

Sex-specific immune response in COVID-19 linked to cellular metabolism

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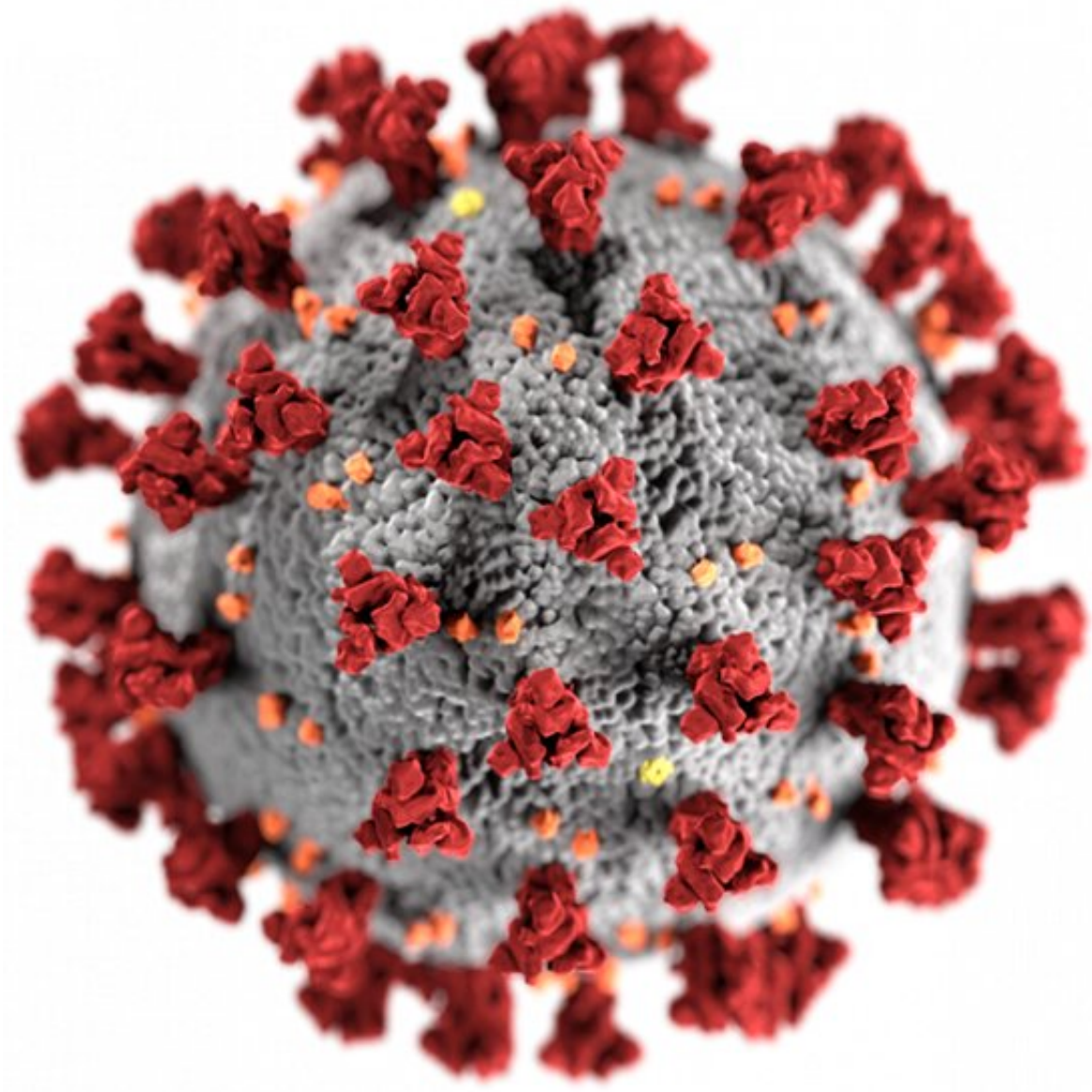


Image of the ultrastructural morphology exhibited by the 2019 Novel Coronavirus (2019-nCoV). Credit: CDC

Researchers studying COVID-19 patients have found a metabolic pathway that is highly correlated with immune responses only in male patients, a group known to be more likely to suffer severe cases and die of the disease, representing a potential target for therapeutic intervention.

In a study published today in the journal *Science Signaling*, the authors report that male COVID-19 patients were more likely than [female patients](#) or healthy control subjects to have elevated levels of kynurenic acid, a product of amino acid metabolism. High levels of kynurenic acid have been linked to several diseases, such as schizophrenia and HIV-related diseases.

Male patients with severe COVID-19 cases were also more likely to have a high ratio of kynurenic acid to kynurenine, a byproduct of the amino acid L-tryptophan which is used to create the nutrient niacin.

"We know that men are at higher risk than women of contracting severe cases of COVID-19 and that sex differences in the body's immune responses present a compelling explanation for this phenomenon," said Caroline Johnson, an assistant professor of epidemiology at Yale School of Public Health and senior author of the study. "We also know that immune responses are regulated in part by metabolites, and so these new findings offer a key window into the mechanisms underlying how this disease affects female and [male patients](#) differently."

With help from Women's Health Research at Yale, Johnson established a collaboration with Akiko Iwasaki, the Waldemar Von Zedtwitz Professor of Immunobiology and Molecular, Cellular and Developmental Biology, who had led a research team this summer in successfully identifying significant differences in how the immune systems of women

and men respond to the virus that causes COVID-19.

With support from Yale School of Public Health's new Rapid Response Fund, Johnson, postdoctoral associate Yuping Cai, and their team studied [blood samples](#) drawn from 22 female and 17 male patients at Yale New Haven Hospital after confirmation of COVID-19 infection. They then compared these samples with samples from 20 uninfected health care providers.

The researchers positively identified 75 metabolites, which are molecular products of digestion and cellular processes. After adjusting for the patients' age, body-mass index, sex, and other characteristics, the researchers determined 17 metabolites were associated with COVID-19 infection. Further analysis revealed the strong relationship between high levels of kynurenic acid as well as high ratios of kynurenic acid to kynurenine in the male [immune response](#) and worse patient outcomes.

"Such sex-specific pathways provide major clues about how this disease infects and sickens individuals," Johnson said. "We can use this knowledge to create more effective treatments for this terrible disease and similar diseases."

More information: Yuping Cai et al, Kynurenic acid may underlie sex-specific immune responses to COVID-19, *Science Signaling* (2021). [DOI: 10.1126/scisignal.abf8483](https://doi.org/10.1126/scisignal.abf8483)

Provided by Yale University

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