Web resources bring new insight into COVID-19

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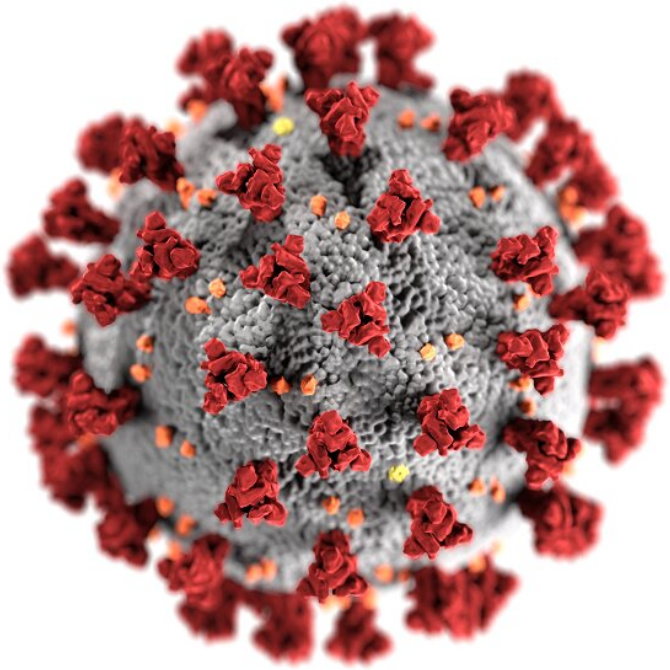

This 3D illustration reveals structural details of coronavirus. Credit: CDC

Researchers around the world are a step closer to a better understanding of the intricacies of COVID-19 thanks to two new web resources developed by investigators at Baylor College of Medicine and the University of California San Diego. The resources are freely available through the Signaling Pathways Project (Baylor) and the Network Data Exchange (UCSD). They put at researchers' fingertips information about

cellular genes whose expression is affected by coronavirus infection and place these data points in the context of the complex network of host molecular signaling pathways. Using this resource has the potential to accelerate the development of novel therapeutic strategies. The study appears in the journal *Scientific Data*.

"Our motivation for developing this resource is to contribute to making research about COVID-19 more accessible to the scientific community. When researchers have open access to each other's work, discoveries move forward more efficiently," said leading author Dr. Neil McKenna, associate professor of molecular and cellular biology and member of the Dan L Duncan Comprehensive Cancer Center at Baylor.

The Signaling Pathway Project

For years, the scientific community has been generating and archiving molecular datasets documenting how genes are expressed as cells conduct their normal functions, or in association with disease. However, usually this information is not easily accessible.

In 2019, McKenna and his colleagues developed the Signaling Pathways Project, a web-based platform that integrates molecular datasets published in the scientific literature into consensus regulatory signatures, or what they are calling consensomes, that rank genes according to their rates of differential expression.

In the current study, the researchers generated consensomes for genes affected by infection with three major coronaviruses, Middle East respiratory syndrome coronavirus (MERS) and severe acute respiratory syndrome coronaviruses 1 (SARS1) and 2 (SARS2, which causes COVID-19).

McKenna and his colleagues provide a resource that assists researchers

in making the most out of coronavirus' datasets. The resource identifies the genes whose expression is most consistently affected by the infection and integrates those responses with data about the cells' molecular signaling pathways, in a sense getting a better picture of what happens inside a cell infected by coronavirus and how the cell responds.

"The collaboration with UCSD makes our analyses available as intuitive Cytoscape-style networks," says McKenna. "Because using these resources does not require training in meta-analysis, they greatly lower the barriers to usability by bench researchers."

Providing new insights into COVID-19

The consensus strategy, the researchers explain, can bring to light previously unrecognized links or provide further support for suspected connections between coronavirus infection and human signaling pathways, ultimately simplifying the generation of hypotheses to be tested in the laboratory.

For example, the connection between pregnancy and susceptibility to COVID-19 has been difficult to evaluate due to lack of clinical data, but McKenna and colleagues' approach has provided new insights into this puzzle.

"We found evidence that progesterone receptor signaling antagonizes SARS2-induced inflammatory signaling mediated by interferon in the airway epithelium. This finding suggests the hypothesis that the suppression of the interferon response to SARS2 infection by elevated circulating progesterone during pregnancy may contribute to the asymptomatic clinical course," McKenna said.

Consistent with their hypothesis, while this paper was being reviewed, a clinical trial was launched to evaluate progesterone as a treatment for

COVID-19 in men.

More information: *Scientific Data*, DOI: 10.1038/s41597-020-00628-6