Editorial: Computational Genomics and Molecular Medicine for Emerging COVID-19

Dong-Qing Wei, Aman Chandra Kaushik, Gurudeeban Selvaraj, and Yi Pan

It is our pleasure and great honor to present this special section of the *IEEE/ACM Transactions on Computational Biology and Bioinformatics*. In 2020, World Health Organization announced Coronavirus disease (COVID)-19 is a pandemic disease, which is devastated the socio-economic life around the world. The disease caused by the zoonotic single-strand RNA virus known as "SARS-CoV-2". To overcome the pandemic, the diagnosis and therapeutics products needs to be developed in short term. Developing therapeutics for infectious diseases, especially viral diseases always a challenging task for the scientific community. However, the utility of high-performance computational resources, artificial intelligence, and machine-learning algorithms can make the process in an affordable way through the usage of genomics, proteomics, pharmacogenomics, and chemical data. Thus, the special section received potential research articles related to computational genomics, molecular medicine, and COVID-19 from reputed scientist around the world. Different articles were employed machine learning, molecular dynamics, computer aided drug design techniques, and emphasizing viral genomics, mutation, drug target, drug candidates, and patient data, were included in this special section.

In "AGTR2, One Possible Novel Key Gene for the Entry of SARS-CoV-2 into Human Cells" by Chunmei Cui, Chuanbo Huang, Wanlu Zhou, Xiangwen Ji, Fenghong Zhang, Liang Wang, Yuan Zhou, Qinghua Cui, it was hypothesized that there could be alternative genes playing key roles in the entry of SARS-CoV-2 into human cells instead of ACE2. In the results authors found that AGTR2 (angiotensin II receptor type 2), a G-protein coupled receptor, interacts with ACE2 and is highly expressed in lung with a high tissue specificity. More importantly, simulation of 3D structure based protein-protein interaction reveals that AGTR2 shows a higher binding affinity with the Spike protein of SARS-CoV-2 than ACE2. In addition, the study predicted many compounds, biologics and traditional medicine to decrease the expression level of AGTR2.

In "Deep Bidirectional Classification Model for COVID-19 Disease Infected Patients," Yadunath Pathak, Piyush Kumar Shukla, and K.V. Arya studied the chest computed Tomography (CT) application on COVID-19 diagnosis, which was alternative to the reverse transcription polymerase chain reaction (RT-PCR) test. In this study, a deep bidirectional long short-term memory network with mixture density network (DBM) model was proposed to classify COVID-19 patient based on the CT images. Comparative analysis reveals that the proposed MADE-DBM model outperforms the competitive COVID-19 classification approaches in terms of various performance metrics that could be used in real-time COVID-19 classification systems.

In "Detection of Phenotype-Related Mutations of COVID-19 via the Whole Genomic Data," Jinxiong Lv, Shikui Tu, and Lei Xu studied both single-locus analysis and joint-SNPs analysis for detection of significant single nucleotide polymorphisms (SNPs) in the phenotypes of symptomatic vs. asymptomatic, the early collection time vs. the late collection time, the old vs. the young, and the male vs. the female. The authors observed the results in three different folds. First, the SNP that locates at the nucleotide position 4321 was found to be an independent significant locus associated with all the first three phenotypes. Moreover, 12 significant SNPs were found in the first two studies. Second, gene orf1ab containing SNP-4321 was detected to be significantly associated with the first three phenotypes, and the three genes, S, ORF3a, and N, were detected significantly in the first two phenotypes. Third, some of the detected genes or SNPs were related to the SARS-COV-2 as supported by the literature survey, which indicates that the results here may be helpful for further investigation.

In "2019nCoVAS: Developing the Web Service for Epidemic Transmission Prediction, Genome Analysis, and Psychological Stress Assessment for 2019-nCoV," Ming Xiao, Guangdi Liu, Jianghang Xie, Zichun Dai, Zihao Wei, Ziyao Ren, Jun Yu, and Le Zhang developed 2019nCoVAS (http://www.combio-lezhang.online/2019ncov/home.html) web interface that not only offers online epidemic transmission prediction and lineage-associated underrepresented permutation (LAUP) analysis services to investigate the spreading trends and genome sequence characteristics. In addition, web interface provides psychological stress assessments based on such an emotional dictionary that we built for 2019-nCoV.

- *Dong-Qing Wei is with the State Key Laboratory of Microbial Metabolism and School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai 200240, China, and also with Peng Cheng Laboratory, Shenzhen, Guangdong 518055, China. E-mail: dqwei@sjtu.edu.cn.*
- *Aman Chandra Kaushik is with Wuxi School of Medicine, Jiangnan University, Wuxi, Jiangsu 214122, China. E-mail: amanbioinfo@sjtu.edu.cn.*
- *Gurudeeban Selvaraj is with the Centre for Research in Molecular Modeling (CERMM), Concordia University, Montreal, QC H4B 1R6, Canada. E-mail: gurudeeban.selvaraj@concordia.ca.*
- *Yi Pan is with the Department of Computer Science, Georgia State University, Atlanta, GA 30302-5060 USA. E-mail: yipan@gsu.edu.*

Digital Object Identifier no. 10.1109/TCBB.2021.3088319

In "High-Throughput Screening and Quantum Mechanics for Identifying Potent Inhibitors against Mac1 Domain of SARS-CoV-2 Nsp3," Chandrabose Selvaraj, Dhurvas Chandrasekaran Dinesh Umesh Panwar, Evzen Boura, and Sanjeev Kumar Singh proposed SARS-CoV-2 Mac1 enzyme is considered as an ideal drug target and inhibitors developed against them can possess a broad antiviral activity against CoV. Considering this, the ADP-Ribose-1"-phosphate bound closed form of Mac1 domain was considered for screening with large database of ZINC. XP docking, QPLD, quantum mechanical studies and molecular dynamics study confirms both substrate and lead molecules are well-adopt to bind with similar binding mode inside the closed form of Mac1.

In "Network-Based Analysis of Fatal Comorbidities of COVID-19 and Potential Therapeutics," Broto Chakrabarty, Dibyajyoti Das, Gopalakrishnan Bulusu, and Arijit Roy investigated angiotensin-converting enzyme 2 (ACE2), transmembrane protease serine 2 (TMPRSS2) and basigin (BSG), as seed nodes and applied the random walk with restart method on the human interactome to construct a protein-protein interaction sub-network. It captures the critical pathways and potential drug candidates for COVID-19.

In "Detection of Binding Sites on SARS-CoV-2 Spike Protein Receptor-Binding Domain by Molecular Dynamics Simulations in Mixed Solvents," Elmeri M. Jokinen, Krishnasamy Gopinath, Sami T. Kurkinen, and Olli T. Pentikainen investigated molecular dynamics simulations in mixed solvents together with virtual screening to identify small molecules that could be potential inhibitors of S protein ACE2 interaction. The most promising binding site on the RBD-ACE2 interface was targeted with virtual screening and DB08248, DB02651, DB03714, and DB14826 are suggested for experimental testing.

In "LUNAR: Drug Screening for Novel Coronavirus Based on Representation Learning Graph Convolutional Network," Deshan Zhou, Shaoliang Peng, Dong-Qing Wei, Wu Zhong, and Xiaolan Xie proposed a new nonlinear end-to-end model called LUNAR. It uses graph convolutional neural networks to obtain the strength of the relationship between different nodes and predict drug candidates that may affect the treatment of COVID-19 based on the known targets of COVID-19. These selected candidate drugs can be used as a reference for experimental scientists and accelerate the speed of drug development.

ACKNOWLEDGMENTS

As guest editors of this special section, we would like to thank the contributing authors, the *TCBB* reviewers who reviewed papers in this special section, and the *TCBB* editorial staff for the support to make this special section possible.

Dong-Qing Wei is currently a tenured professor of bioinformatics with the Department of Bioinformatics and Biostatistics, College of Life Science, Shanghai Jiaotong University, China, and the editor-in-chief of Interdisciplinary Sciences- Computational Life Sciences. He has authored or coauthored more than 450 journal papers, nine monographs with 10000 SCI citations, and an H factor of 60. Over the past three decades, he has made many grand breaking contributions to the development of bioinformatics/AI drug design techniques and their interdisciplinary applications to systems of ever-increasing complexity. He is best known for contributions to the development of molecular simulation and AI tools with applications to a wide range of chemical, physical and biological systems, from electrolytes, to polar liquids, to ferroelectric liquid crystals, to combined Quantum Mechanical/Molecular Mechanical (QM/MM) systems, to membrane proteins, protein-ligand and protein-protein complexes applied to computer aided drug design. His most important contributions in sciences are exemplified by the discovery of ferroelectric nematic liquids crystals, the first complete ab initio MD simulation of explosion (nitromethane), and anti-aging and anti-AD drug candidate WGX-50. He was invited to give invited and plenary talks in more than 100 conferences. He has organized ten international conferences, including the Theory and Computational Chemistry (ACC2008), the AI and Precision Medicine (2017–2018), and the International Conference on Computational and System Biology (ICCSB-2009–2015).

Aman Chandra Kaushik received the PhD degree in bioinformatics from Gautam Buddha University, Delhi, India, while researching at Ben-Gurion University of the Negev, Israel. He is currently an assistant professor with the School of Medicine, Jiangnan University, Wuxi, China. He has authored or coauthored more than100 journal papers, with more than 650 citations, in leading computational biology journals. His research interests include developing computational methods to drive biological discoveries and medical innovations that will benefit public health by analyzing and modeling large-scale biomedical data, especially cancer genomics data. He developed different machine learning tools, including WeiDock, WeiBI, DTI-CDF, SPVec, and A-CaMP, have had an impact on system-based medicine. He was the recipient of the postdoctoral scholar in bioinformatics at Shanghai Jiao Tong University.

Gurudeeban Selvaraj (Member, IEEE) received the BSc degree in biochemistry from Bharathiar University, and the MSc and PhD degrees in marine biotechnology from Annamalai University. He is currently a research associate and the CERMM co-directors search committee member in CERMM, Concordia University, Canada. He has authored or coauthored more than 100 research articles with scholary 1850 citations (H-index-21) in reputed journals, including the *Forinters in Pharmacology, the Current Medicinal Chemistry, the Journal of Biomedical Informatics, the Phytomedicine*, the *IEEE/ACM Transactions on Computational Biology and Bioinformatics*, *Journal of Physical Chemistry C, the Current Pharmaceutical Design, the Current Drug Targets, Journal of Nanobiotechnology*. His research interests include vaccine design, integrating biological omics technologies to understand gene-target interactions using machine-learning algorithms, with applications to genomics and infectious diseases. Prior to joining CERMM, he was a research assistant professor equivalence with the Henan Universtiy of Technology, and postdoctoral research with Istanbul Medeniyet University. He was the recipient of various prestigious research grants, including the MITACS Global link, Bridge funding Concordia University, NSERC (Canada), China Postdoctoral Science Foundation, Henan Postdoctoral Science Foundation, Henan University of Technology research fund (China), TUBITAK (Turkey), and UGC (India). He was an associate guest editor and published special issues in the Bentham Science, the MDPI, and the IEEE journals and reviewed more than 100 papers. He has also participated in more than 40 different international and national conferences and workshops.

Yi Pan received the BEng and MEng degrees in computer engineering from Tsinghua University, China, in 1982 and 1984, respectively, and the PhD degree in computer science from the University of Pittsburgh, USA, in 1991. He is currently a chair professor and the dean of the Faculty of Computer Science and Control Engineering, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, China, and a Regents' professor Emeritus with Georgia State University, USA. From 2005 to 2020, he was a chair of Computer Science Department, Georgia State University. From 2013 to 2017, he was an interim associate dean and the chair of Biology Department. In 2000, he joined Georgia State University, was promoted to full professor in 2004, named a Distinguished University professor in 2013, and designated a Regents' professor, the highest recognition given to a faculty member by the University System of Georgia, in 2015. His profile was featured as a distinguished alumnus in both Tsinghua Alumni Newsletter and the University of Pittsburgh CS Alumni Newsletter. He has authored or coauthored more than 450 papers, including more than 250 journal papers with more than 100 papers published in the IEEE/ACM Transactions or Journals, and he has edited or authored 43 books. His research interests include bioinformatics and health informatics using big data analytics, cloud computing, and machine learning technologies. His work has been cited more than 16000 times based on Google Scholar and his current h-index is 82. He was an editor-in-chief or editorial board member of 20 journals, including seven IEEE Transactions. He is an associate editor-in-chief of the *IEEE/ACM Transactions on Computational Biology and Bioinformatics*. He was the recipient of many awards including one IEEE Transactions Best Paper Award, five IEEE and other international conference or journal best paper awards, four IBM faculty awards, two JSPS Senior Invitation Fellowships, the IEEE BIBE Outstanding Achievement Award, the IEEE Outstanding Leadership Award, the NSF Research Opportunity Award, and the AFOSR Summer Faculty Research Fellowship. He has organized numerous international conferences and delivered keynote speeches at more than 60 international conferences around the world.