b UNIVERSITY OF BERN MULTIDISCIPLINARY CENTER FOR INFECTIOUS DISEASES THESPREAD A NEWSLETTER FROM THE MCID



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News from the Center

Dear readers, we hope you enjoy the latest issue of the MCID newsletter, The SPREAD.

Since the previous issue of The SPREAD, there have been two particular highlights in MCID activities.

On July 6th, the MCID held its annual event. The focus was on the three MCID Core Activities; the BEready Cohort, the BioPreparedness BioBank and the Ethics and Policy Lab. Each Core Activity team presented exciting updates on activities and attendees participated in interactive workshops designed to spark potential collaborations. Thank you to all who were involved!

In Spring 2023, the MCID submitted a proposal for the Co-Leadership of an ARUA-The Guild Cluster of Research Excellence (CoRE), Genomics for Health in Africa (GHA), together with Co-Leads at Stellenbosch University and the University of Tübingen, as well as Core-Partners at several ARUA and The Guild universities. In June 2023 it was announced that GHA will be one of 17 CoREs to receive support from ARUA-The Guild as fundraising, academic exchange and collaborative activities take shape. We are looking forward very much to CoRE-GHA activities getting started. Read more about CoRE-GHA here.

Make sure you keep up-to-date on MCID news and activites by visiting our <u>website</u> and <u>signing up</u> to receive future copies of The SPREAD as well as following us on X (formerly twitter, <u>@MCIDBern</u>) and <u>LinkedIn</u>.

Yours sincerely, Rebecca Limenitakis (MCID Managing Director) Anita Hochuli (MCID Teaching and Outreach Coordinator)





Policy @ the EPL

Article by: PD Dr. Caroline Schlaufer (Manager of Policy @ MCID Ethics and Policy Lab / KPM Center for Public Management)

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The Covid-19 pandemic has demonstrated the importance of scientific knowledge for policymaking: to effectively tackle infectious diseases requires policymakers and scientists to work together. The pandemic has also highlighted how challenging it is to create scientific advisory bodies during a crisis. Pandemic preparedness, thus, also comprises the establishment of a well-functioning collaboration between scientists and policymakers.

The MCID aims to become a resource of expertise and guidance for policy- and decisionmakers in Switzerland and globally. To achieve this goal and to facilitate the transfer of MCID-funded research into public policy, the MCID has established a core activity – the Ethics and Policy Lab (EPL $\underline{\rho}$). The EPL has two main aims:

- 1) To analyze the ethical dimensions of research and policy responses on infectious diseases and to develop constructive solutions for dealing with related ethical conflicts.
- 2) To feed MCID research outcomes into public policy and to facilitate political decisions that are based on scientific evidence.

The EPL offers a variety of services to MCID researchers as well as to policymakers. With regard to policy, the EPL offers support to MCID members, for example, in identifying what parts of their research is relevant to public policy, in enabling contacts with actors from public administration and politics at the federal, cantonal, or municipal levels, or in writing policy briefs and white papers to link research findings to current public issues.

An important way of improving collaboration between scientists and policymakers is to foster improved knowledge about the policymaking process and the political system inside the scientific community. That is why the EPL regularly organizes workshops and events for MCID members about public policy.

The EPL also provides services to policymakers. These services include applied research, policy evaluations, advice on feasible, ethicsbased and socially accepted policy measures, or on policy implementation. So far, the EPL has, for example, written a thesis paper in collaboration with other members of the MCID and researchers from the ISPM on behalf of the Federal Office of Public Health (FOPH) as input for the current revision of the Swiss Epidemics Act¹.



PD Dr. Caroline Schlaufer

In October 2023, the EPL starts a new applied research project to provide empirical knowledge on feasible and socially accepted policy measures to prevent, manage, and control infectious diseases in pets (ϱ). The purpose of the project is to support the Federal Food Safety and Veterinary Office (FSVO) with the involvement of all relevant stakeholders to prepare a strategy for the design and implementation of disease control measures for pets and to increase acceptance of such measures among pet keepers.

Besides supporting MCID-funded projects and offering services to policymakers, the EPL also conducts own research on policy-relevant aspects of infectious diseases, as well as on the use of scientific advice and evidence in policymaking. The current research at the EPL focuses on the following themes:





Research on scientific policy advice

This research analyzes the factors hindering and fostering an effective and democratically accepted use of scientific knowledge in policymaking processes. The goals are to understand the diverse conditions and constraints that shape science-informed policymaking as well as to draw practical conclusions to restructure the institutional settings and procedural norms of scientific policy advice. Members of the EPL and the MCID have been part of a previous study on the use of scientific policy advice in times of crises in Switzerland that compared the use of scientific advice during the COVID-19 pandemic, the financial crisis, and the Fukushima nuclear accident². Current and future research builds on this to discuss the democratic legitimacy of scientific policy advice and to analyze the use of science in policymaking in authoritarian states.

Research on public policy discourse

In this area, the EPL researchers analyze how policymakers and experts publicly communicate and deliberate about public policy. One MCID-funded research project examines how scientific knowledge was presented in public policy debates and how scientists used narratives to influence policy debates during the Covid-19 pandemic in the media in Switzerland ($\underline{\rho}$). A second project funded by the SNSF in the framework of the National Research Program "Advancing 3R" examines the Swiss public debate on research with animals ($\underline{\rho}$).

Contact the EPL if you are interested in receiving support, in collaboration, or if you have questions about our research projects: PD Dr. Caroline Schlaufer on policy-related matters \boxtimes and Dr. Caroline Brall on ethics-related matters \boxtimes



References

¹Althaus, C., Schlaufer, C., Frahsa, A., Hadorn, S., Sager, F., & Zwahlen, M. (2022). Prüfung des Eskalationsmodells (Art. 6 und 7 EpG) unter besonderer Berücksichtigung der Epidemiologie übertragbarer Krankheiten sowie Public-Health-Aspekten: Thesenpapier im Auftrag des Bundesamtes für Gesundheit (BAG) im Rahmen der Revision des Epidemiengesetzes (EpG). Bern. *Q*

² Hirschi, C., Hornung, J., Jalton, D., Mavrot, C., Sager, F., & Schlaufer, C. (2022). Wissenschaftliche Politikberatung in Krisenzeiten in der Schweiz: eine Analyse der Finanzkrise, des Wissenschaftsrats (SWR). Fukushima-Unfalls und der COVID-19 Pandemie. Schlussbericht zuhanden des Schweizerischen Wissenschaftsrats (SWR). Universitäten St.Gallen, Lausanne, Bern. *Q*

RESEARCH





Malaria transmission: is insecticide resistance a problem?

THE SPREAD

A NEWSLETTER FROM THE MCID

Article by: Dr. Jonathan Hamley and Prof. Dr. Deborah Stroka (Department of Visceral Surgery and Medicine, University of Bern, Inselspital / Department of BioMedical Research(DBMR))

At the beginning of this decade, the World Health Organization estimated that half of the world's population were at risk of contracting malaria, with most cases occurring in sub–Saharan Africa, and most deaths in children under the age of five. Malaria is transmitted by *Anopheles* mosquitoes, and although there are several parasite species which cause the disease in humans, *Plasmodium falciparum* is the most common in Africa. An individual can contract the disease when bitten by an infected female mosquito, which requires a blood meal to lay eggs. An effective and widely used method to reduce malaria transmission is to prevent mosquitoes from biting using insecticides. The modern era of insecticide use began in the 1940's, and since the 1970's a group of insecticides called pyrethroids have been commonly used to protect people from being bitten by mosquitoes. Since Anopheles mosquitoes typically bite in the late evening and night-time, sleeping underneath a bed net treated with an insecticide reduces the chance of being infected with malaria, because it repels or kills the mosquito. Insecticides are also sprayed inside houses to kill any mosquitoes which may enter.

Widespread use of insecticides has exerted strong selection pressure on mosquito populations. Mosquitoes containing genetic mutations which provide protection against insecticides reproduce more than those which are susceptible to insecticides, leading to the spread of resistance. To monitor insecticide resistance, mosquitoes are collected in the field, and their survival is checked shortly after an exposure to an insecticide. In many parts of the world, it is now common to find mosquitoes which can survive what were previously lethal doses of insecticides¹.



Dr. Jonathan Hamley



Prof. Dr. Deborah Stroka

At first glance, one might expect that areas in which insecticide resistance is detected should have more cases of malaria, but numerous studies have found that this is not necessarily the case². One explanation for this counterintuitive observation is that the evolution of resistance results in changes in other characteristics of the mosquito. To understand why this is important, we must consider the interactions between the malaria parasite and its mosquito vector. The parasite takes a minimum of 10 days to fully develop inside the mosquito and be transmitted. This means that even a short reduction in the lifespan of the mosquito can reduce the probability of transmission.

It has been suggested that mosquito strains which are resistant to insecticides (i.e., they do not die shortly after being exposed), might still suffer reduced survival later in life. In other words, being resistant to an insecticide is costly to the mosquito. If we took sensitive and resistant mosquito strains but did not treat them with insecticides, the resistant strain would not live as long as the sensitive strain.





The idea that selection for one trait can result in evolutionary changes in another was first recognised by Charles Darwin. However, our understanding of how the processes within mosquitoes determine their evolution, and therefore their ability to transmit malaria is far from complete. A more refined understanding of mosquito evolution will allow us to make more accurate predictions regarding the transmission of malaria. The mosquito must use energy to maintain the machinery for the detoxication of the insecticide and generate an immune response against the malaria parasite. At the same time, the parasite relies on the energy available inside the mosquito for its development. The metabolism of energy creates oxidative stress which contributes to the mortality of the mosquito (figure 1, top panel). Additionally, the depletion of energy reserves is likely to impact the survival of the mosquito. Thus, we can consider the mortality of the mosquito, in part, as a consequence of energy use. As the mosquito evolves to use more of its energy to protect itself against insecticides, this might deplete its energy reserves and result in a more rapid accumulation of oxidative stress.



Figure 1: Energy use within the mosquito determines its survival (top panel). The survival of the mosquito determines malaria transmission (bottom panel).

Our project with the MCID has two parts. The first has involved developing mathematical models to understand the evolution of senescence in disease vectors in the context of energy use. Mathematical modelling is an indispensable tool in biology because it allows us to make predictions which would be difficult to obtain experimentally. However, an ongoing challenge in the use of these models to predict vector evolution and disease transmission is to correctly capture biological processes. Currently we are attempting to inform this theoretical framework with data from experiments on insecticide resistant and sensitive mosquitoes. We are interested in the relative contributions of resource depletion and oxidative stress to survival. Using these data, we can estimate parameters in our model and validate its structure. The second part of the project will integrate these new mathematical representations of within-mosquito dynamics with a model which accounts for malaria transmission between mosquitoes and humans (Figure 1). This model will improve our understanding of how insecticide resistance influences other traits of the mosquito which are important for malaria transmission. This will allow us to more accurately predict how insecticide resistance will impact the number of people who will be infected by the *Plasmodium* parasite.

References

¹World Health Organization. 2016. Test procedures for insecticide resistance monitoring in malaria vector mosquitoes, 2nd ed. 2

²Alout H, Roche B, Dabiré RK, Cohuet A. 2017. Consequences of insecticide resistance on malaria transmission. PLOS Pathogens 13:e1006499. *Q*





Unlocking the Virus-Host Interplay to enhance pandemic preparedness: Focus on the SARS-CoV-2 Protein Nsp1

THE SPREAD

A NEWSLETTER FROM THE MCID

Article by: Dr. Evangelos Karousis (Department of Chemistry, Biochemistry and Pharmaceutical Sciences)

The complex interplay between viruses and the host cells they invade can pose threats to public health and fascinate scientists. Investigating viral mechanisms of host cell invasion also provides key answers to critical social challenges and enhances pandemic preparedness.

A critical element of any viral infection is the dependence of viruses on the host cell's molecular mechanisms. Unable to generate new progeny independently, viruses rely on the host cell metabolism to replicate, often significantly reducing or even halting the host cell's own protein production. Protein synthesis is a necessary step for producing new viruses. The load of virus production falls on the host mRNA translation machinery. Given the importance of mRNA translation in the life cycle of all viruses, it has become a hub of vibrant research over the past few decades. Therapeutic approaches based on understanding mRNA translation during viral infections include drugs targeting Poliovirus, Hepatitis C and HIV infections. Equally importantly, many host cell mechanisms have been revealed by deciphering this interplay.

In recent years, the SARS-CoV-2 virus, responsible for the COVID-19 pandemic, has been in the spotlight of virology research. Among the many proteins produced by the SARS-CoV-2 virus, non-structural protein 1 (Nsp1) plays a crucial role in this host-virus interaction. Non-structural viral proteins catalyse necessary steps for viral propagation or interfere with cellular activities to tilt the metabolic balance to benefit the virus. Even though Nsp1 is not a structural component of the virus, it is a potent tool in the viral arsenal because it inhibits host protein production but allows viral protein synthesis. This phenomenon impacts the severity of the disease because it disrupts cell homeostasis and allows viral propagation.



Dr. Evangelos Karousis

Moreover, as the virus spreads and evolves within the human population, various strains have emerged, each with unique mutations. These variations add complexity to our understanding of the virus and underscore the urgent need to elucidate how these changes may influence the host-virus interaction and alter the course of the disease. However, the part of the viral genome encoding Nsp1 is resistant to mutations, highlighting the importance of this protein for viral propagation.

Guided by these challenges, our research focuses on three central objectives (Figure 1). Our first goal is to gain a more profound comprehension of the mechanism of translation inhibition mediated by SARS-CoV-2 Nsp1. We dissect piece by piece the role of every Nsp1 segment, and we delve into the impact of a particular section of the Nsp1 protein, known as the N-terminal domain, on the host cell's protein production. In this process, we also compare the activity of Nsp1 originating from mutant strains of SARS-CoV-2 in the human population.





Our second aim is to scrutinise the role of Nsp1 from other coronaviruses on host protein production, broadening our perspective beyond just SARS-CoV-2. Lastly, we create a screening platform, enabling us to evaluate small molecules for their potential to hinder host protein production and examine inhibitors of viral proteins that obstruct protein production.



Figure 1: Main research objectives. View of Nsp1 bound to the small ribosomal subunit adapted from ¹

Early after the breakout of the Covid pandemic, we revealed the mechanism of host cell translation inhibition by Nsp1 in collaboration with the research groups of Nenad Ban at ETH Zürich, Oliver Mühlemann and Volker Thiel at the University of Bern¹. We focused on the C-terminal part of the protein, visualised by Cryo-EM bound to the small ribosomal subunit. Biochemical assays verified critical amino acid residues that are important for translation inhibition. We showed that part of the Nsp1 protein binds the ribosome in the region of the mRNA channel. It was essential to decipher how Nsp1, one of the first proteins produced upon SARS-CoV-2 infection, inhibits human translation. However, the role of the N-terminal part of the protein remained unclear, and it could not be explained how viral mRNAs can be translated in the presence of Nsp1.

In a recent interdisciplinary study performed by Nenad Ban, Oliver Mühlemann, Joseph Puglisi and my group, we combined biochemistry, structural biology and single-molecule experiments to decipher the function of the N-terminal domain of the Nsp1 protein from different coronaviruses. In this study, supported by the MCID, we discovered that this protein segment protects viral mRNAs from Nsp1-mediated translation inhibition. This nuanced mechanism showcases the virus's sophisticated strategies for survival and replication within host cells².

Our investigations into Nsp1 proteins from different coronaviruses led to an intriguing finding. Despite their varied origins and sequences, these proteins share common structural features and strategies to impede host protein production by binding the small ribosomal subunit to inhibit translation initiation on host mRNAs. Our results show that different coronaviruses, such as SARS-CoV-2, MERS-CoV, and a coronavirus that infects bats (Bat-Hp-CoV), shut down the production of host cell proteins allowing the production of viral proteins sharing a common mechanism². These discoveries highlight the resourcefulness of these viruses and indicate Nsp1's potential as a promising target for new therapeutic interventions.

Parallel to these explorations, we also develop a screening platform to identify small molecules that disrupt human translation or the virus's takeover of host protein production (Figure 2). Our assay is based on a translation system that we developed recently that allows us to recapitulate the complex mRNA translation reaction in the test tube (cell-free translation). So far, the difficulty of producing translation-competent lysates from living cells is mainly attributed to the variation during cell lysis. Using a method from the chemical industry called dual centrifugation, we can now lyse cells under mild buffer conditions, producing ample amounts of human, translationcompetent lysates³.

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This innovative approach enables us to test potential protein synthesis inhibitors and possible inhibitors of viral proteins that impact translation, opening up new possibilities in developing antiviral therapeutics. These findings represent significant strides in our ongoing efforts to understand and combat these ingenious pathogens.

Our research has provided a clearer picture of the complex interplay between SARS-CoV-2 and host cells, shedding light on the virus's survival strategies and unveiling potential weak points for intervention. Recent findings underscore the crucial role of the Nsp1 protein and its N-terminal domain in the virus's life cycle, offering new possibilities for drug targets. As we continue to live in the shadow of COVID-19, these insights are not just academic curiosities but vital knowledge that could pave the way for more effective prevention and treatment strategies.

We also aim to refine and expand our testing platform. As we uncover more about the activities of viral proteins such as Nsp1, we can better tailor our testing strategies to identify potential inhibitors.



Figure 2: Production of translation-competent lysates and overview of a cell-free translation screening assay. Created with BioRender.com.

Even though we use coronavirus proteins as a proof of principle for our approaches, the insights gained from this research have implications for a broad range of viruses and the very fundamentals of virology. Every bit of knowledge about the interactions between viruses and host cells improves our understanding of viral infections and can guide future research into new treatment and prevention strategies. In a world where viral threats continue to evolve, this type of research is more critical than ever. In a sense, our research is a race against potential threats, and with every piece of the puzzle we put into place, we build up pandemic preparedness. The quest for knowledge is an ongoing journey, and in our fight against viral diseases, each new insight also serves as fuel for training the next generation of scientists.

References

¹Schubert, K. et al. SARS-CoV-2 Nsp1 binds the ribosomal mRNA channel to inhibit translation. Nat. Struct. Mol. Biol. 27, 959–966 (2020). ²Schubert, K. et al. Universal features of Nsp1-mediated translational shutdown by coronaviruses. 2023.05.31.543022. Preprint at ³Gurzeler, L.-A., Ziegelmüller, J., Mühlemann, O. & Karousis, E. D. Production of human translation-competent lysates using dual centrifugation. RNA Biol. 1–12 (2021) 2



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Gain-of-function research: a brief introduction to a hot topic

Article by: Dr. Rebecca Limenitakis (MCID) and Prof. Dr. Carmen Faso (MCID / Institute of Cell Biology (IZB) / Institute for Infectious Diseases (IFIK))

What is gain-of-function research and why is it the subject of heated debate and regulatory guidelines being drawn up in many countries?

Gain-of-function research (GOFR) in its broadest sense encompasses all research in which the phenotype of an organism (one or more of its observable characteristics), is artificially enhanced. When applied to infectious disease agents, GOFR generally concerns enhanced virulence, transmission, infection rate and proliferation of a pathogen. Frequently, but not always, this is achieved through genetic manipulation.

The process of genetic manipulation, also referred to as genetic engineering, relies on technology to actively modify the genetic makeup of an organism, including, for example, the transfer of a gene from one organism to that of another. The first such genetic manipulation process was carried out in 1973, when DNA from one bacterium was successfully introduced into a second bacterial species, resulting in a genetically modified bacterium. Since this time, genetic manipulation has become a standard and increasingly efficient tool in thousands of laboratories around the world and countless genetically modified organisms are generated every day.



Genetic manipulation can allow invaluable insight into the fundamental processes of how different organisms function. Fusing genes of interest with genes encoding fluorescent proteins allows researchers to, for example, locate proteins in the cell. Removing entire genes from an organism can allow the understanding of what role that gene, or often more specifically the protein it encodes, plays. The removal of a specific gene, or even just the changing of a single base pair of DNA, may, for example, prevent a virus entering a specific type of cell, may mean that a parasite is no longer motile, or that a bacterium can no longer be treated with a specific antibiotic. So, ge-





netic manipulation in the case of infectious diseases can help us prevent infection and treat those who become infected. At the same time, the same techniques offer the possibility of creating pathogens that have acquired a mutated and potentially more virulent and less resistant to treatment, phenotype.

This is where we enter into areas of potential concern.

The first described cases of intentional GOFR to investigate virulence were published in 2012, when two research teams independently genetically modified the highly pathogenic avian influenza virus H5N1, not capable of person-to-person transmission, to render it transmissible, via aerosol droplets, between ferrets. While these studies importantly revealed the clear potential of the H5N1 virus to naturally mutate in a way that would allow humanto-human transmission, they also sparked significant concerns regarding the potential risks of generation and potential release of new and/or enhanced infectious agents.

"Why would one set out to make a pathogen more dangerous? Where's the benefit of that?", one might ask. The answer, in a vast majority of cases, is to contribute to preparedness for threats by potentially deadly pathogensto be one, or more, steps ahead of where evolution may naturally take the pathogen. Consider this example: a novel virus is found to be circulating in horses and leading to disease symptoms. How likely is it that the virus can jump to infecting humans? Should widespread measures separating humans from contact with horses be considered? By mutating specific genes of the virus and testing whether or not viruses with single- or multiple differentmutations can infect human cells in culture, information can be gathered on the potential risks associated with this newly identified virus. Such research may also be valuable in the development of a potential vaccine against the virus. The downside, of course, and the one that raises alarm bells, is generation of a virus that is potentially infectious to humans and, which, without manipulation would not have been- or at least not yet.

The possibility, however small, that the Covid-19 pandemic could have been caused by the accidental release of a SARS-CoV-2 from a laboratory has intensified debates around research involving potentially pathogenic organisms and has galvanized public opinion in unprecedented ways. As a population, we were largely unprepared for the sudden spread of a highly infectious virus- and while lessons have been learnt, we may not yet be ready for the next pandemic to arrive. If one discounts any thoughts of malevolence, how is GOFR controlled? Which safety mechanisms are in place and how are they enforced? Should it be happening at all?

These fundamental questions have triggered strong opinions from within political and scientific communities, sometimes clearly at odds with each other. Some of the topics under discussion include if and how proposals for intended GOFR should require official approval- and by who, whether restrictions should be placed on who can perform GOFR, whether any blanket bans should be made on GOFR with certain pathogens and how biosafety and biosecurity of labs performing GOFR can be regulated, including on a global level. Provisional (and very restrictive) guidelines for the authorization of GOFR have been drawn up in the US that aim to minimize the risks associated with gain-of-function research on pathogens that have pandemic potential¹. While these await potential modification and approval, GOFR continues to be a hotly debated topic worldwide, and similar regulations are likely to be drawn up in many countries.

Reference

¹ "Proposed biosecurity oversight framework for the future of science"-DRAFT, National Science Advisory Board for Biosecurity Working Group, US. 2



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Bright and early: meet two MCID early career researchers

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Interview with:

Dr. Bettina Zimmermann, Recipient of MCID Early Career Research Grant for Women (ECRG-W), Institute for Philosophy, and

Dr. Obdulio García-Nicolás, Recipient of Career Development Grant, Institute of Virology and Immunology, Vetsuisse Faculty (IVI)

Can you describe briefly your MCID-funded project and what you aim to achieve?

Bettina: In the ESPRIM project, I aim to describe relationships between science, politics, and the traditional mass media during COVID-19 and contrast those empirical findings with suggestions from the literature on how these relationships should be in Western democracies. I do interviews with scientific advisory board members in Switzerland, Germany, and the United Kingdom and content analyses of policy documents and newspaper articles.



Dr. Obdulio García-Nicolás

Obdulio: I am a co-applicant on the MCID-funded project entitled "Role of sheep and rodent reservoirs for Wesselsbron, a neglected zoonotic flavivirus", together with Prof. Charaf Benarafa. Wesselsbron virus (WSLV) is a mosquito-borne flavivirus endemic of Sub-Saharan Africa, that infects small ruminants (such as sheep and goats), but also other mammals including humans and rodents. We aim to evaluate if events of direct transmission between sheep is possible in absence of mosquitoes, and to identify which body fluids/secretions contain the virus and therefore represent a threat to humans. We are also determining the susceptibility of rodents to identify potential virus reservoir species. In addition, we are establishing diagnostic tools with improved sensitivity and specificity.

How do you think your project can contribute to preparation for infectious disease threats?

Obdulio: WSLV is a classic zoonotic neglected pathogen that has expanded in Africa in recent years. Climate change, trade and travelling activities favor a further spread to other continents. To protect the human and animal population, is therefore crucial to understand the virus's transmission pathways, its reservoir, its pathogenesis and to have specific and sensitive diagnostic tools ready.

Bettina: Pandemics are multi-faceted crises where e.g. social, economic, political, ethical and public health aspects need to be weighed in policymaking. Assessing the relationships between science, politics and the media during the COVID-19 pandemic from an interdisciplinary perspective contributes to a more holistic understanding of how such relationships could be established before and during future pandemics.

What do you see as being the main challenges in multidisciplinary research?

Bettina: Multidisciplinary research is at the core of what I have been doing in my past and present research projects. I was trained in the biomedical sciences but then graduated in bioethics, a field in-between the humanities and the social sciences. So I have been confronted with different research traditions throughout my academic career. One of the challenges, in my experience, is that people bring in fundamentally different understandings of how rigorous science should be conducted. Research interests can be fundamentally different, too, and the publish-or-perish system of science is not helpful in that regard because everyone is pushed to focus on their research discipline. I find the debate and dialogue related to these challenges with open-minded researchers very exciting.



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What excites you about multidisciplinary research?

Obdulio: There is a Spanish proverb that could be translated as "who grasps too much loses everything". This is something I like to think when working in a project that required expertise in different fields. I find it exciting to successfully reach common aims of the project with the contribution of different researchers that master their specific field of expertise.

How do you see the importance of communicating with the public in preparing for times of crisis?

Bettina: For the research project SolPan, my colleagues and I talked to several hundred people that were to represent "the public" in various countries. I take away from their reports and experiences that communicating with the public is a double-edged sword: On the one hand, communication is obviously crucial, because people's behaviour and compliance with mitigation measures is what boosts or hinders infection. On the other hand, I heard many people complaining about too much information, about being confused because of uncoordinated and seemingly contradicting communication from politics and science. So we have to be aware that more communication is not necessarily better and that coordinated, high-quality communication is crucial. I think this is an important part of pandemic preparedness.



Dr. Bettina Zimmermann (photo: Linda Schier)

Obdulio: Communication is key to ensure the success of control measures during crisis. A great example was the COVID-19 crisis, when scientific experts from different fields, public health authorities, and politicians tried to translate to the society the importance to compliance to the different measures to control the spread of SARS-CoV-2 infection. The communication of understandable key messages to ensure why certain control measures are required and why vaccination is beneficial despite its side effects has been a main challenge. A main problem will always be the complexity and dynamics of an epidemic that requires frequent adaptations, misinformation and political abuse of the situation.

How has your career path led to your research as a Member of the MCID?

Obdulio: Since I arrived at the group of Prof Artur Summerfield at the IVI in 2014, I have been studying emerging virus infections with a strong focus on Japanese encephalitis virus (JEV) and related flaviviruses. My focus was on host-virus interactions, possible transmission pathways, species tropism, species adaptation and the immune response. One of the key points leading to our MCID project was the identification of direct pig-to-pig transmission by JEV. Screening the literature indicates that mosquito-independent transmission also occur with other flaviviruses. The question if WSLV can be directly transmitted between animals, and if the virus can be found in mucosal secretions and milk is highly relevant from a One Health perspective, therefore the MCID call was a perfect fit for such a project. Read Obdulio's bio: *Q*

Bettina: I defended my PhD in Bioethics in during the first wave of the COVID-19 pandemic. I was starting a postdoc at the Technical University of Munich and my boss, Alena Buyx, approached me in early March asking if I wanted to be part of an international research project (SolPan) investigating people's lived experiences during the pandemic. We ended up doing qualitative interviews with residents in ten European countries in April 2020, October 2020, and October 2021. I became the co-leader of the Swiss study arm. This project and the opportunity to do cutting-edge empirical research during the pandemic have driven my research interest in infectious diseases, which has led me to apply for an Early Career Research Grant for Women at the MCID. Read Bettina's bio: *Q*







News

MCID Ethics and Policy Lab managers receive mandate from Federal Food Safety and Veterinary Office

MCID Ethics & Policy Lab managers Caroline Brall and Caroline Schlaufer mandated to conduct a project on "Creating political acceptance for disease control measures in household pets: a public policy and ethics perspective". *P*

MCID to Co-lead ARUA-The Guild Cluster of Research Excellence, Genomics for Health in Africa

In June 2023, the African Research Universities Alliance and The Guild of European Research-Intensive Universities announced the launch of 17 Clusters of Research Excellence, one to be Co-Lead by the MCID. Read more overleaf and here *Q*

Possibility of engaging in MCID-funded research, "Pandemic stories", for those in Canton Bern

The team of project "Divided Pandemic Society and Public Health: Polarization in the Covid-19 Pandemic Response in Switzerland", seek people in Bern to share their experiences of the Covid-19 pandemic. Read more and get involved here: Q.

Events

MCID symposium on the revision of the Swiss Epidemics Act

On 16th January 2024, the MCID will host an information event on the revision of the Swiss Epidemics Act. The event (in German) will present the revision process and allow exchange between scientists, politicians and the administration \mathcal{P}

1st European Swine Influenza Network - COST Training School

Between 5th and 8th September 2023, the European Swine Influenza Network COST action (ESFLU) will hold a training school, part-sponsored by the MCID, aimed at young scientists with a keen interest in swine influenza A virus. ESFLU: *Q*

Swiss Meeting for Infectious Disease Dynamics (SMIDDY) 2023

On 20th October, the 2023 SMIDDY event will take place: Modelling infectious diseases during the pandemic: advances in methods and its role for policy making. For more information and registration (until 15th September): *Q*

MCID seminar series

Visit the MCID website to stay up-to-date with the MCID seminar programme. MCID seminars are held in-person and are aimed at a multi-disciplinary audience *Q*

Highlighted publications

Banholzer et al on MCID-funded research looking at SARS-CoV-2 transmission in the classroom

The project team, lead by Lukas Fenner, Phillip Jent, Pascal Bittel and Tina Hascher, report on the effect of mask wearing and air purification on the transmission of SARS-CoV-2 in the school classroom *Q*

Jonathan Hamley et al. on optimising treatment against Oncocerca volvulus, causal agent of river blindness

Jonathan Hamley, MCID Associate Member, and co-authors use modelling approaches to predict the effectiveness of *Oncocerca volvulus* treatment with moxidectrin, determining elimination probabilities under a range of different conditions *Q*

Johanna Hornung and Fritz Sager on evidence usage in policy making on sugar-sweetened beverage taxes

MCID Society and Law cluster members, Johanna Hornung and Fritz Sager investigate why few European countries have adopted a sugar-sweetened beverage tax despite proven benefits on public health; an example of non-use of evidence *Q*

Olivier Guenat et al on a novel inflammation-on-chip model allowing immune cell live imaging during inflammation

MCID Immunity cluster member, Olivier Guenat, and team, develop a novel on-chip model of the lung-endothelial barrier that allows live-imaging of immune cells as they migrate into and through lung tissue during inflammation events *P*

Sebastian Leidel et al on an RNA-linked virulence mechanism in pathogenic yeast

Sebastian Leidel, MCID Immunity cluster member, and colleagues, identify the mechanism through which modifications of the Nsc2 protein affect virulence of both baker's yeast and the common fungal pathogen *Candida albicans Q*

Britta Lundström-Stadelmann on the mechanisms of action of anti-Echinococcus compounds

Britta Lundström-Stadelmann, of the MCID Neglected Diseases cluster, and collaborators, investigate the mechanism of action of the antimalarial mefloquine (and derivatives) in treatment of echinococcosis, identifying potential targets *Q*





Clusters of Research Excellence

In June 2023, Vice-Chancellors and Presidents of the African Research Universities Alliance (ARUA) and The Guild of European Research-Intensive Universities (The Guild) gave their stamp of approval to 17 Clusters of Research Excellence (CoREs). These CoREs aim to tackle issues of global importance in key areas aligned with the Global Gateway's AU-EU Innovation Agenda and with a sharp focus on capacity building and societal impact on the African continent.

The MCID, together with Co-Leads at Stellenbosch University and the University of Tübingen will Co-Lead a CoRE, **Genomics for Health in Africa (GHA)**. This CoRE will focus on genomics, protein structural analysis and informed drug design as tools in infectious disease, rare disease and cancer research and treatment, in and for Africa, striving for continent- wide improvement in public health. The key aim of CoRE-GHA will be capacity building, to be realised through the establishment of an exchange program and a split-site/sandwich doctoral program, with the involvement of all involved CoRE- GHA partners.



The MCID additionally has the role of Core-Partner in a second CoRE, **Advanced Infectious Diseases Research and Training**, to be Co-Lead by the University of Ghana, University of Glasgow and the University of Tübingen. For a full list of all Co-Leads, Core-Partners and other partners involved in both CoREs, see here *Q*. Read more here about the ARUA-The Guild Clusters of Research Excellence *Q*.

Visit of Tulio de Oliveira to the MCID

Prof. Dr. Tulio de Oliveira became a household name during the Covid-19 pandemic for his role in the discovery of the SARS-CoV-2 Beta variant in 2021 and the Omicron variant in 2022 through a massive scale sequencing effort in South Africa. Prof. de Oliveira is professor of bioinformatics at the University of Kwa-Zulu-Natal and Stellenbosch University, where in 2021 he founded CERI, the Center for Epidemic Response and Innovation. Together with Prof. Dr. med. Shahida Moosa he is one of the CoRE-Genomics for Health in Africa Co-Leads.



On 25th June, we were honoured to welcome Prof. de Oliveira to the University of Bern where a number of presentations were given on MCID activities. Tulio was welcomed by Prof. Dr. Hugues Abriel, Vice-Rector Research, the MCID Management Office and a number of MCID Members. Presentations were made on each of the MCID Core Activities, and a small number of MCID-funded or linked projects. This provided an ideal opportunity to identify and discuss common research interests and the MCID looks forward to exploring these further with Tulio and his team within the frame of CoRE-GHA.



MCID MULTIDISCIPLINARY CENTER FOR INFECTIOUS DISEASES







The Multidisciplinary Center for Infectious Diseases (MCID) is a strategic center of the University of Bern, Switzerland, founded through the generous support of the Vinetum Foundation

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