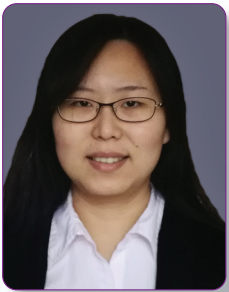


Institut Lady Davis de recherches médicales | Lady Davis Institute for Medical Research

## PAPER OF THE MONTH • MARCH 2021



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Source: MUHC /CUSM)

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# nature medicine

## A Neanderthal OAS1 isoform Protects Against COVID-19 Susceptibility and Severity: Results from Mendelian Randomization and Case-Control Studies

Sirui Zhou, Guillaume Butler-Laporte, Tomoko Nakanishi, . . . Brent Richards

This analysis shows evidence that increased levels of the protein OAS1 has a protective effect against COVID-19 susceptibility and severity. There are already therapies in pre-clinical development that boost OAS1 and could be explored for their effect against SARS-CoV-2 infection.

Recent advances in proteomic technology combined with genetic analyses through Mendelian randomization made possible the delicate work of untangling which proteins affected COVID-19 adverse outcomes. From genetic determinants of 931 circulating proteins, researchers in the Richards lab found that increased OAS1 levels were associated with reduced COVID-19 death or ventilation, hospitalization, and susceptibility in up to 14,134 COVID-19 cases and 1.2 million controls. They proceeded to measure OAS1 levels in 504 patients with different COVID-19 outcomes from the Biobanque Québec COVID-19 and confirmed the findings. They observed a 50% decrease in the odds of very severe COVID-19 per standard deviation increase in OAS1 circulating levels.

This OAS1 isoform likely emerged in people of European ancestry through interbreeding with Neanderthals tens of thousands of years ago. Evolutionary pressure slowly increased the prevalence of this form of OAS1, such that it is now detectable in more than thirty-percent of people of European descent. It is likely that the form of the protein has served as protection against earlier pandemics.