Drug candidate may stop MERS
Chemical disrupts assembly centers of coronaviruses

BY MEGHAN ROSEN
An experimental drug that shuts down construction of virus-making factories within human cells could become a new weapon against MERS and similar respiratory diseases. The chemical, called K22, halts growth of coronaviruses, including the strains that cause MERS and SARS, researchers report May 29 in PLOS Pathogens.

K22 is the latest in a slew of drug candidates to counter coronaviruses, for which no proven drug treatments exist. But K22 stands out from the crowd, says Stanley Perlman, a virologist and pediatric infectious disease physician at the University of Iowa in Iowa City.

K22 hits a part of the viral life cycle that no drug candidate has tackled before. “The ideal drug may be something like this,” Perlman says.

Still, moving the chemical from the lab to the clinic could take years of testing and development, says study coauthor Volker Thiel, a virologist at the University of Bern in Switzerland. “We have no idea how the drug will behave in the body.”

And drug companies might not want to spend the money figuring it out, he says — unless there’s a huge outbreak.

In 2012, scientists documented the first case of MERS, or Middle East Respiratory Syndrome, in Saudi Arabia. MERS has since infected more than 680 people and killed at least 200 (SN: 5/31/14, p. 6). Like SARS before it, which struck more than 8,000 people in a 2002–2003 outbreak, MERS is caused by infection with a coronavirus. Coronaviruses are RNA-based viruses that look like a crown, or corona, under an electron microscope.

These viruses are famous for sneaking into human cells, stealing bits of membrane and erecting tiny chambers for building new viruses. Within cells, the membrane-wrapped virus mills spring up quickly and cluster together like a viral tent city.

In the new study, Thiel, Edward Trybala of Sweden’s University of Gothenburg and colleagues infected human cells growing in dishes with a strain of coronavirus that triggers coldlike symptoms in people. The researchers then added each of 16,671 chemical compounds to different dishes and looked for cells that stayed healthy.

One compound, the small molecule K22, cut viral infection in half compared with cells not exposed to the drug candidate. Thiel and colleagues think that K22 stops the virus from forming the saclike factories inside infected cells.

After infecting a human cell (shown), coronaviruses hijack membranes from the cell to form their own viral factories (cluster of pale circles in center of electron microscope image; dark circle in middle holds new virus particles). A new drug candidate blocks construction of these factories and halts viral growth.

But K22 stands out from the crowd, says Stanley Perlman, a virologist and pediatric infectious disease physician at the University of Iowa in Iowa City.

K22 targets the construction of virus-making factories, a stage that comes after viruses enter the cell. “The idea is that by killing the factory, you’re limiting the virus’s ability to infect more cells,” Perlman says. In addition to shortening the life cycle of the virus, the chemical also limits the amount of virus particles released from cells.

After trying drugs from various companies, Thiel and colleagues were about to test all we have in the freezer.’ ”

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Researchers then tested all 16,671 compounds against the K22 drug candidate against the highly deadly MERS coronavirus. “And it did,” Thiel says. “That was exciting for us.”

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factories inside infected cells. When the team looked at drug-treated cells under a microscope to find the tiny sacs, “we saw that they were all gone,” Thiel says. “That was exciting for us.”

No factories means no new viruses, which stops the infection from spreading to other cells.

Thiel and colleagues were about to publish their findings, he says, but then MERS came along. So the researchers tested whether K22 also blocked growth of the MERS coronavirus. “And it did,” Thiel says. “Then we thought, ‘If it’s inhibiting two coronaviruses, we should test all we have in the freezer.’”

The drug worked against all six of the viruses tested, including the strain that causes SARS as well as viruses that infect cats, birds and mice.

Thiel thinks K22, or similar chemicals that attack the viruses’ factories, could be a new type of weapon in the arsenal of potential drugs for fighting coronaviruses. Having different kinds of ammunition is important to prevent drug-resistant viruses from popping up. “It’s good to combine drugs and target different steps in the virus’s life cycle,” he says. “It’s the lesson we learned from HIV.”

the same cells these astrocytes support, showed signs of listlessness.

Tweaking the behavior of these appetite-regulating astrocytes might be a way to treat obesity, Horvath suggests. But the brain’s leptin machinery is a problematic target, says neuroscientist Jenni Harvey of the University of Dundee in Scotland. Because fat cells produce leptin, obese people generate higher amounts of the hormone in the blood. Faced with a constant barrage of leptin, the brain’s ability to take in the hormone weakens, leading to leptin insensitivity. Adding more leptin wouldn’t do any good, she says. “Targeting the leptin system is unlikely to result in a cure for obesity.”

The newly described role for astrocytes is interesting, but “it’s just scratching the surface,” Harvey says. “There are a lot of questions that need to be answered.”

BY BETH MOLE

Towering waves that rise from cyclones can pulp the frigid waters around Antarctica, potentially wrecking sea ice crucial for maintaining global climate. Because researchers predict climate change will bring more and stronger storms worldwide, the thrashing swells threaten to substantially reduce sea ice.

Around Antarctica, sea ice is forming in some places and disappearing in others, says Alison Kohout, a sea ice researcher at the National Institute of Water and Atmospheric Research in Christchurch, New Zealand. Because sea ice reflects the sun’s rays and insulates the ocean below, the frozen rafts influence global temperatures, storms and ocean circulation. But, Kohout says, scientists don’t know enough about sea ice to predict future changes.

With colleagues, Kohout collected data suggesting that waves from ocean storms may be particularly damaging to sea ice. By collecting observations of ice thickness from around Antarctica and wave-height measurements from five ice-bound sensors off the coast of the southernmost continent, the researchers estimated wave energy. The team then calculated that high waves fueled by distant cyclones could plow through sea ice, packing enough energy to break ice for hundreds of kilometers. The results appear in the May 29 Nature.

The waves, Kohout says, “can travel further than previous theory expected.” Scientists thought that waves diminish exponentially as they slam into floating ice. In other words, ice closer to the continent should experience a small fraction of the wave’s original ramming power. But the new data suggest that storm-generated waves higher than 3 meters weaken linearly as they move across ice, preserving their smashing power for much greater distances.

“The fact that storms have an effect on ice breakup has been known for a long time,” says Claire Parkinson, a climate scientist at NASA’s Goddard Space Flight Center in Greenbelt, Md. But she says the finding that these larger waves can punch deep into ice fields is important.

“Storms could have a bigger impact on the ice cover than had been thought,” she says.

Many scientists expect global warming to boost cyclone activity, Parkinson adds, suggesting that high waves will also increase and potentially crush sections of ice.

Ice-breaking waves need more study, says Julienne Stroeve, a sea ice researcher at the National Snow and Ice Data Center in Boulder, Colo. The thickness of sea ice chunks and how closely they’re packed together influence how much damage waves can cause, she says. But because the study focused on young, 1-year-old ice up to 1 meter thick, which is common on the edges of sea ice, the results are probably a good indicator of how big waves will affect sea ice in the future, she says.

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