Bethlehem and their colleagues acknowledge that their study suffers from a problem endemic in neuroimaging studies — a remarkable lack of diversity. The brain scans they collected come mainly from North America and Europe, and disproportionately reflect populations that are white, university-aged, urban and affluent. The study includes only three data sets from South America and one from Africa — accounting for around 1% of all the brain scans used in the study.

Billions of people worldwide lack access to MRI machines, making diverse brain-imaging data difficult to come by, Laird says. But the authors haven't stopped trying. They have launched a website where they intend to update their growth charts in real time as they receive more brain scans (see go.nature.com/3rctwfd).

Big data sets, big responsibility

Another challenge was determining how to give proper credit to the owners of the brain scans used to construct the charts. Some of the scans came from open-access data sets, but others were closed to researchers. Most of the closed-data scans hadn't yet been processed in a way that would allow them to be incorporated into the growth charts, so their owners did extra work to share them. These scientists were then named as authors of the paper.

Meanwhile, the owners of the open data sets received only a citation in the paper — which doesn't hold as much prestige for researchers seeking funding, collaborations and promotions. Seidlitz, Bethlehem and their colleagues processed these data. In most cases, Bethlehem says, there was essentially no direct contact with the owners of these data sets.

There are a number of reasons that data sets might be closed: for instance, to protect the privacy of health data. But this doesn't make it fair that the researchers who opened their data sets didn't get authorship, Bethlehem and Seidlitz say. They contend that authorship guidelines from journals, including *Nature* — which say that each author is expected to have made "substantial contributions" to, for example, the analysis or interpretation of data — are an obstacle. (*Nature*'s news team is editorially independent of its publisher.)

A *Nature* spokesperson responds that the issue was "considered carefully by the editors and authors according to our authorship policies" and that "all data sets were appropriately credited per our data citation policy".

Ultimately, these concerns can be traced back to how researchers are evaluated by the scientific enterprise, says Kaja LeWinn, a social epidemiologist at the University of California, San Francisco. She says that stakeholders — including funders, journals and research institutions — need to re-evaluate how brain science can be properly recognized and rewarded, especially as these types of large-scale study become more common.

INFECTED IMMUNE CELLS HOLD CLUES TO SEVERE COVID

The virus SARS-CoV-2 can infect immune cells, prompting a massive inflammatory response.

By Smriti Mallapaty

Immune cells infected with SARS-CoV-2 can trigger a massive inflammatory response that contributes to severe COVID-19, suggest two papers.

Since the early days of the pandemic, research has suggested that inflammation leads to significant respiratory distress and organ damage, hallmarks of severe COVID-19. But scientists have struggled to pinpoint what triggers the inflammation.

The latest studies implicate two types of white blood cell — monocytes in the blood and macrophages in the lungs — which, once infected with the virus, trigger inflammation. The studies also provide conclusive evidence that the virus can infect and replicate in immune cells, and reveal the receptor it exploits to enter those cells. Evidence for such infections has been mixed until now.

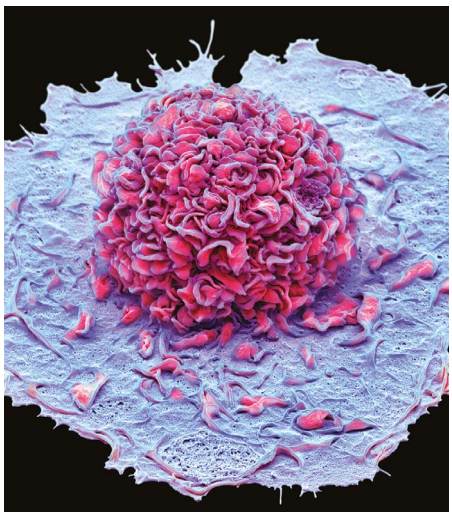
The studies offer a plausible explanation for how severe COVID-19 progresses, says Malik Peiris, a virologist at the University of Hong Kong. "I don't think it is the only or most important pathway, but it is certainly interesting."

Still, infected immune cells could offer a potential target for drug development, says Jian Zheng, an immunologist at the University of Iowa in Iowa City.

In a paper published in *Nature* on 6 April, Judy Lieberman, an immunologist at Boston Children's Hospital in Massachusetts, and her colleagues looked at blood samples from people with COVID-19 (C. Junqueira *et al*. *Nature* https://doi.org/hppt; 2022). They found that about 6% of monocytes — 'early responder' immune cells that patrol the body for foreign invaders — were undergoing a type of cell death associated with inflammation, known as pyroptosis. To see so many cells dying is unusual, she says.

When the researchers looked at the dying cells, they found they were infected with SARS-CoV-2. The team suggests the virus was probably activating inflammasomes, large molecules that trigger a cascade of inflammatory responses that end in cell death.

The researchers also looked at another type of immune cell, macrophages, in the lungs of people who had died of COVID-19. Because macrophages collect cellular garbage, including viral debris, it has been difficult to show whether they were infected with SARS-CoV-2 or just sopping up this debris. The team found that about one-quarter of macrophages had activated inflammasomes, and a fraction of those had indeed been infected with the virus. Other infected lung cells, from tissue called the epithelium, did not display the same response.



STEVE GSCHMEISSNER/SPL

SARS-CoV-2 can infect macrophages (pictured) in the lungs.

The results align with those of the second study, posted on the preprint server bioRxiv by Esen Sefik, an immunologist at Yale University School of Medicine in New Haven, Connecticut, and her colleagues, and yet to be peer reviewed (E. Sefik *et al*. Preprint at bioRxiv https://doi.org/hppw; 2022). They found that the virus could infect and replicate in macrophages in human lung cells and in a mouse model of the human immune system. The macrophages showed the same inflammatory response as described by Lieberman, and eventually died.

The macrophages' response could be their way of stopping SARS-CoV-2 from replicating, says study co-author Richard Flavell, an immunologist also at Yale. When inflammasomes were activated, the virus stopped replicating in the cells. When the researchers blocked inflammasomes, the macrophages started producing infectious virus.

But Stanley Perlman, a virologist at the University of Iowa, says studies will be needed to work out how important infected immune cells are in inducing severe COVID-19, compared with other possible mechanisms.