COVID-19 Biomarkers in Research and Associations with Comorbidities

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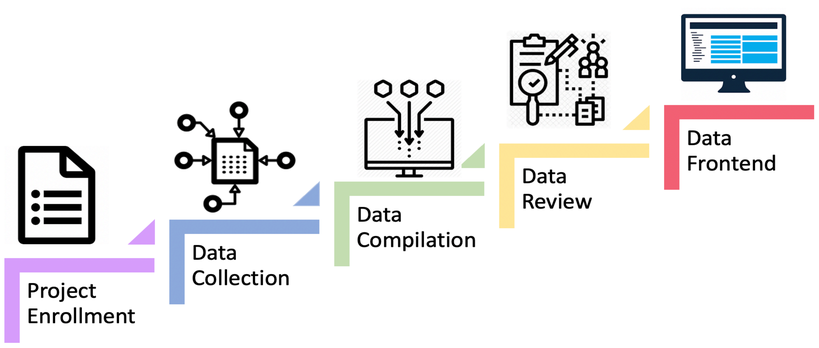
ABSTRACT

Signature molecules, including genes, proteins, target panels, and glycans termed as biomarkers, are becoming increasingly significant in the Coronavirus disease 2019 (COVID-19) pandemic. High-throughput molecular characterization technologies have greatly accelerated the development of tests for risk assessment, diagnosis, prognosis, disease monitoring, and therapeutic evaluation. The disease complexity emphasizes the need for biomarker characterization that can help stratify patients based on their variable clinical manifestations and the presence of comorbidities. Powered by an NCI ITCR funded, comprehensive data model built to capture cancer biomarker data (OncoMX), and incorporating crowdsourced data collection and integration techniques, we have efficiently harmonized COVID-19 biomarker data. As of now, we have 146 potential biomarkers for COVID-19. Most biomarkers are associated with the immune system (including complement factors, inflammatory modulators, and pro-inflammatory factors) as well as coagulation factors. These trends suggest a vascular pathobiology of the COVID-19 disease. Utilizing this collated biomarker data, we propose to identify common features and attributes of COVID-19, with cancer and other metabolic syndromes. Preliminary analysis shows biomarkers such as ACE2, IL-6, IL-4, and IL-2 have similar expression profiles in COVID-19 and cancer. Furthermore, COVID-19 biomarkers such as D-dimer, neutrophil to lymphocyte ratio (NLR), C-reactive protein (CRP), and low-density lipoprotein (LDL) shed light on the underlying physiological or pathological association with metabolic syndrome, diabetes, and hyperlipidemia. **The importance of this study lies in identifying specific biomarkers that can successfully stratify patients based on distinct clinical presentations and the presence of comorbidities. Exploration of these patterns will benefit researchers and diagnosticians alike.**

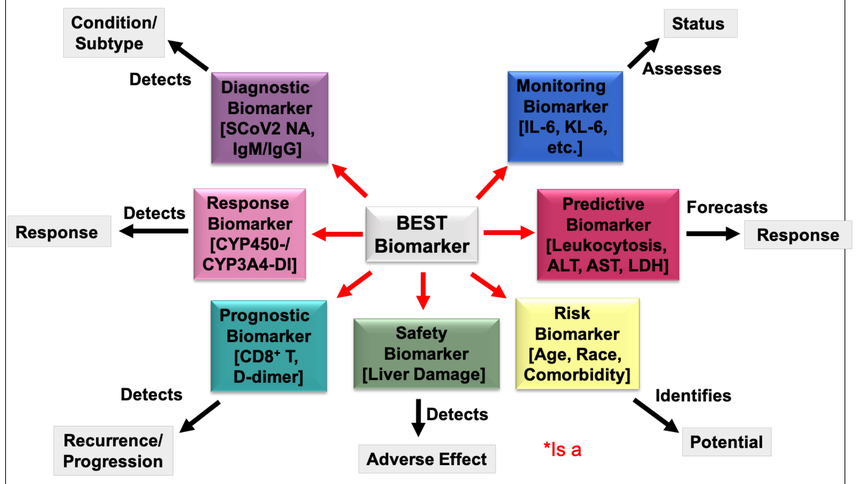
WORKFLOW



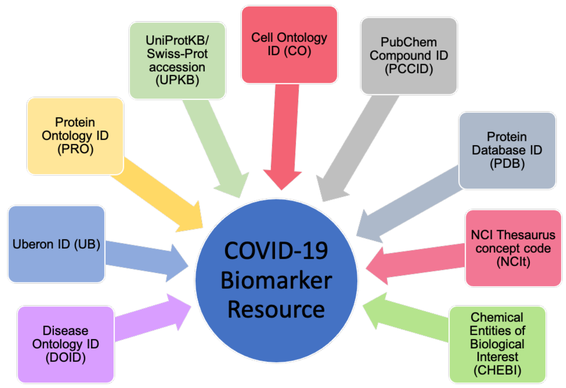
Project Overview: Steps for collection, organization, standardization and integration of the data elements in the COVID-19 biomarker resource data model.

COVID-19 BIOMARKER DATA MODEL

Crowdsourcing has allowed us to annotate and cross-validate 145 biomarkers. Biomarkers have a wide range of applications depending on their usage in different stages of the disease. By leveraging existing standards and ontologies, we propose a COVID-19 biomarker data model that promotes extensibility and sustainability.



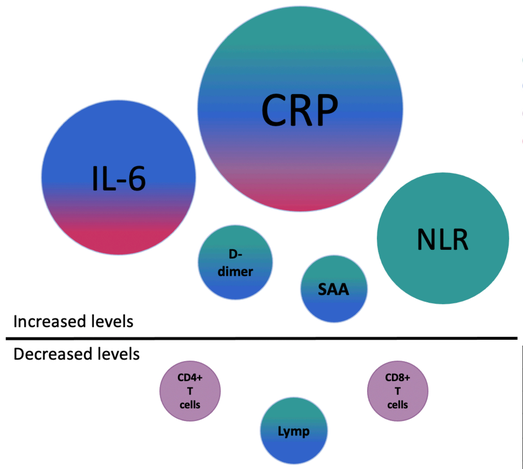
Model of BEST biomarker subtypes. BEST biomarker types modeled on disease progression. Each category of BEST biomarker fulfils a distinct role ”as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention.



Rubric for Biomarker data type and column content: Harmonization of biomarker-centric knowledge (including terms, definitions, synonyms), enriched with objects imported from related reference ontologies under a unified framework.

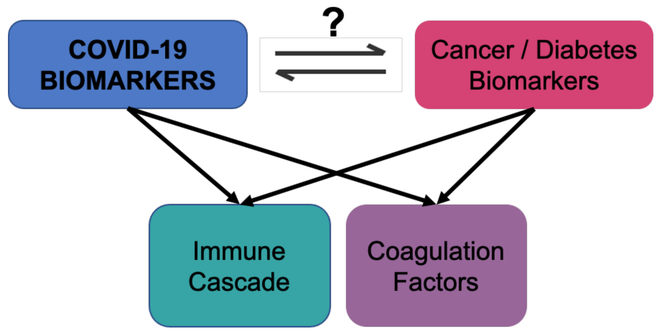
TRENDS IN COVID-19 BIOMARKER DATA

COVID-19 Biomarker Highlights: Top biomarkers are depicted as increased or decreased levels. The size of the circle is indicative of the number of articles supporting the biomarker. The color of the circle corresponds to the BEST biomarker type (Monitoring – blue, Prognostic – green, Diagnostic – purple, Predictive – pink).



Acronym	Biomarker Name
CRP	C-reactive protein
IL6	Interleukin-6
NLR	Neutrophil-to-Lymphocyte ratio
SAA	Serum amyloid A protein
Lymp	Lymphocyte

Data suggests that hyper-activation of the immune system, coagulopathies and the targeting of specific types of cells are the primary *modus operandi* of SARS-CoV-2. It also sheds light on the underlying physiological or pathological association with cancer as well as metabolic syndrome, diabetes, and hyperlipidemia.



Impact: In the early stages of understanding the pathology of this infectious disease, we provide this biomarker resource to support continued research around the world to better understand and manage COVID-19. We encourage collaborations and contributions to the resource.

ACKNOWLEDGEMENTS

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DATA AVAILABILITY

All data reported is freely available at https://data.oncomx.org/covid19 under the Creative Commons CC-BY-4.0 license.

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