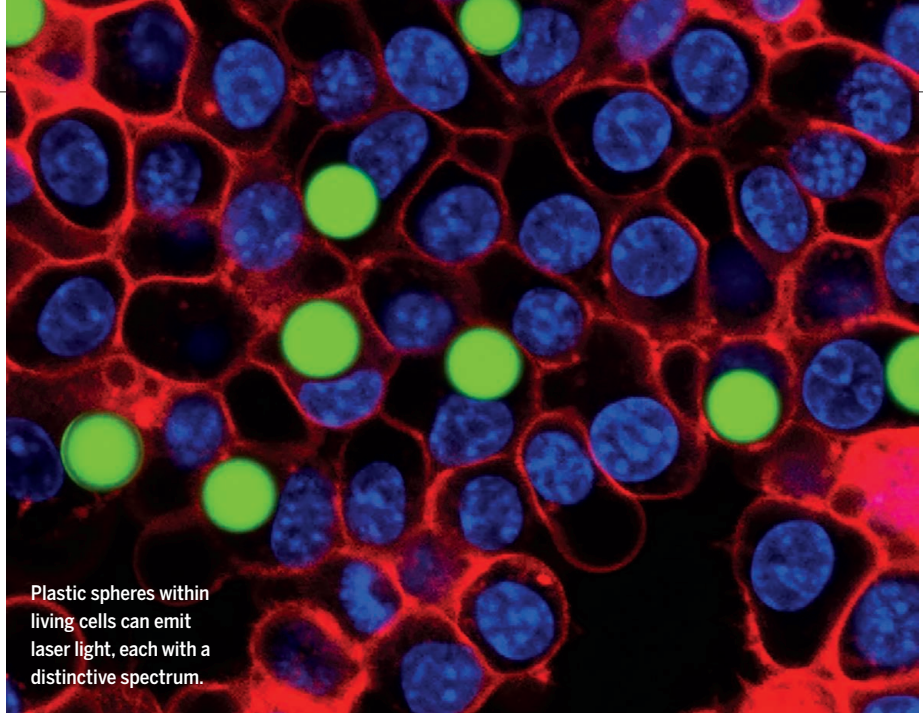

Plastic spheres within living cells can emit laser light, each with a distinctive spectrum.

IMAGE: M. SCHUBERT ET AL., *NANOLETT* (2015); ACS

pendently, using much the same technique.

The hard part is putting a cavity in a cell. Gather and colleagues got cells to do that for themselves. In culture, they mixed cells with tiny plastic spheres 5 to 10 micrometers in diameter that had been "doped" with a fluorescent dye. The beads served as the cavities, the dye as the medium. The cells absorbed the spheres through endocytosis, the same process by which immune cells gobble up pathogens, the team reported online on 17 July in *Nano Letters*. The trick worked with four types of cells, including human macrophages, a type of white blood cell.

The researchers then applied a 5-nanosecond pulse of light to excite the dye. It emitted light that raced around the sphere's equator, held in by a process called total internal reflection. Specific wavelengths—those for which a whole number of light waves wrapped exactly around a bead's circumference—resonated and grew more intense, until the bead "lased" at a couple of those wavelengths.

Yun and his HMS colleague Matjaž Humar also managed to get cells to take up plastic beads, and they created two other kinds of resonating spheres as well, they reported online on 27 July in *Nature Photonics*. They injected cells with droplets of dyed oil and also showed that the natural lipid globules in fat cells could be made to serve as resonating spheres.

The most obvious application of the lasers would be to track the movements of individual cells, Yun and Gather say. Each plastic bead has a slightly different diameter and optical properties, so it shines at distinctive wavelengths, which serve as a barcode to identify a cell. Gather and colleagues tracked a handful of macrophages in culture for 19 hours, and Yun and Humar did a similar demonstration.

The lasers' ability to shine at narrowly defined wavelengths should give them an edge over rival cell-tracking techniques such as fluorescent tags. Because a fluorescent molecule gives off a spectrum of wavelengths, researchers cannot tag many cells before the tags' spectra overlap. But the lasers' spike-like spectra should make it possible to track thousands of the tiny beacons simultaneously. Researchers might even be able to expand the number to millions or billions by loading each cell with multiple spheres. Every cell would then lase at a distinctive combination of wavelengths.

But that prospect is a way off. First, the teams need to show that various types of cells will take up the spheres, especially in living tissue. Gather predicts that won't be a problem. "I'm confident that this [technique] is generalizable," he says. Developers must also reduce the size of the plastic beads. Now, the beads stuff the cells full, Yun acknowledges. "You feel a bit of pity for them," he says. However, both he and Gather have shown that they can use smaller glass beads instead of the plastic ones.

The tiny lasers might be put to use in research right away to track cultured immune cells as they migrate in response to chemical stimuli, Franze says. A bigger payoff would come if they can be used in vivo, he says, for example, to track cells in developing embryos, the immune system, or cancerous tumors. To do that, researchers would need to get light into and out of living tissue. Zebrafish, which can be made transparent, would be an ideal organism to start experimenting with, Franze says.

Ultimately, laser cells might find uses nobody has imagined. "Regardless of anything else," McGloin says, "it's very cool." ■

INFECTIOUS DISEASES

Risk of 'leaky' vaccines debated

Controversial finding suggests they can speed the spread of deadly pathogens

By **Kai Kupferschmidt**

When people talk about the impact of vaccines, they usually mean the millions of humans saved from disease and death. But Andrew Read, an evolutionary biologist at Pennsylvania State University, University Park, likes to think about what vaccination does to pathogens. In 2001, he published a theory in *Nature* suggesting that some vaccines may cause viruses and bacteria to become more deadly.

Now, Read has some evidence to back that up—at least in animals. A paper published in *PLOS Biology* this week suggests that widespread vaccination against Marek's disease, a viral infection in chickens, explains why it has evolved to become more lethal the past few decades. Something similar might happen with certain human vaccines, Read cautions.

But other researchers say the study has little relevance for public health. Read "should stop scaremongering," says vaccine researcher Adrian Hill of the University of Oxford in the United Kingdom. He and others worry that the paper—and news stories like this one—will only play into the hands of the antivaccine movement.

Read's ideas are built on the widely accepted idea that pathogens often evolve to become less lethal over time. After all, killing their host quickly reduces their chances of being passed on, whereas causing mild symptoms, or none at all, should aid their spread. So-called leaky or imperfect vaccines, which don't prevent infection but merely reduce symptoms, upend that notion, Read argues. They allow the spread of deadlier pathogens that would normally burn out quickly.

Leaky vaccines are common for animal infections, including Marek's disease. Most human vaccines, on the other hand, actually prevent infection, but that may soon change. With diseases like malaria or HIV, for which protection is very hard

to achieve, researchers may settle for vaccines that save lives by preventing severe disease, but not infection.

In the study, Read and his co-workers, working at the Pirbright Institute in Compton, U.K., showed that unvaccinated birds infected with highly virulent strains of Marek's disease didn't shed much virus; they also died too fast to pass the disease on to healthy, unvaccinated birds. But just as Read predicted, the opposite occurred in vaccinated birds: They shed more virus when infected with a virulent strain, readily infecting and killing unvaccinated cagemates. To Read, the result suggests that vaccines can favor strains that would otherwise be too lethal to spread.

It's a convincing study, says Michael Lässig, who studies influenza evolution at the University of Cologne in Germany, "But it's a very special set of circumstances ... I would be careful about drawing general conclusions." Hill also thinks that Marek's disease may be a special case; nothing suggests that human vaccines have ever made a disease more virulent, he says. What's more, natural immunity is "leaky," too, Hill argues, allowing infected people to survive and transmit a disease that is deadly to others. "For malaria, whatever today's vaccine does is a drop in the ocean of all the immunity that is happening in Africa from all the infections," he says.

> ***"It's a very special set of circumstances ... I would be careful about drawing general conclusions."***
> **Michael Lässig**, University of Cologne

Read suspects the phenomenon is more widespread. Feline calicivirus, which causes a respiratory infection in cats, also appears to have increased in virulence as a result of vaccination, Read says, and he is worried about the same thing happening with avian influenza, which some countries keep at bay with poultry vaccines. "You could have the emergence of superhot strains," he says.

As for human disease, the study offers no support whatsoever for those who oppose vaccination, Read stresses. And if leaky vaccines are proven safe and effective, they should be used, he adds, but perhaps with closer monitoring and additional measures to reduce transmission, such as bed nets for malaria. "We need to have a responsible discussion about this." ■

PHOTO: (LEFT) BGI; (TOP) © CULTURA/CORBIS

SCIENCE AND THE LAW

Forensic labs explore blind testing to prevent errors

Evidence examiners get practical about fighting cognitive bias

By **Kelly Servick**

Shaken by revelations of unreliable results in crime labs, some forensic scientists are urging their colleagues to adopt a basic research practice: the blind experiment. Last week, at the first International Symposium on Forensic Science Error Management in Arlington, Virginia, nearly 500 scientists, lab managers, and other practitioners confronted the factors that lead them to make mistakes. A key problem, many said, is that people who evaluate evidence from crime scenes have access to information about a case that could bias their analysis.

This subconscious influence can take many forms, explained Itiel Dror, a cognitive neuroscientist at University College London. It can arise from irrelevant contextual information, such as the nature of the crime, the race of a suspect or a victim, and police investigators' beliefs about a suspect's guilt. It can also arise from the physical evidence itself. For example, seeing a suspect's fingerprint before analyzing one from a crime scene might change how an examiner interprets ambiguous features. "That's backward reasoning," Dror told the audience. "You go to such trouble not to contaminate the evidence physically, so take account of cognitive contamination."

Dror has been a longtime critic of the lack of blinding procedures in forensic science. His presence at the meeting, organized by the National Institute of Standards and Technology (NIST), was one sign of the field's eagerness for reform after a decade of humbling revelations. A 2009 report from the National Research Council concluded that many forensic disciplines lacked a firm foundation in science and produced inconsistent, unreliable results. In response, NIST and the Department of Justice assembled both a national commission on forensic science to suggest policies that will strengthen the field and 24 discipline-specific expert committees to make practical recommendations to more than 400 U.S. labs.

Meanwhile, a handful of studies—many led by Dror—have revealed how cognitive bias might contribute to forensic errors. DNA examiners who did not know that an assailant in a gang rape case had implicated another suspect, for example, were more likely to conclude that this suspect's DNA was absent from a vaginal swab of the victim. Another study revealed that, at least in untrained volunteers, exposure to emotional background stories and crime scene photos made people more likely to declare a match between fingerprints whose similarities were ambiguous.

Last week's meeting explored practical steps to combat such bias. Dror, whose consulting company has given workshops to various labs, including ones run by the FBI