

## Research brief

### Seeing double

Scientists have discovered that high concentrations of conjoined immune cells, or doublets, in blood samples can signal severe cases of diseases such as tuberculosis and dengue fever. Having anecdotally noticed the association, they substantiated it in analysis of blood samples from patients from the USA, Sri Lanka, and Peru. They showed that the doublets were the combination of a T cell and a monocyte, which they say makes sense, given that monocytes are reservoirs for disease in these two infections, so T cells will be more likely to find, interact closely, and form doublets with them. The finding could lead to laboratory tests to predict disease progression or vaccine effectiveness.

### LASER ART

Findings from a study in mice have shown that a combination of treatments can eliminate replication-competent HIV DNA from about a third of treated animals. Researchers combined a DNA-excising treatment based on CRISPR-Cas9 with a new strategy known as long-acting slow-effective release (LASER) antiretroviral therapy (ART). The scientists posit that the LASER ART can suppress viral replication long enough for the CRISPR-Cas9 treatment to completely eliminate HIV, which it can't do on its own. The mice were engineered to produce human T cells susceptible to HIV infection. The next steps would be tests in non-human primates.

### Antibiotics for viral infections?

The use of antibiotics to prophylactically treat bacterial infections might inadvertently increase the risk of viral infections such as influenza. So say the findings of a study in mice, which gave a mechanistic explanation to the commonly seen association between oral antibiotic treatment and increased viral infection risk. Mice with enhanced baseline type 1

interferon signalling, which confers increased resistance to influenza virus infection, were more susceptible to infection after 2–4 weeks of antibiotic treatment. Faecal transplants subsequently restored protection, suggesting a protective role of the gut microbiota. The researchers next want to understand the exact mechanisms by which gut bacteria communicate with the lung.

### Reservoir droplets

A new imaging method has shown promise for detection of how tuberculosis drugs work. Using the method, which combines correlated light, electron, and ion microscopy, researchers showed how bedaquiline sequesters in lipid droplets in *Mycobacterium tuberculosis*-infected human monocyte-derived macrophages. Unsure of whether the lipid droplets were preventing the drug from reaching the bacteria, they disturbed the formation of the droplets and saw a greater concentration of the drug inside the bacteria. The droplets thus form a reservoir from which the drug can attack the bacteria. Such imaging can give fresh insights into understanding how antibiotics work and guide development of new treatments against tuberculosis and other pathogens.

### Malaria coming in from the cold

Even slight climate change could increase the spread of malaria, despite previous findings suggesting that the plasmodium parasite wouldn't reproduce fast enough to spread sufficiently well in cooler climes. By contrast with a foundational 1930s study, which modelled potential spread using experiments in a Eurasian species *Anopheles maculipennis*, the new study assessed parasite development in two of the most important malaria vectors globally, *Anopheles stephensi* and *Anopheles gambiae*. At 18°C, the findings showed, the parasite takes 31 days to

develop, which, when modelled, makes sustained transmission likely. With even slight global warming, the disease could inch up from endemic areas into presently unaffected high-elevation areas in places such as east Africa and South America.

### Infection now, MS later?

Findings from a study of mice suggest that transient viral infections in childhood might predispose an individual to the development of multiple sclerosis later in life. Scientists exposed adult and young mice to transient viral infections before injecting them with self-reactive immune cells when the animals were fully grown. Mice that had infections in adulthood were protected from the action of the immune cells, but in mice infected in early life, the immune cells entered the brain and attacked the exact locations where the infection had been, leading to the development of lesions characteristic of multiple sclerosis.

### The exercise bug

Analysis of faecal samples from marathon runners has identified a bacterial species associated with improved capacity for exercise. In runners, bacteria from the genus *Veillonella* were more abundant after running a marathon than they were before. And the bacteria were absent in samples from sedentary people. Researchers isolated one species, *Veillonella atypica*, and showed that mice that were given it had greater capacity for exercise. The bacteria metabolise lactic acid, producing the short-chain fatty acid propionate as a metabolite. Giving propionate alone to mice improved their running capacity, leading the researchers to suggest that *Veillonella* spp supplements might one day help people improve their exercise capacity and thus avoid diseases such as diabetes.

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For more on **doublets and infection** see *eLife* 2019; **8**: e46045. DOI:10.7554/eLife.46045

For more on **eliminating HIV** see *Nat Commun* 2019; **10**: 2753. <http://dx.doi.org/10.1038/s41467-019-10366-y>

For more on **antibiotics, the gut, and viral infection** see *Cell Rep* 2019; **28**: 245–56.e4. <https://doi.org/10.1016/j.celrep.2019.05.105>

For more on **imaging and bedaquiline** see *Science* 2019; **364**: 1279–82. DOI:10.1126/science.aat9689

For more on **climate and the spread of malaria** see *Biol Lett* 2019; **15**: 20190275. DOI:10.1098/rsbl.2019.0275

For more on **viral infection and multiple sclerosis** see *Sci Transl Med* 2019; **11**: eaav5519. DOI:10.1126/scitranslmed.aav5519

For more on **exercise and the microbiota** see *Nat Med* 2019; published online June 24. DOI:10.1038/s41591-019-0485-4