Introduction

Introduction to the thematic issue on infectious diseases: Highlights of the Brazilian virology conference 2022 and International Experimental Biology and Medicine Conference (IEBMC), Brazil 2022

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Between 17 and 20 of October 2022, the Brazilian Society for Virology (SBV) and the Society for Experimental Biology and Medicine (SEBM) got together in the beautiful city of Porto Seguro, Brazil, for the 33rd Brazilian Congress of Virology, the 17th Mercosur Virology Meeting, and the 9th annual International Experimental Biology & Medicine Conference (Figure 1). This fantastic scientific congregation came together at the Arraial D'Ajuda village, a place known to be the first Brazilian landscape seen by Portuguese sailors, in the 1500s, after they set sail eastwards to find new navigation routes from Europe to India. Therefore, it was a very auspicious location that marked the first joint meeting held by SBV and SEBM. The SBV and International Experimental Biology and Medicine Conference (IEBMC) Infectious Diseases Thematic Issue celebrates this scientific congregation by inviting speakers from the joint conferences to publish their work either in the form of original research or state-of-the-art reviews, all within the Infectious Diseases theme. The chosen theme was particularly pertinent, considering that the SBV/SEBM joint meeting marked the return of presential conferences after 2 years of remote meetings, due to the lockdowns caused by the COVID-19 pandemic. Indeed, the coronavirus pandemic has been a painful demonstration of how susceptible we still are to infectious diseases in the 21st century and this thematic issue approaches concerns and aspects of some troublesome emerging, re-emerging, or established human infectious diseases.

We have learned many tough lessons from the COVID-19 crisis, and we are still learning. Nonetheless, two particular aspects stand out: first, the importance of vaccines for fighting the disease burden upon the human population; and second, how important fast, specific, and affordable diagnostics are for epidemic/pandemic management and decision-making by public health officials and physicians. In this respect, this Special Issue brings some relevant contributions and discussions.

In the paper by Souza-Silva *et al.*,[1] the authors discuss the state-of-the-art knowledge about dendritic cells (DCs) and how the activation of different DCs' subpopulations affects the immune response outcome. Moreover, they present how targeting antigenic peptides to DCs has turned into an attractive vaccine strategy, in which recombinant proteins fused to antibodies that recognize DC-specific surface receptors can direct the fused antigens straight to these cells. In the last years, a plethora of monoclonal antibodies (mAbs) that recognize DC surface receptors have been used, including mAbs directed at C-type lectin endocytic receptors such as DEC205, CLEC9A, CLEC12A, mannose receptor 1, DC SIGN, CD207, DCIR; DCIR2, and dectin-1, among others. The first studies were done through DC delivery of ovalbumin (OVA), leading to intensive immune responses to the antigen. Later on, clinically relevant antigens were tested and, once again, important and protective immune responses were achieved. These included targeting DCs with antigens from *Plasmodium*, *Leishmania*, *Trypanosoma*, and *Toxoplasma* parasites, HIV, among other pathogens. Thus, the main message presented by the authors is that antigen-targeting to DCs may represent a powerful yet underused immunization strategy, either as a main vaccine or an auxiliary immunization strategy.

As for diagnostics, two papers in the Special Issue approached diagnostic challenges and solutions regarding infectious diseases. In the work by Lopes-Luz *et al.*,[2] the authors discussed what is new in leprosy diagnostics, bringing forth new serological and molecular methods. Indeed, although multidrug therapies are available and effective against the *Mycobacterium* infection, early diagnostics contribute strongly to disease control. Nonetheless,

Figure 1. Logo of the 33rd Brazilian Congress of Virology and 9th annual International Experimental Biology & Medicine Conference, representing the SBV/SEBM joint meeting held in Bahia, Brazil, between 17 and 20 of October 2022.

the most frequent forms of diagnosis in prevalent countries are still based on clinical findings or labor-intensive bacilloscopy of intradermal scrapings. Alternative solutions are present and discussed, including ELISA tests and immunochromatographic, point-of-care strategies, using recombinant *Mycobacterium leprae* protein markers such as the PGL-I antigen and fusion, chimeric proteins encompassing ML0405, ML2055, and ML2331 antigens. However, although serology is quite useful in detecting multibacillary leprosy, diagnosing paucibacillary patients is a challenge due to the typical low immune responses found in such patients. To that end, molecular tests employing quantitative polymerase chain reaction (PCR) or loop-mediated isothermal amplification (LAMP) techniques are presented, as well as attractive DNA targets such as the high copy number gene coding for the *M. leprae*-specific repetitive element (RLEP). The combination of serologic and molecular tests has expanded the diagnostic capabilities of public health systems in affected countries and is a definitive step in controlling leprosy. Indeed, LAMP molecular tests, such as the one discussed above, have been considered attractive tools for fast, accurate, and cheap point-of-care diagnostics. In the study by De Souza *et al.*,[3] authors present improved protocols to express and purify the recombinant enzymes *Bst*-DNA Polymerase and HIV-Reverse Transcriptase, used in Reverse transcription quantitative PCR to detect RNA viruses. Optimized, patent-free protocols are presented, compared to commercial kits, and evaluated using either laboratory or clinical samples.

However, effective vaccines and accurate diagnostics will always depend on a thorough knowledge of the target pathogen biology as well as how they interact with their hosts and, eventually, how they become resistant to therapeutic interventions. In this regard, five excellent papers are included in the Special Issue. The study of Bezerra *et al.*[4] brings insights into the Sabia virus (*Brazilian mammarenavirus*); the only BSL4 category infectious agent ever isolated in Brazil. This new-world arenavirus presents several shared biological characteristics with old-world arenaviruses but also has unique structural and antigenic properties. The authors have used bioinformatic and empiric tools to characterize the structural features of the virus particle and its protein components, identifying potential targets for antiviral drugs and immune responses. The paper presents a review of such studies.

If the Sabia virus represents a grave but rare infection, malaria, on the contrary, constitutes an immediate threat and an ongoing public health problem in several countries on the American and African continents. Malaria is the most frequent parasitosis and can be caused by seven members of the *Plasmodium* genus. *Plasmodium vivax* is the leading cause of malaria in Latin America, responsible for thousands of malaria cases every year. In the article by Ferraboli *et al.*,[5] the authors have conducted a comprehensive review of what is known about *P. vivax* transcriptomics. To that end, the authors revised important information on dominant protein expression in each life stage of the parasite, identifying transcription patterns related to pathogenesis and immune

escape, as well as potential targets for vaccine development and anti-malarial therapy. Gene-expression markers that define each stage of the parasite are discussed and, indeed, while metabolism-related genes are upregulated in schizonts, for instance, parasite forms associated with the early infection of human hepatocytes present a strong transcriptome bias toward the activation of immune escape-related genes, including genes coding for proteins involved in decommissioning host pro-inflammatory and stress responses. Finally, the authors discuss how transcriptomics in the blood stages of the parasite are strongly devoted to the process of human reticulocyte invasion and infection.

Respiratory viral infections also constitute a major threat to the public health, but on a much wider scale than malaria. Indeed, infections caused by important respiratory viruses such as Influenza A virus (IAV), respiratory syncytial virus (RSV), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) are a major cause of mortality and morbidity all over the globe. Much of the pathogenesis of these infections is related to aberrant, widespread inflammation, leading to tissue damage and secondary bacterial pneumonia. In the review by Tavares *et al.*,[6] an alternative approach to diminish the excessive inflammation caused by viral respiratory infections is presented, and the potential for specialized pro-resolving mediators (SPMs) in fighting host mortality and morbidity caused by disseminated inflammation after infection is discussed. SPMs are molecules derived from fatty acid catabolism and are active immune mediators able to resolve inflammation and still induce antimicrobial responses. Natural killer (NK) cells, for instance, have a protective effect during certain stages of IAV and RSV infection; nonetheless, sustained activation of NK cells can lead to increased cytotoxicity and aberrant inflammation. In this context, SPMs can regulate NK function and deter further inflammatory exacerbation. SPMs are also able to modulate other cells and inflammatory signals, including Treg cell function, but at the same time, induce host anti-pathogen responses, especially by triggering activation of adaptative immune responses during IAV or RSV infections. Not surprisingly, both IAV and RSV are known to disrupt SPM production and signaling. The use of SPMs is discussed as an auxiliary treatment in preventing damage caused by exacerbated inflammation induced by respiratory virus infections.

The recent *Monkeypox virus* (Mpox) outbreaks in many countries where the disease had never been reported before are evidence of how human activity has altered epidemiological patterns, leading to unpredictable emergence and/or re-emergence of infectious diseases. In the specific case of poxviruses, the eradication of the deadliest orthopoxvirus—variola virus, the causative agent of smallpox—happened before more refined technologies to study virus biology and cell/virus interaction were developed. Thus, many gaps in this knowledge about Mpox and other poxviruses exist. In the paper by Lourenço *et al.*,[7] the authors evaluated how circulating, zoonotic strains of *Vaccinia virus* (VACV) interact with the unfolded protein response (UPR) pathway to achieve replicative success and deter cell death from apoptosis as well as pro-inflammatory signaling by infected cells. The presented results show that at least two of the three main signaling, receptor-mediated pathways are disrupted, completely or in part, during infection by VACV, improving virus resilience in infected cells.

Finally, even when all seems to be right and an appropriate therapeutic intervention exists for a given infection, microorganisms respond to selective pressure by evolving drug resistance. This is discussed in the review by Bertonha *et al.*,[8] in which bacterial resistance to β-lactams and other important, cell-wall biogenesis-related antibiotics is the main theme. Because resistance to drugs like penicillin has become widespread, alternative components of the cell wall biosynthetic pathway may represent new opportunities for drug development. One particularly attractive pathway is the role of penicillin-binding proteins (PBPs), which are responsible for cross-linking peptidoglycan stem peptides during the bacterial cell wall synthesis. Structural biology studies on the PBP and β-lactams interaction have helped to identify previously unknown catalytic pathways and new molecular ligands, contributing to the design of new drugs. More interestingly, such approaches have led to the development of drugs active not only against gram-positive bacteria, but for gram-negative bacteria as well. Many different types of anti-bacterial compounds acting on the PBPs of gram-positive or gram-negative bacteria are presented and discussed.

In summary, this Special Issue represents a fraction of all important discussions held during the SBV and the SEBM joint meeting that took place in the beautiful Arraial D'ajuda village, in Bahia, Brazil, in 2022. The event celebrated not only the return of presential meetings after 3 years of the COVID-19 pandemic but also emphasized how much scientists from Brazil, United States, and other countries can achieve when working together, to assure a better future for humans and for the planet as well.

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All authors wrote, revised, and approved this article.

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