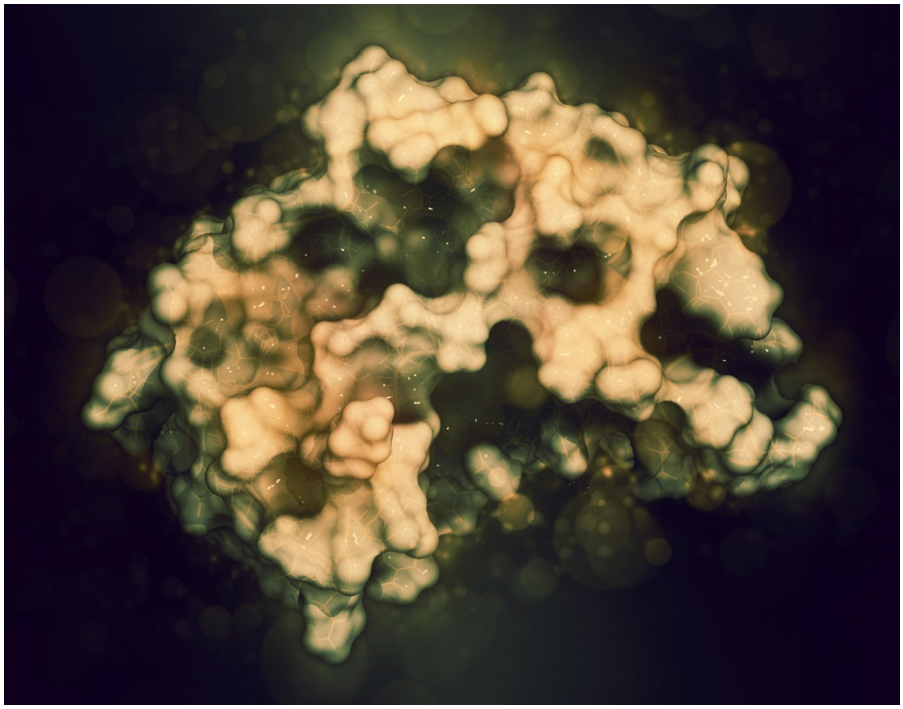

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Problem protein: An illustration of interleukin-6, one of the inflammatory proteins implicated in depression.

group of participants with depression in that trial did benefit from anti-inflammatory treatment. In 2015, McIntyre and his team in Toronto initiated a clinical trial using the same drug, infliximab, to treat depression. However, in this study, one of the criteria for participation is a CRP level above the value that predicted a reduction in depression in response to the antibody drug in the 2013 trial. "We designed our study informed by the results of the Emory study," McIntyre says.

Another ongoing clinical trial, run by Janssen Pharmaceuticals, is dosing patients who have depression with an antibody called sirukumab, which acts to neutralize the inflammatory protein interleukin-6. The experimental new drug, which is not yet approved for any illness, was originally developed to treat rheumatoid arthritis. Janssen's depression study is focused on how this drug will work in participants who have high CRP levels. The company made this decision on the basis of Miller's findings, says Wayne Drevets, a psychiatrist and disease-area leader in mood disorders at Janssen. Another antibody to interleukin-6, tocilizumab, is being used in a clinical trial by a team at Brigham and Women's Hospital to treat depression. Tocilizumab, marketed under the brand name Actemra, is currently indicated to treat rheumatoid arthritis.

These anti-inflammatory treatments might also have applications for other mental illnesses, such as schizophrenia. Ragy Girgis, a psychiatrist at the Columbia University Medical Center, saw Miller's 2013 study and immediately noted its potential use for schizophrenia. "I read it and said, 'We have to be able to do something like this in schizophrenia,'" Girgis says. Research shows that interleukin-6 levels are elevated in people with this condition, so Girgis used tocilizumab in a clinical trial that finished collecting data in February. The results are not yet available. Girgis is hopeful that the findings will be positive. There's already a large amount of overlap between existing treatments for depression and treatments for schizophrenia, he adds. "Chances are that treatments for one could very well be effective for the other."

But once the clinical trials researching depression and schizophrenia finish, even assuming the response is good, getting approval to use an anti-inflammatory medication for these disorders could take years. Drevets says that it could be almost a decade or longer. Moreover, in their current form, immunosuppressants are expensive: in the US, a single dose of infliximab can cost thousands of dollars per infusion.

Cost is one of the reasons that the treatment isn't intended as a one-size-fits-all drug, Drevets says. Instead, the drugs could specifically target the subset of people with depression who don't respond to other treatments, or who have results on future inflammatory-biomarker tests that indicate immunosuppression might work for them. Most researchers are working under the assumption that these treatments are not going to benefit everyone. "We're thinking about developing drugs that might work particularly well for a particular subgroup," Bullmore says. "I think that a lot of people in industry would think that is the right thing to do."

Even Miller doesn't think the immunosuppressant therapies are ready for prime time just yet. "Don't play with fire unless you really know what you're dealing with," Miller says. "The immune system is very complicated." His current work focuses on the role that the neurotransmitters glutamate and dopamine have in inflammation and depression. He thinks that the way dopamine interacts with inflammatory pathways in the brain could make it a potential treatment target.

Scientists in this field remark that the landscape has changed dramatically in the past ten years. "Now, if you go to a psychiatry meeting, there are tons of mainstream talks on inflammation, and the place is packed," McIntyre says. The crowded rooms are a good thing, Miller notes, despite the extra pressure the attention brings: "It's easier to work in the shadows, sometimes, than it is to work in full sunlight. People get more competitive. But I think it makes the science better."

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Correction

In the August 2017 issue, the story "Breaking through: How researchers are gaining entry into barricaded bacteria" (*Nat. Med.* **23**, 907–910, 2017) misstated that the pharmaceutical company Achaogen would be filing a New Drug Application with the FDA in 2018. The company will be filing an Investigational New Drug application. The article was also unclear in wording the progress of siderophore-conjugated antibiotics. Such antibiotics have made it to clinical trials, but none so far have made it to market. The errors have been corrected in the HTML and PDF versions of the article as of 23 August 2017.