Drug development

The hunt for covid-19 drugs

Many drugs and vaccines are now being developed and tested

Debora MacKenzie

AS THE number of coronavirus cases escalates, a massive research and development effort is under way, with human trials planned.

What the thousands of people who already have the covid-19 virus would benefit from is a drug that can stop it replicating. To find what may do this, people are ransacking lists of existing drugs that could be repurposed with minimal further testing.

Leading the pack is remdesivir, an experimental antiviral drug now undergoing large trials in patients in China and the US, including 13 people who were on the Diamond Princess cruise ship.

It is hoped that the drug, which failed in trials against Ebola in 2014 but passed safety tests, can stop the covid-19 virus replicating by blocking a crucial enzyme. Its maker, US firm Gilead Sciences, is building manufacturing facilities ahead of trial results in April.

Trials are also planned for kaletra, a combination of two anti-HIV drugs that stops viral replication and has reportedly worked on covid-19 in China.

Chloroquine, an antimalarial drug that most malaria now resists, might also hold promise. Studies suggest that it stops the related SARS virus replicating and invading cells, and that it works against the covid-19 virus. Treatment guidelines in China now recommend two 500 milligram doses daily.

Another approach is to use proteins called monoclonal antibodies that target specific viruses for destruction by the immune system. Vir Biotechnology in the US has made monoclonal antibodies for the covid-19 virus for an experimental diagnostic test. It now plans, with Chinese firm WuXi Biologics, to test them as a treatment. US firm Regeneron is brewing similar antibodies.

A team at Imperial College London has used artificial intelligence to assess approved drugs for promising candidates, and identified a rheumatoid arthritis drug, baricitinib (*The Lancet*, doi.org/dph5). This blocks the pathway the covid-19 virus uses to invade cells, as well as

42 days

How quickly one firm was able to make enough vaccine for trials

interfering with interleukin-6, the signalling molecule that triggers the lethal runaway immune response that can kill in severe cases. An antibody called tocilizumab is already being used in China to block interleukin-6 in people with covid-19.

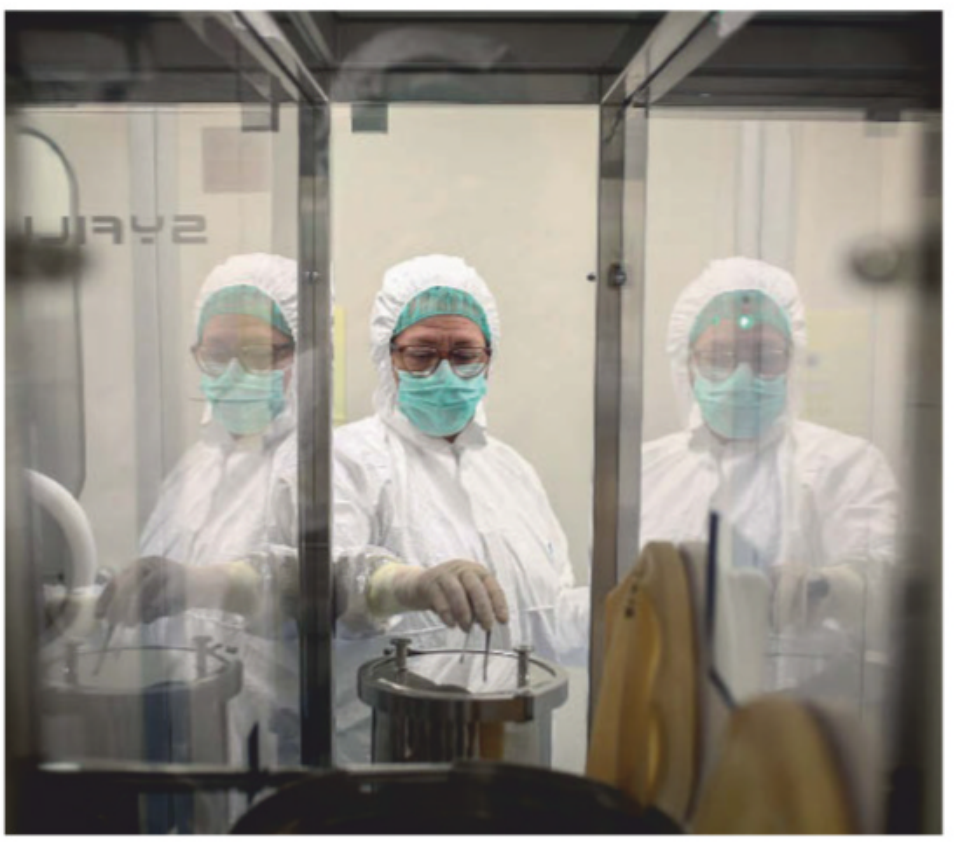
For people who don't catch the virus during this outbreak – and future generations – a vaccine will be needed. French firm Sanofi is working on hybridising the covid-19 virus with a harmless baculovirus already approved for its flu vaccine, which it can make in mass quantities to test if it works as a covid-19 vaccine.

The Coalition for Epidemic Preparedness Innovations (CEPI) is backing several other drug candidates. It was launched in 2017 by the Gates Foundation and several governments to develop vaccines for new diseases. "We were set up to respond to exactly this situation," says spokesperson Jodie Rogers.

CEPI plans to have at least one vaccine in human trials by May. If trials succeed, it plans to make "hundreds of millions of doses available" by early 2021.

This week, CEPI announced that it would back a vaccine developed by the University of Oxford that is made of Vaccinia virus, once used in smallpox vaccine, carrying an external spike protein from covid-19. The group will also support a vaccine from US firm Novavax made of "nanoparticles" of the spike protein plus an immune-stimulating chemical.

Many labs are working on drugs to prevent or fight infection with coronavirus



OLIVER BUNIC/BLOOMBERG VIA GETTY IMAGES

CEPI has already launched four other covid-19 projects. US firm Inovio had been working on a DNA vaccine for the related MERS virus, and says it had one for covid-19 just 3 hours after the gene sequence for the virus was published on 10 January. It plans clinical trials in April and to have a million doses by December, if the approach works.

DNA vaccines are rings of genetic material that enter our cells and make viral proteins that induce immunity. However, they have never been approved for humans for fear they might affect our own genes or induce damaging immune reactions.

Messenger RNA vaccines don't pose the same problems. CEPI is backing one from CureVac in Germany and another from Moderna in the US, which recently made enough vaccine for human safety trials in the record time of 42 days.

Supporters say that DNA or RNA vaccines, unlike some conventional vaccines, can't cause disease, are stable, cheap to mass-produce and effective in small doses – all boons in a pandemic emergency. By the time they are fully tested, however, covid-19 may no longer be an emergency. It may even be hard to find test subjects not already immune.

The coalition is also supporting more conventional vaccines, including a process to make viral proteins from the University of Queensland, Australia, and a viral protein vaccine from China's Clover Biopharmaceuticals plus an immune-boosting additive from British firm GSK. A further 48 proposals are still being considered.