

1 **Artificial Intelligence and Machine Learning to Fight COVID-19**

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25 Coronavirus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome
26 coronavirus 2 (SARS-CoV-2) (13), has become an unprecedented public health crisis.
27 Coronavirus Resource Center at Johns Hopkins University of Medicine has reported a
28 total of 23,638 deaths as worldwide COVID-19 infections surpass 500,000 (as of 5pm
29 EST on March 26, 2020). On March 16, 2020, the White House collaborating with
30 research institutes and tech companies has issued a call to action for global artificial
31 intelligence researchers for developing novel text and data mining techniques to assist
32 COVID-19 related research. The Allen institute for AI in partnership with leading
33 research groups issued an open-source, weekly updated COVID-19 Open Research
34 Dataset (2), which continuously documents COVID-19 related scholar articles to
35 accelerate novel research projects urgently requiring real-time data. The large-scale
36 data of COVID-19 patients can be integrated and analyzed using advanced machine
37 learning algorithms to better understand the pattern of viral spread, further improve
38 diagnostic speed and accuracy, develop novel effective therapeutic approaches, and
39 potentially identify the most susceptible people based on personalized genetic and
40 physiological characteristics. Inspirationally, within a short period of time since COVID-
41 19 outbreak, advanced machine learning techniques have been used in taxonomic
42 classification of COVID-19 genomes (8), CRISPR-based COVID-19 detection assay (6),
43 survival prediction of severe COVID-19 patients (11), and discovering potential drug
44 candidates against COVID-19 (4).

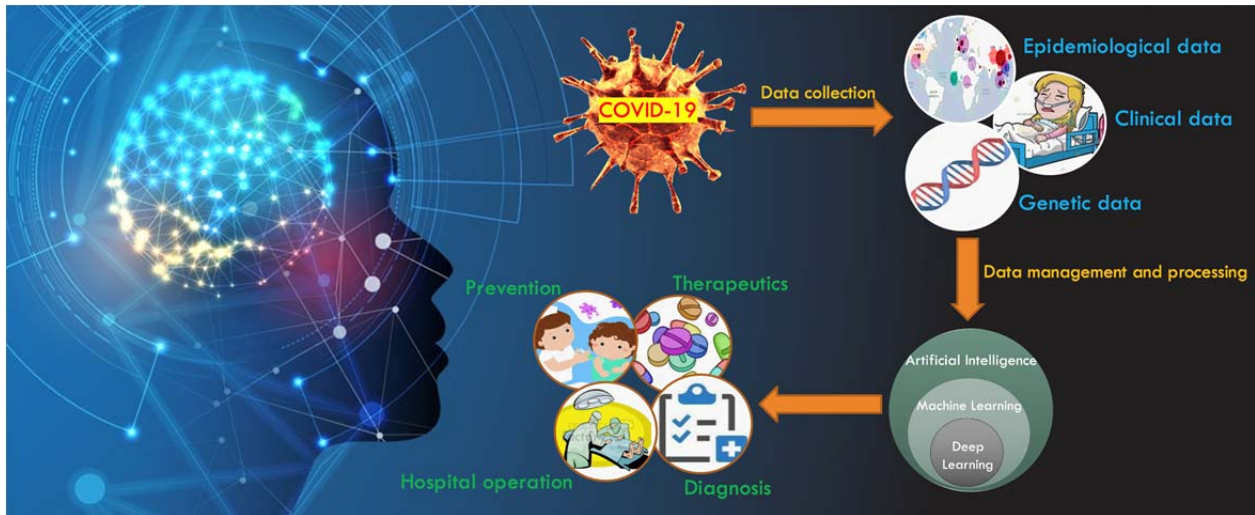
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46 Personalized protective strategies can greatly benefit from precise classifications of the
47 population based on categorized COVID-19 susceptibility. The earlier observation that

48 elderly people have a higher risk to COVID-19 is challenged by a recent finding that
49 more and more young adults suffer from severe COVID-19 symptoms, indicating an
50 urgent need of a comprehensive risk evaluation based on personalized genetic and
51 physiological characteristics. Human angiotensin-converting enzyme 2 (ACE2),
52 expressed in epithelial cells of lung, small intestines, heart and kidneys, is an entry
53 receptor for SARS-CoV-2 spike glycoprotein (3, 13). Fang et al. hypothesized that
54 increased expression of ACE2, by using ACE2-stimulating drugs to treat hypertension
55 and diabetes, could actually worsen clinical outcomes of COVID-19 infection (3).
56 Indeed, this hypothesis should be further tested with strict experimental designs and
57 long-term clinical observations. Therefore, biochemistry (e.g., ACE2 expression level)
58 and clinical data (e.g., age, respiratory pattern, viral load and survival) of COVID-19
59 patients with underlying medical conditions can be analyzed using machine learning
60 approaches to not only identify any reliable features (e.g., ACE2) for risk prediction, but
61 also further perform risk classification and prediction for a balanced preparation of
62 ongoing disease treatment and COVID-19 defense (Figure 1). ACE2 genetic
63 polymorphism, represented by diverse genetic variants in human genome, has been
64 shown to affect virus-binding activity (1), suggesting a possible genetic predisposition to
65 COVID-19 infection. Therefore, machine learning analysis of genetic variants from
66 asymptomatic, mild or severe COVID-19 patients can be performed to classify and
67 predict people based on their vulnerability or resistance to potential COVID-19 infection,
68 by which the machine learning model can also return those prioritized genetic variants,
69 such as ACE2 polymorphism, in their decision-making process as important features for
70 functional and mechanistic studies (Figure 1).

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74 Figure 1. Application of artificial intelligence and machine learning in the fight against
75 COVID-19.

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77 Currently, ongoing efforts have been made to develop novel diagnostic approaches
78 using machine learning algorithms. For example, machine learning based screening of
79 SARS-CoV-2 assay designs using a CRISPR-based virus detection system was
80 demonstrated with high sensitivity and speed (6). Neural network classifiers were
81 developed for a large-scale screening of COVID-19 patients based on their distinct
82 respiratory pattern (10). Similarly, a deep-learning based analysis system of thoracic CT
83 images was constructed for automated detection and monitoring of COVID-19 patients
84 over time (5). Rapid development of automated diagnostic systems based on artificial
85 intelligence and machine learning can not only contribute to increased diagnostic
86 accuracy and speed, but will also protect healthcare workers by decreasing their
87 contacts with COVID-19 patients (Figure 1).

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89 An effective therapeutic strategy is urgently needed to treat rapidly growing COVID-19
90 patients worldwide. As there is no effective drug proven to treat COVID-19 patients, it is
91 critical to develop efficient approaches to repurpose clinically-approved drugs or design
92 new drugs against SARS-CoV-2. A machine learning based repositioning and
93 repurposing framework was developed to prioritize existing drug candidates against
94 SARS-CoV-2 for clinical trials (4). Additionally, a deep learning based drug discovery
95 pipeline has been used to design and generate novel drug-like compounds against
96 SARS-CoV-2 (12). AlphaFold (9), which is a deep learning system developed by Google
97 DeepMind, has released predicted protein structures associated with COVID-19, which
98 can take months using traditional experimental approaches, serving as valuable
99 information for COVID-19 vaccine formula. Moreover, COVID-19 vaccine candidates
100 were proposed by a newly developed Vaxign reverse vaccinology tool integrated with
101 machine learning (7). The tremendous amount of COVID-19 treatment data in
102 worldwide hospitals also require advanced machine learning methods for analyzing
103 personalized therapeutic effects for evaluating new patients, such as hospitalization
104 prediction, which can not only provide better care for each patient but also contribute to
105 local hospital arrangement and operation (Figure 1).

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107 As artificial intelligence and machine learning scientists have been eagerly searching
108 and waiting for real-time data generated by this pandemic around the world, timely
109 delivery of COVID-19 patient data, such as physiological characteristics and therapeutic
110 outcome of COVID-19 patients, followed by subsequent data transformation for easy

111 access, is extremely important, but challenging. Figure 1 is a schematic representation
112 of the workflow, but there are several steps in the process that currently limit the
113 application of machine learning and artificial intelligence to combat COVID-19.
114 Availability of COVID-19 related clinical data, which can be managed and processed
115 into easily accessible databases is a key current barrier. Thereby, development of
116 cyber-infrastructure to fuel world-wide collaborations is important. To this end, the US
117 federal agencies are already promoting the formations of consortia and funding
118 opportunities (<https://www.nsf.gov/pubs/2020/nsf20055/nsf20055.jsp>). In addition to
119 these initiatives, Integrating COVID-19 related clinical data with existing biobanks, such
120 as the UK Biobank, with pre-existing data of those patients (if already in biobanks), such
121 as their genotype and physiological characteristics, could maximize our efforts towards
122 a faster, feasible means to the end of meaningful data-mining by bioinformaticians and
123 computational scientists. A centralized collection of worldwide COVID-19 patient data
124 will be beneficial for future artificial learning and machine learning research to develop
125 predictive, diagnostic and therapeutic strategies against COVID-19 and similar
126 pandemics in future.

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