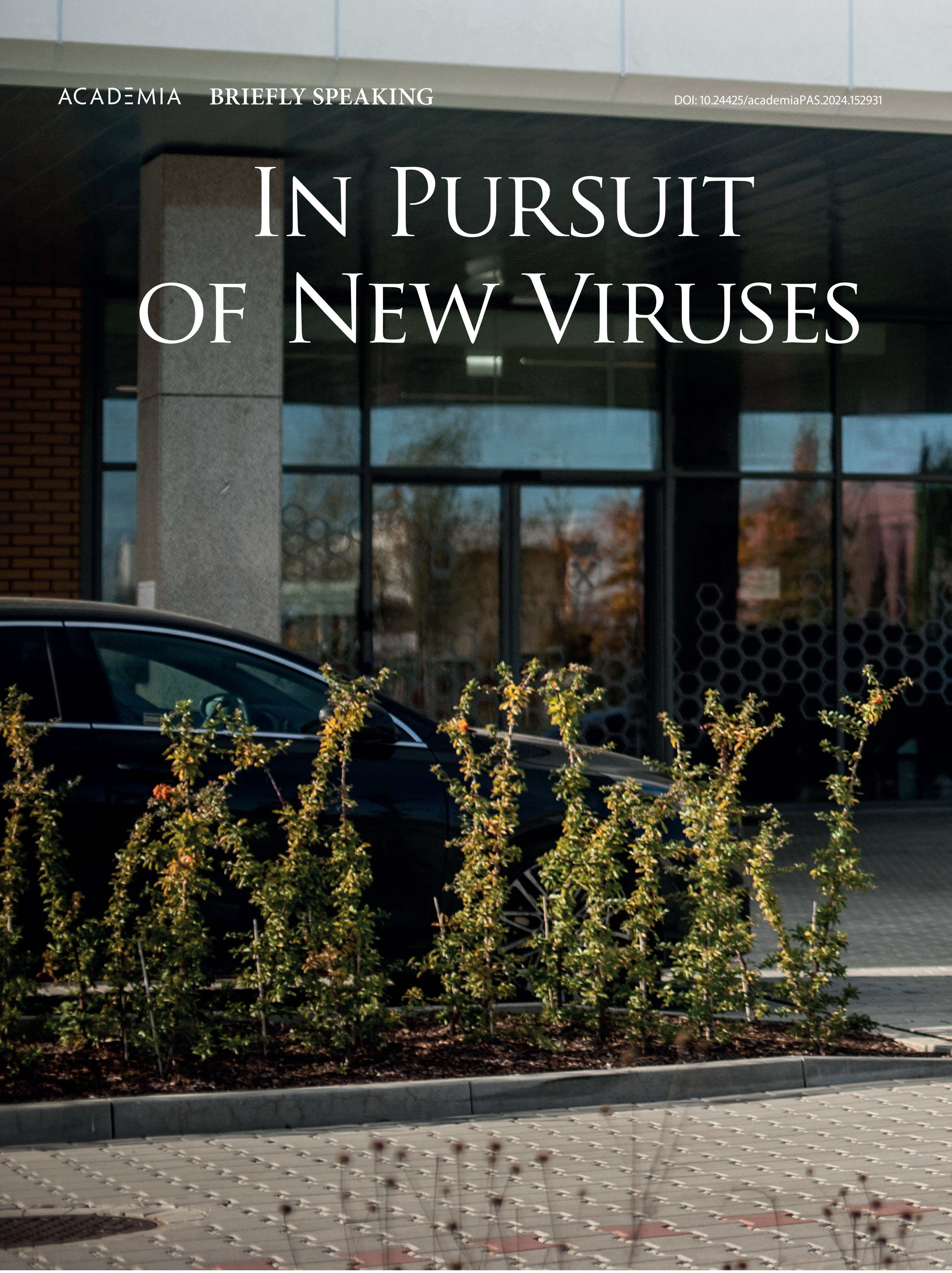
In Pursuit of New Viruses



Prof. Krzysztof Pyrć, head of the BSL3+ Virology Laboratory at the Małopolska Centre of Biotechnology, Jagiellonian University (MCB UJ), and a member of the Climate Crisis Committee of the Polish Academy of Sciences, talks about his work as a virologist and the challenges posed by climate change.

SYLWIA PIWOWAR

Do you remember when you first thought about becoming a biologist?

KRZYSZTOF PYRĆ: No, because I never became a biologist per se; in fact I'm a *molecular biologist*. Biology and molecular biology are entirely different fields. Both are important, but their foundations are completely distinct. I often joke that it's much easier for me to tell animals apart by examining their cells than by looking at them as a whole.

But to answer your question, I first thought about becoming a molecular biologist back in high school. I was fascinated by chemistry and considering medicine when I learned about a new field called *biotechnology*, which largely focused on molecular biology. A field that combined chemistry, biology, and physics was exactly what interested me. A single cell, a single tissue, the mechanisms driving processes in living organisms – the very essence of life.

Yet out of all living organisms, you became most interested in "non-living" viruses. Why them?

My interest in viruses started purely by chance. During my graduate studies, I was researching cancer and had plans to go to Amsterdam on an Erasmus scholarship to further develop my skills in this area. Unfortunately, the trip was canceled, and by a twist of fate, I joined the team of Prof. Benjamin Berkhout, a world-renowned virologist. Along with Lia van der Hoek, they gave me the opportunity to work on various projects. That's when I got involved in searching for new viruses. This was before advanced genome sequencing technologies became available, so the work wasn't straightforward.

I quickly resolved some technical issues and began analyzing patient samples. During my research, I identified the cause of a disease in one patient and, in the process, discovered a new human coronavirus – NL63.

OWN ARCHIVE KRZYSZTOF PYRĆ

This was a major scientific breakthrough. Around more or less the same time, the SARS-CoV-1 virus emerged, which demonstrated that what we were working on was important.

After spending several years abroad in the United States and the Netherlands, you returned to Poland, building research infrastructure and gathering materials. How did that come about?
It was a gradual process. At the time, there wasn't a proper virology lab in Poland capable of conducting advanced research. Initially, I worked in a microbiology lab equipped to handle microorganisms but not fully adapted for virology. I started by organizing a second-class biosafety laboratory, a basic facility where we can work with viruses encountered in everyday life, such as those causing colds or diarrhea, including low-pathogenic coronaviruses (the less dangerous ones).

However, I soon began considering broader societal needs and became involved in the project to establish the Małopolska Centre of Biotechnology. This initiative led to the creation of a completely new institute, where I now work. During this time, the idea of establishing a BSL3+ laboratory within the institute emerged, enabling work with infectious agents that pose real societal threats, capable of causing fatalities or permanent harm. This marked the beginning of Poland's first purely research-focused facility of this kind.

How do scientists react to working with such dangerous biological material? How did you go about building a research team?
Good science in this field is never done alone – it's always a team effort, no matter where you are in the world. What's more, you need to have creative, curious people who can make decisions. This isn't assembly-line work; in our lab, every team member acts as their own creative director.

As for whether we're afraid to work with dangerous viruses, the answer isn't simple. Everyone needs to feel safe. I have a certain rule: when working with agents that could be lethal, our protection comes not only from physical safeguards but also from our experience, strict procedures, and a thorough understanding of the risks. We review our protocols every year, and the entire team thinks about what we can improve. There are no bad suggestions or comments – anyone who feels unsafe can speak up, and we address the issue immediately.

Clear communication is also essential. If there's a problem or accident, it's always openly discussed. Trust within the team is crucial as well. A newly trained team member only joins once the entire team agrees that the person is ready to work safely. There have even been cases where the team has said, "We understand you want this person to join the lab, but we're not comfortable with the idea." In such situations, the individual doesn't receive authorization and has to limit their work to less hazardous topics.

What other research areas are you involved in besides working on viruses?
After returning to Poland, I worked in a microbiology lab at the Department of Microbiology, Faculty of Biochemistry, Biophysics, and Biotechnology at Jagiellonian University. For many years, the lab focused on *Porphyromonas gingivalis* bacteria. At the time, we were studying interactions between bacteria and viruses. We wanted to see whether co-infections by different pathogens could interact and pose a greater threat to the host. *Porphyromonas gingivalis* wasn't the only bacteria we worked with – we also studied *Staphylococcus aureus* (golden staph) and several others.

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Now, we're revisiting this topic because one of my colleagues, Dr. Aleksandra Mielewska, received a grant from the National Science Centre for a project which we'll carry out together with one of the top experts in bacterial infections, Prof. Jan Potempa. This research remains fascinating and is still incredibly important from a societal perspective.

Do virus research and bacteria research proceed in similar ways?
Actually, no. While both fall under the umbrella of microbiology, the methods used for researching viruses and bacteria are entirely different. Bacteria are living organisms, while a virus is essentially a piece of information encoded in a complex structure of proteins and nucleic acids. To understand viruses, we need to examine how this information interacts with a host cell, like a human cell.

If I had to compare virology to other fields of biomedicine, it's closer to cell biology, genetic engineering, and tissue engineering. In our research, we use highly advanced models of the human body, such as three-dimensional, fully functional models of bronchial tissue, lungs, or intestines.

You're a member of the Climate Crisis Committee of the Polish Academy of Sciences. What role does a virologist play in this group?
On that committee I focus on infectious diseases whose spread or emergence is connected to climate change. Recently, the West Nile virus appeared in Poland, brought here by migratory birds. There have also been reports of dengue virus spreading further north. Forecasts suggest that Poland may soon see the arrival of *Hyalomma* ticks, which can transmit the Crimean-Congo hemorrhagic fever (CCHF) virus. I truly value the opportunity to work with experts in climate change, and I try to sensibly contribute my own expertise in infectious diseases to the conversation.

> Pandemics have happened before and will happen again. We must recognize that with climate change and urbanization, such threats are likely to appear more frequently.

What would have to happen for diseases previously unknown in Poland to become a reality here?
Several factors play a role, but I'll highlight three. The most direct is simply higher average temperatures, which create better conditions for pathogens to thrive. For example, in the Polish town of Rzeszów last year, there were cases – and sadly, some deaths – caused by *Legionella*, a bacterium that thrives in warm water. When temperatures are high, this bacterium can multiply in air conditioning systems, water supplies, or public fountains. If a fountain is located in a populated area, it's not hard to imagine the potential for serious outbreaks. In most cases, infections result in what's called Pontiac fever, a relatively mild or even asymptomatic condition. Unfortunately, some cases progress to Legionnaires' disease, which can be severe and even fatal.

As temperatures rise, indirect effects also come into play. For instance, animals begin migrating to stay within their optimal temperature range, altering their natural habitats. This includes ticks and mosquitoes that originally lived only in warmer regions but are now appearing further north. Unfortunately, these arthropods often carry diseases that are unfamiliar to us. For example, the Asian tiger mosquito (*Aedes albopictus*) is a carrier of several viruses, including dengue, which was previously unheard of in this part of the world. Sadly, we're increasingly hearing reports of its presence in neighboring countries, and someone recently sent me a photo of a tiger mosquito spotted near Wadowice in southern Poland.

It's not just arthropods that are migrating – larger animals like bats and fur-bearing mammals are also on the move. This poses another potential risk. Wild animals in new environments experience stress, which can lead to more frequent outbreaks of disease. What's more, species that previously lived in separate regions are now coming into contact. These new and prolonged interactions increase the likelihood of cross-species transmission, which could eventually result in the emergence of new viruses that infect humans.

So more pandemics are in store for us in the future?
Pandemics have happened before, and they will happen again. In the twenty-first century, we've already experienced two major ones: swine flu and COVID-19. We need to recognize that with climate change and urbanization, such threats are likely to appear more frequently. Unfortunately, I feel that not everyone – especially policymakers – fully understands that something serious could happen again. We still lack strategic plans for dealing with the next pandemic. For several years now, we've seen waves of the Mpox virus, which also poses a potential threat.

Given the last pandemic and the growing risks, how much has progress has virology made in recent years?
In terms of the science itself, I don't think the field has accelerated significantly since the pandemic. The increased global interest in virology in recent years has drawn many people to the field, but often they were not specialists. This led to a flood of derivative research, while the most valuable studies had already been conducted before the pandemic. For instance, the vaccines against SARS-CoV-2 were developed based on research carried out long before the pandemic, as part of efforts to combat MERS (a coronavirus that has been present on the Arabian Peninsula since 2012). Similarly, the only drug (remdesivir) available in the early phase of the pandemic was originally developed for a different purpose and was first described in *Science Translational Medicine* in 2017. We were the ones who proposed its use as a possible treatment

for coronavirus pandemics. In 2006, we also wrote about molnupiravir, suggesting it as a broad-spectrum inhibitor for coronaviruses. Unfortunately, the public often only hears that "some company has released a new drug," without realizing it's actually the result of years of research and the hard work of scientists around the globe.

What *has* changed in recent years is the scientific community's approach – there's a greater awareness of the need to share materials, data, and collaborate. For example, my team is part of the European project DURABLE, which connects several excellent academic institutions across Europe. Our joint efforts aim to prepare us for the next potential pandemic – or, ideally, to stop such threats in their early stages. We're also working to monitor what's happening in the animal world and identify viruses in the environment that could pose risks to us. For instance, our research on the presence of avian flu in cats is part of this broader effort. We're also developing research platforms that will allow us to assess the risks of specific pathogens more quickly and effectively and propose countermeasures.

How would you assess public awareness regarding the risks posed by viruses?

The public is highly polarized on this issue. There are numerous sources of misinformation – is now commonly called "fake news." In addition, many individuals speak with an air of authority on the subject despite having no expertise in it at all. Then there are various public figures – celebrities, influencers, or politicians – who, without fully understanding the weight of their words, can easily sow confusion. For example, when a country's president publicly questions vaccines or admits they've never even had a flu shot, the societal impact of such statements is overwhelmingly negative. I'm not sure if this stems from a lack of understanding of their influence or other reasons, but the result is the same: many people are left unsure of what to believe, and the information landscape becomes chaotic.

What research is your team now planning?

Our research focus has remained consistent for many years: emerging viruses that could infect humans and pose challenges, either on an individual or societal level. These include coronaviruses and influenza viruses, but we also study other pathogens, such as flaviviruses and alphaviruses, which are transmitted by mosquitoes and have either already reached Poland or are expected to do so in the near future. In our work, we concentrate on the early stages of infection. For instance, we aim to identify the factors that influence a virus's ability to jump from animals to humans and evaluate how a virus's evolution might affect the course of the disease. Simply put, we're trying to predict whether a new variant of SARS-CoV-2 – or even a completely new SARS-CoV-3 – might soon emerge. Beyond that, we're also exploring ways to respond effectively so that society doesn't face the same high costs as it did during the last pandemic.

INTERVIEW BY **MARIUSZ GOGÓL**

SYLWIA PIWOWAR

Prof. Krzysztof Pyrć, PhD, DSc

is a scientist, professor, and president-elect of the Foundation for Polish Science (FNP). He specializes in virology, with a focus on the mechanisms and pathology of infections, using ex vivo cultures that replicate the human body in laboratory conditions. He established the BSL3+ and ABSL3+ laboratories at the Małopolska Centre of Biotechnology, Jagiellonian University. He has authored over 140 publications in prestigious journals such as Nature Medicine, Science Translational Medicine, Nucleic Acids Research, and PNAS. His work has been cited nearly 14,000 times (*h*-index = 52). He serves as a reviewer and expert for research funding institutions in Poland and worldwide. Prof. Pyrć holds patents that have led to the creation of two spin-off companies. He has led and coordinated numerous national and international research grants, as well as projects funded by commercial entities. Currently, he serves as an advisor to the European Commission and the Polish Ministry of Health, and he has previously advised Polish municipal governments, the Polish Ministry of Science, the Prime Minister, and the President of Poland.

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