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Editorial overview: Special issue on virus structure and expression in current opinion in virology

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The Covid-19 pandemic has shaken the world, with a massive impact on the economy, education, lifestyle, and health systems. Over the last two years, the scientific community has worked enormously to decipher all the possible aspects of the SARS-CoV 2 virus and its replication within the host, search for new antiviral strategies and develop vaccines. The incredibly fast gain of knowledge related to SARS-CoV 2 and COVID19 was only possible because of the enormous orchestration of financial and human resources, all focused on common global goals. Nonetheless, the accelerated scientific development in the years previous to the current pandemic cannot be underestimated. Indeed, the knowledge accumulated over years of research on viruses' structure and replication played a vital role in this endeavor. This Special Issue on Virus structure and infection coincided with the period of the Covid-19 pandemic. Besides the impact of the pandemic on the submission schedules and over laboratory work conditions, this Special issue could not be more providential. The authors and their published researchers have reviewed technological and methodological advances on viral structure and expression in this current issue. The most advanced experimental techniques used to characterize virus particles and virus proteins, including cryogenic electronic microscopy and nuclear magnetic resonance, were thoroughly reviewed [1,2]; new developments in molecular dynamics simulation and other computational strategies to study virus structure and proteins were also described [3]; an elegant integrative approach combining experimental and computational methods to characterize at atomic-level the structures and dynamics of HIV-1 capsids were carefully shown [4]; pivotal examples of the structure and functional characterization of important targets for antiviral development against SARS-CoV 2 and flaviviruses were described [5–7]. Also, discoveries on giant viruses, which have recently shaken the virology community, were aborbed, and revisions on important viral protein drug targets were made [8,9].

The recent advances in experimental techniques applied to the study of structural biology enabled the structural characterization of viruses at a near-atomic scale. The revolutionary Cryogenic electron microscopy, Cryo-EM, is now a robust methodology and gold-standard experimental approach for studying the virus's structure and function. Cryo-EM provides a combination of resolution and broad applicability over viruses' size, which other traditional techniques such as X-ray Crystallography could not achieve. De Oliveira and Silva [1] summarized the advances in Cryo-EM and its application on structural virology, showing recent examples that reveal

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the vital contribution of Cryo-EM, like the solving of the SARS-CoV 2 spike protein structure both in the prefusion and postfusion conformations.

Among the structural biology techniques, Nuclear magnetic resonance (NMR) is unique since it combines atomic resolution with the capability to study very flexible proteins and characterizes protein dynamics over a broad timescale. Because of those qualities, NMR can identify conformational epitopes, which is very important in structural vaccinology. The disadvantage of NMR is the size limitation of the analyzed protein complex. Valente and Manzano-Rendeiro [2] organized a minireview on mapping conformational epitopes by NMR spectroscopy, showing different methodologies that can be applied to characterize viral antigens and their interactions with polyclonal, monoclonal, and antibodies fragments by NMR.

Another revolution in the field of viral biophysics is strongly supported by molecular dynamic simulation. The implementation of accurate physical models, faster algorithms, new easy-to-use workflows, and software combined with hardware development, such as installing High-Performance Computing (HPC) infrastructures and improving GPUs, has contributed to turn MD simulation into a gold standard method to study biomolecular dynamics. Machado and Pantano [3] pointed out the recent achievements and the yet-needed developments of MD simulation applied to study viruses' structure and dynamics.

The characterization of virus structures, morphology, and dynamics is challenging due to the size, complexity, and morphology diversity observed in viruses' structures. Combining several experimental techniques with advanced computational methods, such as molecular dynamics, is essential to produce more realistic and detailed models of virus particles and proteins. In this regard, Polenova *et al.* [4] described a brilliant example of combining several experimental and computational methods to solve the structure and dynamics of the HIV-1 capsid structure. The mentioned HIV-1 structural models have been developed thanks to advances in Cryo-EM, cryo-electron tomography (Cryo-ET), magic angle spinning NMR spectroscopy (MAS NMR), and large-scale molecular dynamics (MD) simulation. The impact of these new structural models on the searching of new HIV-1 antiviral developments was also appointed.

The contributions of Hillen [5], da Poian *et al.* [7], and Moraes *et al.* [6] exemplified the considerable impact the structural virology is providing to fight global-impacting viruses: the SARS-CoV 2, the HIV-1, and flaviviruses. Hillen [5] reviewed the structure and function of SARS-CoV 2 polymerase, one of the most promising drug targets against SARS-CoV 2, and organized an overview of current coronavirus RdRp structures, together with many functional studies; Da Poian *et al.* [7] reviewed the structure and function of flaviviruses' capsid proteins that interact with viral RNA to form the flaviviruses nucleocapsid. They showed how vital the quaternary organization and the dynamics of the flaviviruses' capsid proteins are for its function and virion morphogenesis. Moraes *et al.* [6] focused on an important target for antiviral development against Dengue virus and other flaviviruses: the non-structural protein 5, NS5.

Recent discoveries have shown how diverse and intriguing viruses can yet be despite our actual knowledge of viruses' structure and their proteins functions. Recent findings over giant viruses with larger sizes, huge DNA coding capacity, complex structures, and diverse morphologies have recently surprised the virology scientific community. Cortines *et al.* [8] reviewed the

structure and physiology of giant DNA viruses. Indeed, many different giant viruses have been discovered since the first identification of the *Acanthamoeba polyphaga mimivirus* in 2003. These giant viruses possess diverse morphology and genomes over 0.4–2.5 Mpb that encode more than 400 proteins. The discovery of giant viruses challenges the preconceived standers of virus structure and complexity, and these aspects are discussed. Large and giant DNA viruses are a monophyletic group constituting the recently established *phylum Nucleocytoviricota*. Abrahão *et al.* [9] addressed the origin and evolution of large and giant viruses, exploiting the correlation between the virus's entry mechanisms, host preferences, and similarities in viral particle assembly conserved over the evolution. The authors reinforced the monophyletic of the *phylum Nucleocytoviricota* and its probable origin from less complex viruses.

References

1. de Oliveira GA, Silva JL: **Cryo-EM to visualize the structural organization of viruses.** *Curr Opin Virol* 2021, **49**:86-91.
2. Valente AP, Manzano-Rendeiro M: **Mapping conformational epitopes by NMR spectroscopy.** *Curr Opin Virol* 2021, **49**:1-6.
3. Machado MR, Pantano S: **Fighting viruses with computers, right now.** *Curr Opin Virol* 2021, **48**:91-99.
4. Perilla JR, Hadden-Perilla JA, Gronenborn AM, Polenova T: **Integrative structural biology of HIV-1 capsid protein assemblies: combining experiment and computation.** *Curr Opin Virol* 2021, **48**:57-64.
5. Hillen HS: **Structure and function of SARS-CoV-2 polymerase.** *Curr Opin Virol* 2021, **48**:82-90.
6. Fernandes PO, Chagas MA, Rocha WR, Moraes AH: **Non-structural protein 5 (NS5) as a target for antiviral development against established and emergent flaviviruses.** *Curr Opin Virol* 2021, **50**:30-39.
7. Neves-Martins TC, Mebus-Antunes NC, Caruso IP, Almeida FCL, Da Poian AT: **Unique structural features of flaviviruses' capsid proteins: new insights on structure-function relationship.** *Curr Opin Virol* 2021, **47**:106-112.
8. dos Santos Oliveira J, Lavell AA, Essus VA, Souza G, Nunes GHP, Benício E, Guimarães AJ, Parent KN, Cortines JR: **Structure and physiology of giant DNA viruses.** *Curr Opin Virol* 2021, **49**:58-67.
9. Rodrigues RAL, de Souza FG, de Azevedo BL, da Silva LC, Abrahão JS: **The morphogenesis of different giant viruses as additional evidence for a common origin of Nucleocytoviricota.** *Curr Opin Virol* 2021, **49**:102-110.