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Commentary

Biomedical Research Goes Viral: Dangers and Opportunities

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Researchers around the globe have been mounting, accelerating, and redeploying efforts across disciplines and organizations to tackle the SARS-CoV-2 outbreak. However, humankind continues to be afflicted by numerous other devastating diseases in increasing numbers. Here, we outline considerations and opportunities toward striking a good balance between maintaining and redefining research priorities.

The world is currently facing a global pandemic without precedence within our lifetime, and there is an urgent need of research breakthroughs. It is encouraging and exciting to observe how leading research organizations and scientists across all disciplines are actively redeploying efforts to help identify and implement solutions, bringing a constellation of the brightest minds working on the COVID-19 acute societal challenge together. The importance of such global effort has also catalyzed rapid mobilization of funding bodies in support of these operations, accelerated eagerly anticipated changes in research culture, and brought about a beautiful manifestation of exercising research freedom. Across the world, leading scientists and research organizations are united in the joint fight against the devastating threat we are all currently facing. Many research centers have redeployed trained personnel to actively join in helping at local hospitals and health departments, in addition to providing instruments and reagents to colleagues in need of those to better fight the pandemic and repurposing research facilities to accelerate translational impact. Virologists, immunologists, geneticists, molecular biologists, lung biologists, epidemiologists, and computational biologists, among others from all fields of biomedical sciences, together with clinicians of numerous disciplines are working feverishly to answer COVID-19-related questions, accelerate diagnostic testing, and enable development of vaccines and therapeutics. Scientists across the board, from early-career trainees to seasoned department heads, are rolling up their sleeves to make a scientific contribution that may help overcome the crisis sooner with fewer casualties and less societal damage. There is no question that this historic worldwide effort is impressive and should enforce society's trust in science while inspiring the next generation of budding scientists to find their calling.

It is clear that experts with appropriate training and long-accrued experience in fighting pandemics ought to be and are indeed leading the way in our current challenge and also that they ought to be ably supported and assisted by scientists worldwide in their monumental efforts. Along those lines, new approaches from basic research can plug in fast for innovative therapeutics, such as Cas-based technology. In addition, widely adopted digital tools such as smartphone applications are now being rapidly developed, deployed, and used to track contact and symptoms. Population-based biobanks and epidemiological cohorts across the world are joining forces to empower large-scale surveillance and research in infection trajectories, pathophysiology, outcomes, and underlying genomics. These approaches benefit from an interdisciplinary approach and have started to make progress in understanding transmission patterns in recent weeks, for example.

However, widespread redeployment of world-class expertise from other areas into the current acute phase of COVID-19 research can lead to substantial loss of focus. A longer-term diversion of resources runs the risk of stifling much-needed new basic research and technological breakthroughs that have the potential to revolutionize biomedicine. For example, the development of CRISPR-Cas genome and transcriptional engineering tools has the potential to considerably transform biomedicine (including the fight against COVID-19). Therefore, similar basic research breakthroughs with major potential for transformative societal benefits should not be prevented, risked, or delayed. A refocus on COVID-19 research activities is likely to engender adverse effects on society's clear and urgent need for sustained research into major diseases, which will continue to afflict humankind and remain leading causes of death and disability well beyond the end of the acute COVID-19 challenge. Such a dynamic carries the risk of hindering breakthroughs and can dilute, delay, and

Figure 1. Keeping the Eye on the Ball
While acting swiftly and decidedly to fight the pandemic, the scientific field cannot afford to lose focus on important research missions to fight other growing health challenges. Illustration: Charlie Padgett.

disrupt ongoing team efforts to tackle these equally devastating health challenges.

Clearly, this is neither the time to be divided nor to act without decisiveness. However, as a global research community, it is important to keep an eye on the fact that, worldwide, people (including children) are still dying of diseases other than COVID-19. These numbers will go up for a long time to come if clinical, translational, and basic researchers shift their focus away from fighting these killers. It is impossible to predict in detail what this hiatus could mean for grand challenges we have collectively been striving to combat for decades. Here, we comment on societal threats and research challenges using the representative examples of cardiometabolic diseases and cancer, which will continue to plague humankind in the future (Figure 1). We further highlight lessons to be learned from the current acute response to the COVID-19 threat and outline opportunities not to be missed for accelerating, rather than hampering, progress for biomedical research more widely. Importantly, beneficial developments like international teams working together rather than in competition, faster processing by regulatory bodies, and fast sharing of data are all positive developments likely to speed up translation of research results in the future.

Cardiometabolic Diseases

Obesity is still imposing a major global threat to human health. Obesity numbers continue to grow exponentially across the globe, thus making metabolic dysfunction a long-term challenge for global health care systems. The immense impact of obesity on population health is illustrated by both the fact that the consequences of over-nutrition have bypassed under-nutrition as a leading global burden to human health and by the role of obesity-related metabolic dysfunction as a risk factor for further long-term cardiovascular complications (Finucane et al., 2011). Most notably, type 2 diabetes affects more than 400 million people worldwide today, and the closely correlated cardiovascular diseases remain the main cause of death in Western societies, with a similar upward trajectory in low- and middle-income countries commensurate with recent demographic shifts (WHO, 2016). Halting or slowing down scientists' and clinicians' efforts to predict, treat, and eventually cure metabolic complications may thus endanger direly needed progress in (1) defining diabetic sub-populations with specified requirements for treatment and complications prevention, (2) developing personalized therapeutic strategies to counteract diabetic metabolic dysfunction and their long-term (cardiovascular) complications, and (3) employing pancreatic beta cell regeneration and functional restoration to finally overcome the disease. Of note, beyond the classical obesity- and diabetes-related complications, recent global research has further highlighted that defects in energy homeostasis serve as prime risk factors for many cancers, thereby rendering obesity and diabetes prevention and therapy into a critical measure to protect against malignant diseases in the long run (García-Jiménez et al., 2016). Finally, the mutual impact of metabolism and immune responses ("immuno-metabolism") has gained significant attention by the global research community. Indeed, numerous examples have been discovered on how metabolism in obesity and/or diabetes affect the recruitment and function of immune cells and vice versa. Decades of research on immuno-metabolic pathways will support our fight against long-term chronic metabolic dysfunction (Li et al., 2020). Even if it is not as front and center in the pubic media or our minds today, we cannot afford to lose this fight, as it concerns hundreds of millions of patients with numbers constantly and rapidly increasing. Diverting focus or support away from the important long-term efforts to fight cardiometabolic diseases has consequences that will certainly be as devastating and as lethal as the COVID-19 pandemic.

Cancer

Worldwide, the number of newly diagnosed cancer patients will increase from 18 million today to approximately 30 million in the year 2040, posing a substantial challenge to cancer care systems and to cancer research (https://gco.iarc.fr/today/). Most of this growth will occur in low- and medium-income countries, but the number of cancer cases will continue to rise at least in the coming decade in high-income countries as well. The reasons for this alarming forecast are a growing world population, increasing life expectancy with a cancer risk that increases with age in a number of countries, and higher exposure to unhealthy lifestyle factors. For example, about 40% of all cancers could be prevented if all currently known risk factors were avoided by all citizens (https://www.who.int/). Importantly, many of these risk factors also contribute to other widespread health threats. In addition, non-malignant diseases such

as chronic inflammation, non-alcoholic steatohepatitis, diabetes, and a range of different infections may per se be a causative factor for cancer—calling for joint research across different fields of health sciences (de Martel et al., 2020; Gallagher and LeRoith, 2015; Malehmir et al., 2019).

Another important concern of oncologists and cancer researchers is the growing number of cancer survivors, which already represents a multiple of the number of new cancer cases and will continue to grow as cancer care improves (Shapiro, 2018). Cancer survivors are exposed for very long times, if not for life, to the risk of recurrence, secondary cancer, morbidity caused by neoplastic disease or therapeutic interventions, psychological sequelae, and reduced quality of life as well as socioeconomic disparities. A growing challenge is also that the average age of cancer patients will increase in the coming years. Translational and clinical cancer research has in the past mainly been performed in small, selected cohorts of relatively fit younger and elderly patients, which may not be representative of the more frail and multimorbid cancer populations to be treated in the future (Overgaard, 2015). As a final example, the majority of cancer patients in the future will live in countries that have so far been heavily underrepresented in both preclinical and clinical cancer research. This carries substantial risk that new strategies might lead to unexpected results.

To address these and other challenges, research of the biology of cancer and healthy tissues at risk of side effects must be conducted together with population sciences, and the development of new diagnostic and therapeutic approaches needs to be performed in populations that reflect the future global cancer burden. The results of this research are expected to feed into three major anti-cancer strategies: (1) primary prevention as the only option to reduce the burden of new cancer cases, (2) early detection of cancer at stages that are curable with therapies are already at hand, and (3) improved diagnostic-therapeutic interventions that widen the therapeutic window between tumor control and damage to healthy tissues or impairment of quality of life.

Pronounced biological heterogeneity exists between tumors of the same type in different patients, as well as between subvolumes of the same tumor and primary tumors and metastases. Tumor biology also changes over the course of tumor progression and therapy. Additional heterogeneity exists between healthy organs of different patients. Therefore, all anti-cancer strategies mandate an increasingly personalized approach (Baumann et al., 2016; Dagogo-Jack and Shaw, 2018). Personalized bioassay-based oncology, mainly in the field of drug-based cancer treatment, has in many aspects paved the way for personalized medicine in general. This approach must be strengthened by global networking and should also be extended toward personalized primary prevention and early detection beyond the few examples already established today. A translational framework covering the continuum from discovery research to outcome and population research appears to be best suited to address the very substantial challenges that cancer and other major diseases will pose on our societies in the decades to come (Eggermont et al., 2019; Ringborg, 2019; Wild et al., 2019). To be successful on a global scale, the vast disparities existing in the world need to be taken into account. It is therefore of paramount importance that the COVID-19 pandemic is not interpreted as a calling to refocus but as a calling to unite and a unique chance to learn lessons toward integrating, balancing, and improving biomedical research programs across disciplines.

Opportunities for Biomedical Research Going Forward

The COVID-19 crisis has engendered a rapid shift in research focus and culture. Biomedical research going forward ought to capitalize on this disruptive effect. There exist several areas of these recent changes that can stand the wider biomedical science field in good stead going forward. Indeed, success in global mobilization of research endeavors can and should be co-opted and adapted to speed progress for research on cancer, diabetes, and other big societal health challenges. Open data sharing and implementation of the FAIR principles have become common goals and are in fact increasingly mandated. Rapid peer review and publication of results has served the community well. Regulatory processes by institutional review boards and authorities, sometimes a hurdle to fast translational successes, have been rapidly adapted to more efficient workflows. Global collaboration has flourished, with shared resources, exchange of materials, expertise and technologies, open communication, and transparency allowing for quicker, better, more impactful research insights. Hospital departments and research labs have quickly worked hand in hand in a bidirectional translation approach, which was often not pragmatic only few months ago. Interdisciplinary teams have formed and quickly learned to understand each other's languages, with excellent examples of success stories emerging already. Harmonization of efforts to enable meaningful meta-analysis is leading to better-powered research and impactful outcomes. The requirement for social distancing, which also holds true for scientists all over the world, together with the suddenly increased pressure to come up with novel solutions to new and old challenges, has culminated in innovative digitization of scientific processes. Forced integration of data science tools (apps), real-world studies (new cohorts), artificial intelligence, and cutting-edge laboratory research into one rapidly adaptive global research program constitutes developments that will not be reversed but rather will accelerate progress across disciplines long after the COVID-19 pandemic has been brought under control.

Further, we need to understand why certain diseases—cancer, obesity, and diabetes among them—appear to be predisposing to more serious progression of COVID-19 cases. This could indeed lead to improvements in precision prevention and personalized therapy of virus infections and additionally offer insights into aspects of metabolic disease, of which scientists were previously not aware, thus providing a better understanding of mechanisms that underpin co-morbidity across the board.

Perhaps the most significant change catalyzed by the pandemic has been raised societal and political awareness of three basic pillars underpinning the promise of improving human health for all.

First, the usefulness, safety, and ultimately also economic value of investing

in long-term basic research and medical science including population studies and technology platforms have come into focus. Second, the importance of prevention medicine tools such as vaccines and vaccine development platforms has deservedly returned to the fore. Finally, the need for functioning and balanced public-private partnerships, effectively translating academic insights into approved drugs in quality and amounts capable of stopping worldwide threats, has been recognized as a sine qua non in delivering solutions at a global and equitable scale.

Conclusion

The world is currently facing a research challenge of unprecedented proportions in living memory. The pandemic has deservedly attracted resources and has brought scientists together in order to tackle this huge societal challenge. However, research strategies, programs, and resources built over decades to prevent or eradicate even bigger and equally urgent health threats are at risk of experiencing a major setback with potential dire implications for our society. The research community must decide carefully how to best fight the terrible pandemic that currently paralyzes much of our lives, while protecting the expertise and knowledge base accrued longitudinally, and how to maximize output from infrastructural and research development investments to also protect society from diseases that may feel comparably familiar but remain just as lethal. We are currently being made aware, again, of what a valuable commodity health is and that a well-functioning health system can also be an economic advantage. Scientists, society, and those in power must realize that the challenge posed by the pandemic offers opportunity to improve health care in a sustainable way that pays off in the long term. In the past, we have failed to fully capitalize on similar opportunities, such as the development of new rapidly adaptable vaccine platforms following epidemics such as Ebola or avian flu. While this should not happen again now, we categorically cannot let the pendulum swing in the opposite direction and neglect research focusing on preventing and eradicating other major diseases. Instead, based on what we have learned during the current COVID-19 crisis, smart, lasting, balanced, and joint investments in improving our health as one global society are warranted.

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DECLARATION OF INTERESTS

In the past 5 years, Dr. Michael Baumann attended an advisory board meeting of MERCK KGaA (Darmstadt), for which the University of Dresden received a travel grant. He further received funding for his research projects and for educational grants to the University of Dresden by Teutopharma GmbH (2011–2015), IBA (2016), Bayer AG (2016–2018), Merck KGaA (2014–open), Medipan GmbH (2014–2018). He is on the supervisory board of HI-STEM gGmbH (Heidelberg) for the German Cancer Research Center (DKFZ, Heidelberg) and is also a member of the supervisory body of the Charité University Hospital, Berlin. As former chair of OncoRay (Dresden) and present CEO and Scientific Chair of the German Cancer Research Center (DKFZ, Heidelberg), he has been or is still responsible for collaborations with a multitude of companies and institutions, worldwide. In this capacity, he discussed potential projects with and has signed/signs contracts for his institute(s) and for the staff for research funding and/or collaborations with industry and academia, worldwide, including but not limited to pharmaceutical corporations like Bayer, Boehringer Ingelheim, Bosch, and Roche and other corporations like Siemens, IBA, Varian, Elekta, and Bruker. In this role, he was/is further responsible for commercial technology transfer activities of his institute(s), including the DKFZ-PSMA617 related patent portfolio [WO2015055318 (A1), ANTIGEN (PSMA)] and similar IP portfolios. Dr. Baumann confirms that to the best of his knowledge none of the above funding sources was involved in the preparation of this paper.

Dr. Matthias Tschöp is a member of the scientific advisory board of ERX Pharmaceuticals, Cambridge, Mass. He was a member of the Research Cluster Advisory Panel (ReCAP) of the Novo Nordisk Foundation between 2017 and 2019. He attended a scientific advisory board meeting of the Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, in 2016. He received funding for his research projects by Novo Nordisk (2016–2020) and Sanofi-Aventis (2012–2019). He was a consultant for Bionorica SE (2013–2017), Menarini Ricerche S.p.A. (2016), and Bayer Pharma AG Berlin (2016). As former Director of the Helmholtz Diabetes Center and the Institute for Diabetes and Obesity at Helmholtz Zentrum München (2011–2018), and since 2018, as CEO of Helmholtz Zentrum München, he has been responsible for collaborations with a multitude of companies and institutions, worldwide. In this capacity, he discussed potential projects with and has signed/signs contracts for his institute(s) and for the staff for research funding and/or collaborations with industry and academia, worldwide, including but not limited to pharmaceutical corporations like Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Medigene, Arbormed, BioSyngen, and others. In this role, he was/is further responsible for commercial technology transfer activities of his institute(s), including diabetes related patent portfolios of Helmholtz Zentrum München as, e.g., WO/2016/188932 A2 or WO/2017/194499 A1. Dr. Tschöp confirms that to the best of his knowledge none of the above funding sources were involved in the preparation of this paper.

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