## News in focus

Scientists straying from their field of expertise in this way are examples of what Nathan Ballantyne, a philosopher at Fordham University in New York City, calls "epistemic trespassing". Although scientists might romanticize the role and occasional genuine insight of an outsider – such as the writings of physicist Erwin Shrödinger on biology – in most cases, he says, such academic off-piste manoeuvrings dump non-experts head-first in deep snow.

Many trespassers have good intentions, Ballantyne says, and crossing disciplinary lines can be positive for research. But he says that outsiders should collaborate with a genuine expert – and that studies that do not list such an expert as a co-author should raise a red flag to other researchers and the media.

Some funders have recognized the threat of covidization. Matthias Egger, president of the National Research Council of the Swiss National Science Foundation, warned earlier this year of the "instant experts" thrown up by the pandemic. "Colleagues who had spent their academic careers far removed from viruses and lung inflammation have now miraculously revealed themselves as experts," he wrote in an opinion piece. Throwing money at COVID-19 at the expense of other science could be a mistake. he said, and researchers should concentrate on the questions they decided to pursue. "There will be no covidization of research here." he said. "Whether your chosen field is the coelacanth, exoplanets, social inequality or global warming, please keep doing what you do."

## HOW KIDS' IMMUNE Systems can Evade covid

Children's untrained immune cells and other factors seem to be key to eliminating SARS-CoV-2.

## By Bianca Nogrady

oung children account for only a small percentage of COVID-19 infections – a trend that has puzzled scientists. Now, a growing body of evidence suggests why: kids' immune systems seem better equipped to eliminate the virus SARS-CoV-2 than are adults'.

"Children are very much adapted to respond – and very well equipped to respond – to new viruses," says Donna Farber, an immunologist at Columbia University in New York City. Even when they are infected with SARS-CoV-2, children are most likely to experience mild or asymptomatic illness.

Another clue that children's response to the virus differs from that of adults is that some children develop COVID-19 symptoms and antibodies specific to SARS-CoV-2 but never test positive for the virus on a standard test using the technique RT-PCR. In one study, three children from the same family developed SARS-CoV-2 antibodies<sup>1</sup> – and two of them even experienced mild symptoms – but none tested positive on RT-PCR, despite being tested 11 times over 28 days while in close contact with their parents, who had tested positive.

Their immune system sees the virus "and it just mounts this really quick and effective immune response that shuts it down, before it has a chance to replicate to the point that it comes up positive on the swab diagnostic test", says Melanie Neeland, an immunologist at the Murdoch Children's Research Institute in Melbourne, Australia, who studied the family.

Even in children who experienced the severe but rare complication called multisystem inflammatory syndrome in response to SARS-CoV-2 infection, studies report that the rate of positive results on RT-PCR is 50% or below<sup>2</sup>.

Farber says the types of antibody children develop offer clues about what is going on. In a study<sup>3</sup> of 32 adults and 47 children aged 18 or



Children rarely show symptoms of COVID-19.

younger, she and colleagues found that children mostly produced antibodies aimed at the SARS-CoV-2 spike protein, which the virus uses to enter cells. Adults generated similar antibodies, but also developed antibodies against the nucleocapsid protein, which is essential for viral replication. Farber says the nucleocapsid protein is typically released in large quantities when a virus is widespread in the body.

That kids lacked nucleocapsid-specific antibodies suggests that they aren't experiencing a significant infection, says Farber. Children's immune responses seem to be able to eliminate the virus before it takes over, she says.

## Adaptive versus innate

Farber suggests that the reason children can neutralize the virus is that their T cells are relatively naive. T cells are part of the body's adaptive immune system, which learns to recognize pathogens it encounters over a lifetime. Farber says that because children's T cells are mostly untrained, they might have a greater capacity to respond to new viruses.

But other evidence suggests the situation is not so straightforward: a study<sup>4</sup> of people with COVID-19 that included 65 children and young people under the age of 24, along with 60 adults, found that the adults had a stronger T-cell response to the virus's spike protein than did the children and young people. Farber says the study measured memory T-cell responses, which are much less developed in children, rather than naive T-cell activity.

Children's ability to neutralize the virus might also be linked to the fact that they have a strong innate immune response from birth, says Alasdair Munro, who studies paediatric infectious diseases at University Hospital Southampton, UK. But this effect is difficult to study, and raises the question of why it isn't seen with other viruses that can cause disease in children, he says.

Children are also the main reservoir for seasonal coronaviruses that cause the common cold. Some researchers have suggested that antibodies for these viruses might confer some protection against SARS-CoV-2, but the evidence is mixed, says Munro.

Meanwhile, there is evidence that when children are exposed to the virus, they receive a smaller dose than adults, because their noses contain fewer ACE2 receptors, which the virus uses to gain access to cells. This might also explain why COVID-19 is less prevalent in children than in adults, say researchers.

Munro says it is unlikely that there is a single explanation for why COVID-19 seems to affect children less than adults. "Biology is rarely so straightforward."

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