



## Research brief

For more on an **emerging parasitic disease in Brazil** see *Emerg Infect Dis* 2019; published online Sept 30. <https://doi.org/10.3201/eid2511.181548>

For more on the **immunology of lymphatic filariasis** see *PLoS Negl Trop Dis* 2019; **13**: e0007697

For more on **dimerisation and influenza** see *PLoS Pathog* 2019; **15**: e1008034

For more on **vitamin C and sepsis** see *JAMA* 2019; **322**: 1261–70

For more on the **heat-stable candidate chikungunya vaccine** see *Sci Adv* 2019; **5**: eaaw2853

For more on **lncRNA and HIV** see *MBio* 2019; **10**: e02016–19

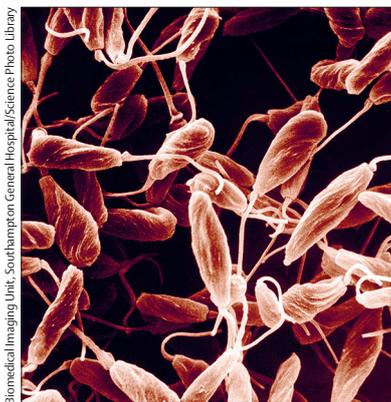
For more on **L-form switching** see *Nat Commun* 2019; **10**: 4379

### A potential emerging disease

Researchers in Brazil might have identified an emerging, treatment-resistant parasitic disease similar to visceral leishmaniasis. In an HIV-negative man in his mid 60s who had symptoms similar to visceral leishmaniasis, including an enlarged liver and spleen and widespread skin lesions, but who died despite standard leishmaniasis treatment, bone-marrow and skin-lesion samples showed that he harboured protozoan parasites closely related to *Crithidia fasciculata*, a parasite that usually colonises mosquitoes. Parasites isolated from the patient were able to infect the liver and cause skin lesions when given to mice.

### Host vs worm

Treatment for lymphatic filariasis often causes adverse events, with these events thought to be caused by the body's response to dying filarial worms rather than by the drugs per se. To better understand these immunological shockwaves, researchers assessed blood samples from nearly 100 people receiving treatment. They detected post-treatment spikes in plasma concentrations of both filarial antigens and host cytokines. Transcriptional analysis comparing nine people who had moderate adverse events with nine matched controls showed upregulation of 744 genes in affected individuals, with many of these genes involved in immune signalling.



Biomedical Imaging Unit, Southampton General Hospital/Science Photo Library

### Stop flu on a dime

The influenza virus's constant evolution and antigenic drift is why it continues to be a public health concern. The virus's RNA polymerase is formed of three subunits that continuously change configurations, but it was hitherto unknown if these structural changes confer functional benefits. By assessing the polymerase structures of related strains, researchers showed that polymerase subunits co-evolve to ensure optimal intersubunit interaction and dimerisation (the joining of two monomer subunits). Using reverse genetics and cell-based reconstitution of the viral polymerase, the researchers showed that the dimerisation process is essential for efficient vital RNA replication and might thus be a strong candidate to target with antiviral treatment approaches to restrict genetic reassortment.

### A study with a twist

Researchers assessing whether intravenous vitamin C treatment protects patients with sepsis from organ failure saw no association, but instead detected encouraging suggestions that it might help reduce people's mortality risk and help them to recover quicker. In the CITRUS-ALI trial, they randomised 167 patients with sepsis and acute respiratory distress syndrome to receive either vitamin C infusions or a water placebo. 30% of those given vitamin C died by day 28 vs 46% given placebo. On average, people in the vitamin C group spent 3 fewer days in intensive care (7 days vs 10 days at day 28) and 7 fewer days in hospital (15 days vs 22 days at day 60) than those given placebo.

### Chikungunya: in from the cold

Using a synthetic protein scaffold, UK and French researchers have developed a candidate chikungunya vaccine that does not need to be refrigerated. The heat-stable particle,

called ADDomer (an adenovirus-derived multimeric protein-based self-assembling nanoparticle scaffold), has what they describe as a flexible, exposed surfaced and was engineered to express immunogenic epitopes from the chikungunya virus. The particle was shown to have good biodistribution and immunogenicity in mice. This so-called plug-and-play vaccine technology, the researchers suggest, could potentially be applied to vaccines against other viruses.

### HIV: a long kiss goodnight?

Researchers might have identified a crucial component in the process that activates dormant HIV, that if targeted might help flush out HIV reservoirs that can otherwise persist after antiretroviral treatment. The component is a long non-coding RNA (lncRNA), a type of RNA that does not translate into a protein but instead orchestrates how other genes are turned on and off. A genome-wide expression analysis of HIV-infected macrophages isolated one lncRNA, with the acronym HEAL, that when silenced or removed with CRISPR CAS-9, prevented HIV from recurring after antiretroviral treatment. Next steps: animal models.

### Harrydium houdiniae

Bacteria have been shown to be able to slip their cell walls to escape being targeted by cell-wall-targeting antibiotics such as penicillin. Samples from 29 of 30 elderly patients with urinary tract infections contained wall-less, so-called L-form state bacteria such as *Escherichia coli* and *Staphylococcus* species. In laboratory experiments, researchers showed that wall-targeting antibiotic treatment causes bacteria to undergo L-form switching. They also filmed bacteria reforming their cell wall 5 h after shedding it, and used transparent Zebra fish to show that the switching can occur within organisms.

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