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CHEMICAL & ENGINEERING NEWS

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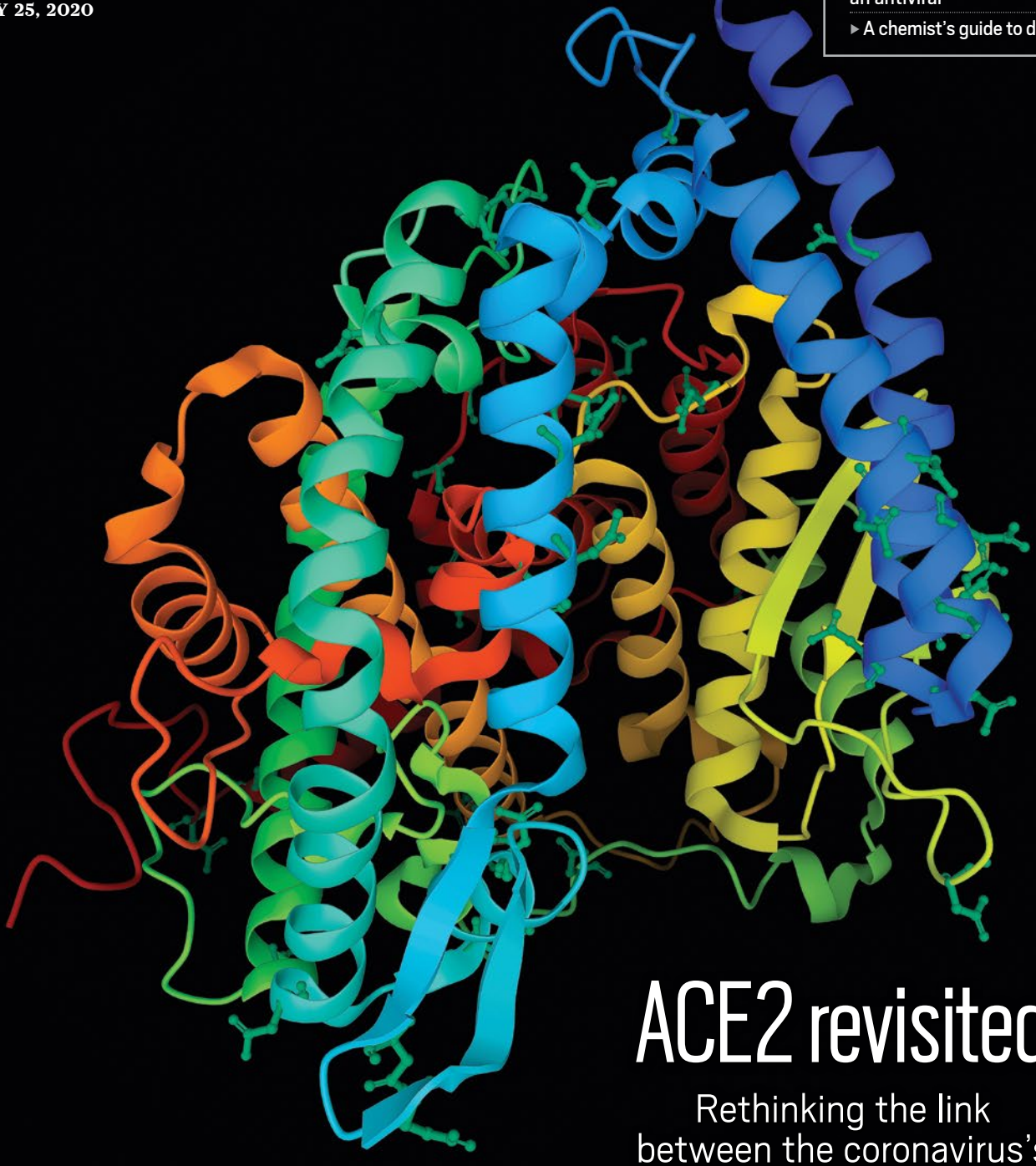

ACE2 revisited

Rethinking the link between the coronavirus's human entry point and blood pressure drugs

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VACCINES

New malaria vaccines show promise

Genetically engineered, weakened parasites may generate a stronger immune response

Two experimental malaria vaccines have delivered promising results in first-in-human trials, demonstrating how genetic engineering is driving a new wave of vaccines that could protect people from this killer disease.

The World Health Organization estimates that there are more than 200 million cases of malaria each year, causing almost half a million deaths. Although malaria can be treated with drugs, researchers have spent decades trying to develop vaccines that could prevent and potentially even help eradicate malaria. In 2019—after 32 years of development and clinical trials—a vaccine called Mosquirix (also known as RTS,S) was finally rolled out to young children in pilot programs across three African countries.

Mosquirix acts against the most deadly form of human malaria, caused by the parasite *Plasmodium falciparum*. It is the only malaria vaccine to move beyond Phase III clinical trials, but it is no silver bullet. The vaccine only prevents about 40% of malaria cases, and the protection wanes after a few years. More than 20 other vaccines, which are still moving through the development pipeline, aim to improve on that performance.

One of the big challenges for these vaccines is that malaria parasites have a very complex life cycle, shape-shifting as they move through mosquitoes and human hosts. Mosquirix tackles the parasite when it is a sporozoite—the form that mosquitoes inject into their victims' bloodstreams, and which then infects liver cells. The vaccine contains a circumsporozoite protein (CSP) that induces the human body to generate antibodies against sporozoites.

Two new vaccines also target the liver stage, but contain whole sporozoites that have been attenuated—they are alive, yet unable to cause malaria. Since sporozoites carry dozens or hundreds of proteins that could trigger an immune response, researchers think the two vaccines may offer more robust protection than the lone CSP in Mosquirix.

The first vaccine, *Pb*Vac, uses *Plasmodium berghei*, a relation of *P. falciparum* that infects rodents but does not cause disease in humans. "The parasite is naturally attenuated, so it's inherently safe in that way," says Miguel Prudêncio at the University of Lisbon, part of the team behind *Pb*Vac. The researchers genetically modified *P. berghei* sporozoites to express *P. falciparum* CSP.

Mosquitoes inject *Plasmodium falciparum* sporozoites into their human hosts, causing malaria.

Volunteers who were treated with *Pb*Vac and then infected with malaria had, on average, a 95% reduction in *P. falciparum* in their livers. In vitro tests showed that the vaccine triggered an antibody response that stopped sporozoites entering liver cells (*Sci. Transl. Med.* 2020, DOI: 10.1126/scitranslmed.aay2578). Prudêncio says that it should be possible to further engineer *P. berghei* sporozoites to carry other antigens in addition to CSP.

The second vaccine, PfSPZ-GA1, was developed by a team in the Netherlands, in collaboration with biotechnology company Sanaria. It contains *P. falciparum* sporozoites that lack two genes the parasite needs in order to develop in the liver. Volunteers who were given the vaccine and then infected with malaria produced antibodies against CSP, along with T cells (*Sci. Transl. Med.* 2020, DOI: 10.1126/scitranslmed.aaz5629).

"Ultimately, these are promising results," says Stefan H. I. Kappe, a malaria researcher at Seattle Children's Research Institute. "I think we are at the beginning of developing a very potent attenuated whole-parasite vaccine."—MARK PEPLOW, special to C&EN

BIOMATERIALS

Stretching the brain to image it

Seeing inside someone's heart. Stretching the mind. These aren't just turns of phrase but something that researchers can physically do with help from polymer science and microscopy. Massachusetts Institute of Technology chemical engineer Kwanghun Chung has found a way to turn organs into flexible, transparent hydrogels (*Nat. Methods* 2020, DOI: 10.1038/s41592-020-0823-y).

When he was a postdoc, Chung helped develop a way to render brain tissue transparent and fixed in polyacrylamide, but the resulting samples were brittle. Chung and his team have now adjusted the amounts of acrylamide, cross-linker, and initiator to create an entangled hydrogel rather than a cross-linked one. Because the long polymer chains are entangled, the links can slip around one another, giving the gel structural integrity but also flexibility and stretchability. The team call the technique ELAST (entangled link-augmented stretchable tissue-hydrogel).

When their polymer formulation infuses biological tissues, cells and molecules become entangled in a stretchy gel. That makes fragile tissues easier to handle and can speed up the process of fluorescently labeling cells or biomolecules. Instead of waiting for imaging probes to diffuse through a thick sample, they can stretch out ELASTicized samples and apply a solution of fluorescent probes, maximizing the contact between the labels and the samples and speeding up the labeling process. When the gel snaps back to its original shape, it's ready for imaging and the next round of labeling. Chung hopes to use the technique to make a comprehensive map of the human brain.—LAURA HOWES

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