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Commentary

Systems Biology of COVID-19 and Human Diseases: Beyond a Bird's Eye View, and Toward One Health

Srishti Banerjee, Shreyayukta Chakraborty, and Sandipan Ray

Abstract

As we gaze into the future beyond the current coronavirus disease 2019 (COVID-19) pandemic, there is a need to rethink our priorities in planetary health, research funding, and, importantly, the concepts and unchecked assumptions by which we attempt to understand health and prevent illness. Next-generation quantitative omics technologies promise a more profound and panoptic understanding of the dynamic pathophysiological processes and their aberrations in diverse diseased conditions. Systems biology research is highly relevant for COVID-19, a systemic disease affecting multiple organs and biological pathways. In addition, expanding the concept of health beyond humans so as to capture the importance of ecosystem health and recognizing the interdependence of human, animal, and plant health are enormously relevant and timely in the current historical moment of the pandemic. Notably, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19, can affect our body clock, and the circadian aspects of this viral infection and host immunity need to be considered for its effective clinical management. Finally, we need to rethink and expand beyond the false binaries such as humans versus nature, and deploy multiomics systems biology research if we intend to design effective, innovative, and socioecological planetary health interventions to prevent future pandemics and ecological crises. We argue here that juxtaposing ecology and human health sciences scholarship is one of the key emerging tenets of 21st-century integrative biology.

Keywords: COVID-19, systems biology, One Health, planetary health, integrative biology, ecology

Perspective

The last two decades witnessed tremendous advances in omics-scale molecular profiling technologies. This provided a plethora of new insights into large-scale complex biological and ecological problems and multifactorial human diseases. Systems approaches and computational biology have also progressed radically to engage with big data-driven inquiries in health sciences and ecology. In this overarching context, coronavirus disease 2019 (COVID-19) calls for a systems biology approach as well as a "One Health" conceptual framing to coronavirus and zoonotic disease surveillance.

As noted recently, "an improved understanding of viral diversity and species-specific shedding dynamics is important for designing informed zoonotic disease surveillance and spillover risk reduction efforts" (Lane et al, 2022). Because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing COVID-19, has impacts beyond the respiratory system, including the reproductive system, systems biology of COVID-19 can help decipher the multidimensional consequences of the virus, for example, on fertility and pregnancy in hosts (Harb et al, 2022). Notably, SARS-CoV-2 can affect our body clock, and circadian aspects of this viral infection and host immunity need to be considered for its effective clinical management (Ray and Reddy, 2020).

Department of Biotechnology, Indian Institute of Technology Hyderabad, Hyderabad, India.

As we gaze into the future beyond the current pandemic, there is a need to rethink our priorities in planetary health, research funding, and, importantly, the concepts and unchecked assumptions by which we attempt to understand health and prevent illness. Expanding the concept of health beyond humans so as to capture the importance of ecosystem health and recognizing the interdependence of human, animal, and plant health are enormously relevant and timely in the current historical moment of the pandemic. We also need to rethink and expand beyond the false binaries such as

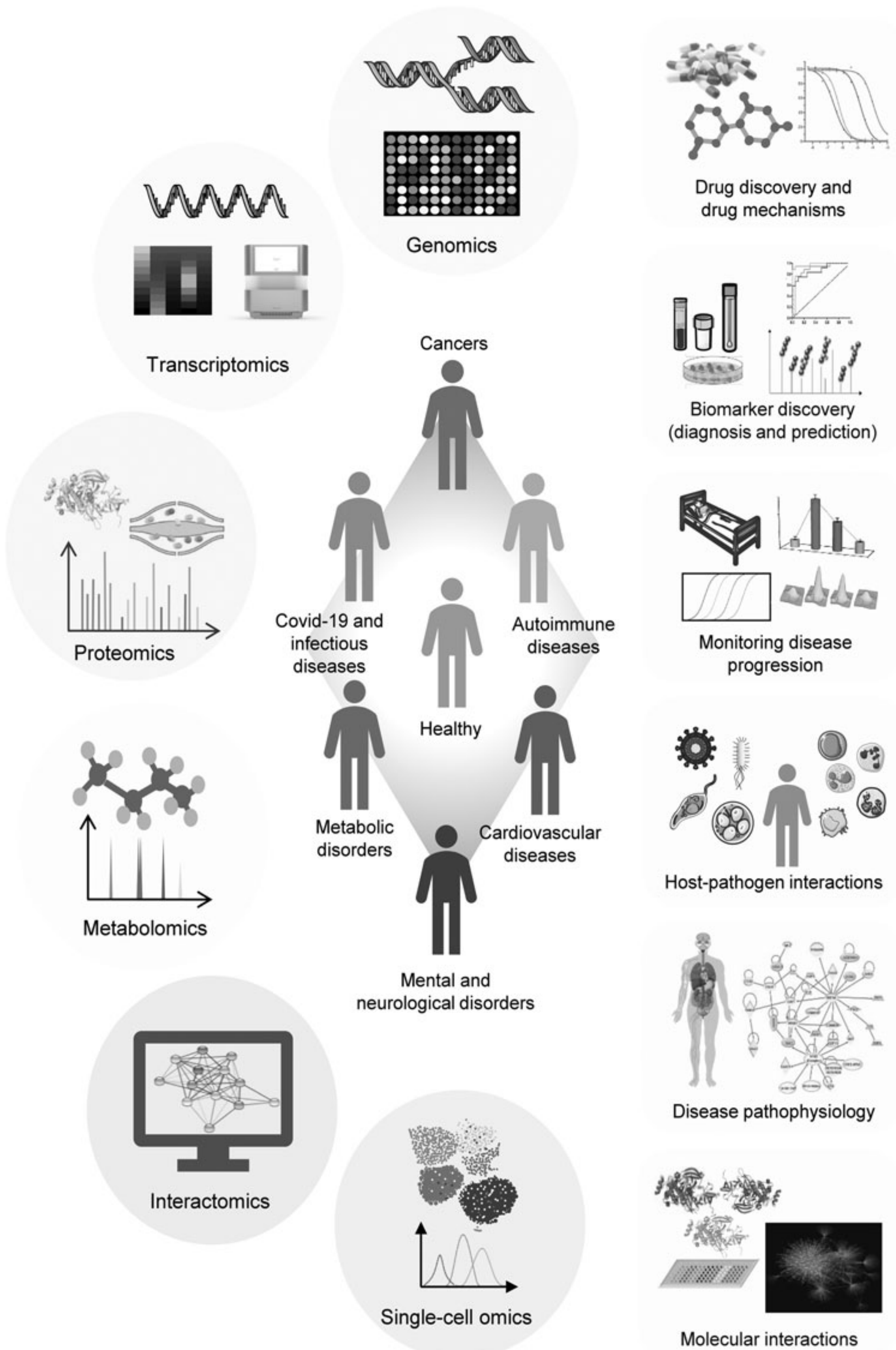

FIG. 1. Multidimensional systems-level omics technologies for the study of COVID-19 and multifactorial complex human diseases. Parts of Figure 1 are drawn using pictures from Servier Medical Art, provided by Servier, licensed under a Creative Commons Attribution 3.0 unported license.

humans versus nature, and deploy unbiased multiomics systems biology research, if we are to design effective, innovative, and socioecological planetary health interventions to prevent future pandemics and ecological crises (Özdemir et al, 2020; Wang et al, 2021).

Next-generation quantitative omics technologies offer the promise to obtain a more profound and panoptic understanding of the dynamic pathophysiological processes and their aberrations in diverse diseased conditions in a tissue-specific manner that was never achievable before. Consequently, systems-level integrated multiomics approaches are being effectively implemented in almost all extents of biomedical research, including understanding disease pathogenesis, identifying novel biomarkers, elucidating mechanisms of drug action, and discovering new therapeutic targets (Fig. 1). In this vein, omics-scale comprehensive studies provide novel insights into complex pathophysiology of COVID-19 and its therapeutic interventions (Ray and Srivastava, 2020).

Prospects of systems biology in translational health research are substantial. However, one major criticism of such omics-scale studies often arising is that those are generally restricted in providing only a ''Bird's eye view'' of the overall process rather than any precise inferences. Here we wish to argue that systems biology research can provide extremely useful information regarding human health and diseases if the experiments are carefully conceived, and the data are appropriately interpreted by considering metadata as well as newly generated experimental data.

For instance, integrative personal omics profile (iPOP) to forecast medical risks in an individual, including type 2 diabetes (Chen et al, 2012) and other common human diseases, is noteworthy and timely. Monitoring personalized omics profiles can help infer healthy and diseased conditions in a tailored manner, which is critical for obtaining deeper mechanistic insights into highly heterogeneous and complex chronic human diseases, such as cancers or metabolic syndrome, not to mention COVID-19 that is a systemic disease that calls for a systems medicine approach.

With recent advances in systems biology, large-scale omics profiling approaches turned more specific toward each organ and tissue or even at single-cell expression levels (Jiang et al, 2020; Karlsson et al, 2021). Comprehensive single-cell RNA sequencing enables us to classify the protein-coding genes according to their expression profiles in various cell types (Karlsson et al, 2021). Mapping the cell type or tissue-specific expressions of proteins and enzymes is critical for understanding the spatial distribution of human metabolism and physiological pathways, which may contribute to more precise therapeutic targeting under diseased conditions.

The majority of chronic human diseases and severe acute infections exhibit complex pathophysiology and clinical manifestations by affecting multiple physiological pathways. Thus, defining the disease-associated molecular networks through integrating multidimensional molecular and physiological systems-level information may offer a much more comprehensive and nuanced understanding of the complex pathophysiological underpinnings of human diseases (Schadt, 2009). Systems-level molecular information can also substantially improve the disease classification and severity grading processes, particularly when clinical manifestations alone are inadequate to handle the enormous disease heterogeneity.

Integrating proteome-level information with genomics and transcriptomics is critical for translating systems biology into innovative health care applications. In this vein, in the postgenomic era, the Human Proteome Project (HPP) is informing multiomics and translational research (Adhikari et al, 2020). Besides, the successful completion of the Integrative Human Microbiome Project (iHMP) provided a vast amount of complementary information on dynamic interactions between humans and microbiomes and their influence on health and diseases (iHMP Research Network Consortium, 2019).

The cumulative benefits of the omics breakthroughs on planetary health are poised to become more apparent and a tangible reality if we are able to expand our conceptual frames on translational medicine under One Health and similar integrative lenses. After all, multiomics integration is one part of such an integrated conceptual approach, and juxtaposing ecology and human health scholarship is one of the key emerging tenets of 21st-century integrative biology.

Author Disclosure Statement

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Address correspondence to:
Sandipan Ray, PhD, MRSB
Department of Biotechnology
Indian Institute of Technology Hyderabad
BT317, Biotechnology and Biomedical Engineering Building
Kandi, Sangareddy
Hyderabad 502284
Telangana
India

E-mail: sandipan.ray@bt.iith.ac.in

Abbreviations Used

COVID-19 = coronavirus disease 2019
iHMP = Integrative Human Microbiome Project
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2