cultures and showed by cryo-electron microscopy that the coat proteins form helixes that assemble into long filaments with a single-stranded DNA molecule in the middle.

Next, the authors mixed the purified phages with the polymers alginate or hyaluronan; the first is abundant in the biofilm matrix whereas the second is produced and secreted by host cells. Under these conditions, which mimic the environment that the bacteria encounter during infection, Pf4 filaments spontaneously formed liquid crystalline droplets. Notably, the droplets were spindle shaped and over 4 µm in length, which is similar to the length of *P. aeruginosa* cells. Indeed, when the authors also added bacterial cells, the droplets formed around the cells, encasing them in a phage 'shield'.

To confirm whether the droplets protect *P. aeruginosa* from antibiotics, the authors treated the cultures with aminoglycoside antibiotics or the last-resort antibiotic colistin. Only cells in the condition that promoted droplet formation (Pf4 and polymer present) were protected from the antibiotic; neither the phage nor the polymer alone had an effect. Previous work had suggested that negatively charged phage DNA sequesters the positively charged antibiotics. Although this effect might still have a role, Tarafder et al. showed that droplets formed by empty phages without the central DNA also were protective.

In summary, the study shows that phage droplets surrounding bacterial cells protect *P. aeruginosa* from antibiotics. Interestingly, filamentous inoviruses such as Pf4 are also present in many other Gram-negative pathogens, which suggests that physical protection by phages might be widespread.

Ursula Hofer

ORIGINAL ARTICLE Tarafder, A. K. et al. Phage liquid crystalline droplets form occlusive sheaths that encapsulate and protect infectious rod-shaped bacteria. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1917726117 (2020)
RELATED ARTICLE De Smet, J. et al. *Pseudomonas* predators: understanding and exploiting phage–host interactions. *Nat. Rev. Microbiol.* **15**, 517–530 (2017)

were tagged with GFP, and potential recipient cells expressed mCherry. Consequently, cells that successfully received a plasmid were positive for both fluorescent markers.

The authors used this assay to test the transfer of two particularly concerning plasmids, pCT (encoding an ESBL) in *Escherichia coli* and pKpQIL (encoding a carbapenemase) in *Klebsiella pneumoniae*. They screened a library of over 1,200 already approved drugs for their ability to inhibit plasmid transmission. After removing known biocides and antibacterials, as well as compounds that reduced growth in the assay, the authors identified seven hits, including abacavir and azidothymidine. Both drugs are nucleoside analogues that inhibit the reverse transcriptase of HIV, and they are in wide clinical use.

Azidothymidine showed more consistent and stronger inhibition than abacavir, reducing transmission of both pCT and pKpQIL by over 80% compared with untreated controls. Previous work had suggested that azidothymidine has antibacterial effects. Importantly, for both drugs the concentrations that inhibited plasmid transfer were well below the minimum inhibitory concentration for the bacterial strains used. When the authors tested mutant strains that became resistant against the antibacterial action of azidothymidine, they found that inhibition of plasmid transmission also was abolished. Resistance arose through a deletion in the gene encoding the thymidine kinase needed to activate azidothymidine, which is a prodrug. This result confirms that azidothymidine activity is indeed responsible for plasmid inhibition, potentially through insertion of the active drug into replicating plasmids, leading to termination of DNA chain elongation.

Drugs that inhibit plasmid spread or persistence could be useful to purge antimicrobial resistance plasmids from bacterial populations, for example in the human gut or wastewater, and approved antiretrovirals are promising leads.

Ursula Hofer

ORIGINAL ARTICLE Buckner, M. C. et al. HIV drugs inhibit transfer of plasmids carrying extended-spectrum β-lactamase and carbapenemase genes. *mBio* **11**, e03355–19 (2020)

IN BRIEF

VACCINES

An imperfect vaccine reduces pathogen virulence

Leaky vaccines prevent the development of disease symptoms, but do not protect against infection and the onwards transmission of pathogens, which has been a concern because the consequences for unvaccinated contact individuals are unknown. Bailey et al. performed transmission experiments using Marek disease virus in chickens and found that the herpesvirus of turkeys vaccine significantly reduced feather viral load in both vaccinated birds and unvaccinated contact individuals. The authors found that contact birds were less likely to develop disease and die, and that they displayed milder symptoms and shed less virus, when infected by vaccinated birds, potentially because of a lower infectious dose. This study highlights that sterilizing immunity is not always needed to control the spread and severity of disease, and that leaky vaccines may have a role in disease management.

ORIGINAL ARTICLE Bailey, R. I. et al. Pathogen transmission from vaccinated hosts can cause dose-dependent reduction in virulence. *PLoS Biol.* **18**, e3000619 (2020)

MICROBIOME

Bacterial signatures in internal tissues

The human body is home to trillions of microorganisms that colonize the gut and surfaces exposed to the environment, but a detailed analysis of microorganisms within internal tissues such as fat and the liver has been lacking, partly because of the challenge in obtaining uncontaminated tissue samples. Anhê, Jensen et al. obtained blood, liver and three types of fat tissue samples from 40 individuals with obesity during bariatric surgery. The authors used 16S rRNA sequencing to analyse bacterial DNA within the samples and identified tissue-specific differences in taxa and amount of bacterial DNA and found bacterial signatures in visceral fat that were specific to individuals who have type 2 diabetes (T2D). In mesenteric fat of individuals with diabetes, there was a reduction in diversity with fewer Gram-positives and more opportunistic Gram-negative Enterobacteriaceae. This study suggests that internal tissues are exposed to bacteria or bacterial DNA, which could be used as a biomarker of T2D.

ORIGINAL ARTICLE Anhê, F. F. & Jensen, B. A. H. et al. Type 2 diabetes influences bacterial tissue compartmentalisation in human obesity. *Nat. Metab.* https://doi.org/10.1038/s42255-020-0178-9 (2020)

VIRAL INFECTION

Turning up the heat on virus transmission

Vector-borne pathogens can influence the physiology of their vectors and hosts, enhancing pathogen transmission and affecting their ecology. Porras et al. found that infection with the barley yellow dwarf virus (BYDV) elevated the surface temperature of infected host plants by an average of 2 °C and led to the upregulation of three heat-shock protein genes in the BYDV aphid vector *Rhopalosiphum padi*, enhancing thermal tolerance by 8 °C. Remarkably, the authors found that this enhancement in thermal tolerance allowed aphids to inhabit higher and warmer regions of infected host plants when they became displaced from cooler regions by *Rhopalosiphum maidis*, a larger aphid species. These results show that viral infection can have profound effects on thermal biology of hosts and vectors, resulting in drastic changes to the environmental niche of the vector.

ORIGINAL ARTICLE Porras, M. F. et al. Enhanced heat tolerance of viral-infected aphids leads to niche expansion and reduced interspecific competition. *Nat. Commun.* **11**, 1184 (2020)