IN BRIEF

PUBLIC HEALTH

Super-spreading of *Mycobacterium tuberculosis*

Genomic analysis can be used to reconstruct outbreak dynamics; however, transmission chains of slowly mutating pathogens, such as *Mycobacterium tuberculosis*, can be difficult to determine because of low genetic diversity between isolates. Lee et al. used deep sequencing at 10–20 times the depth of previous analyses to investigate a tuberculosis outbreak in the Canadian Inuit. Earlier work had shown two distinct clusters of cases whereby isolates differed in a single nucleotide polymorphism (SNP), but no link could be found between the two clusters. Deep sequencing has now revealed that one patient actually harboured both strains, the one with and the one without the SNP. Based on this result and epidemiological data, the authors conclude that the most likely explanation is a super-spreading event in which this patient infected up to 17 other individuals, giving rise to the two clusters.

ORIGINAL ARTICLE Lee, R. S. et al. Previously undetected super-spreading of *Mycobacterium tuberculosis* revealed by deep sequencing. *eLife* **9**, e53245 (2020)

ANTIMICROBIALS

Triple hit against *Plasmodium*

With rising rates of antimalarial drug resistance, new compounds with novel targets and mechanisms of action are urgently needed. Screening a library of aspartic protease inhibitors has now identified compounds that target two essential proteases of *Plasmodium falciparum*: plasmepsin IX and X. Further in vitro and in vivo experiments revealed that the inhibitors block liver, blood and mosquito stages of *Plasmodium* spp. The two protease targets are involved in processing a wide range of parasite proteins important in invasion, egress and parasite development. This broad and multi-stage activity is reflected in a high barrier to resistance development and makes cross resistance for these new compounds less likely in parasites that are already resistant against other antimalarials.

ORIGINAL ARTICLE Favuzza, P., de Lera Ruiz, M. et al. Dual plasmepsin-targeting antimalarial agents disrupt multiple stages of the malaria parasite life cycle. *Cell Host Microbe* https://doi.org/10.1016/j.chom.2020.02.005 (2020)

VIRAL INFECTION

Entering and breaking for HIV?

As a retrovirus, HIV needs to deliver its genome to the nucleus and reverse transcribe it before integration. There is a longstanding debate, with various, often contradictory results, about when and where the capsid that surrounds the HIV genome disassembles, that is, 'uncoats'. Burdick et al. now suggest that uncoating only happens after HIV has entered the nucleus and reverse transcribed its genome, delivering it close to integration sites. They labelled capsid with GFP by inserting the fluorescent marker between matrix and capsid and mutating a protease cleavage site to avoid loss of the marker. When they tracked labelled viral cores, they found, in contrast to previous studies that had suggested uncoating in the cytoplasm, that cores remained intact or nearly intact until they had reached their nuclear destination. Furthermore, their results suggest that interaction with the host protein cleavage and polyadenylation specificity factor 6 supports entry through nuclear pores. Once in the nucleus, reverse transcription happened inside the cores, and viral DNA was only released shortly before integration, potentially protecting it from innate DNA sensing.

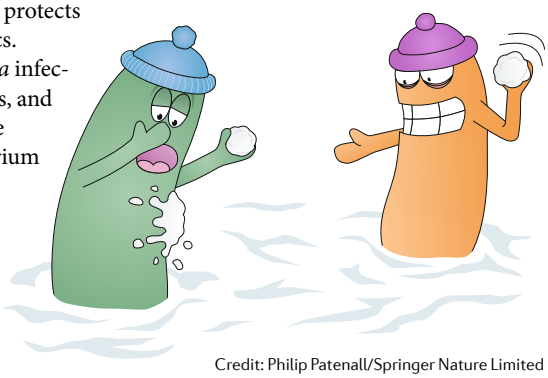
ORIGINAL ARTICLE Burdick, R. C. et al. HIV-1 uncoats in the nucleus near sites of integration. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1920631117 (2020)

ANTIMICROBIAL RESISTANCE

Phage liquid crystals protect *Pseudomonas*

Pseudomonas aeruginosa can cause chronic and difficult to treat infections, in a large part owing to the many ways in which it tolerates or resists antibiotics. A new study now identifies a new mechanism of antibiotic tolerance, in which a phage produced by the bacterium forms liquid crystalline droplets around the cells and thereby protects them from antibiotics.

Most *P. aeruginosa* infections involve biofilms, and previous studies have found that the bacterium strongly upregulates the production of Pf phages when it forms biofilms. Furthermore, samples from patients with cystic fibrosis or chronic wound infection contain substantial amounts of Pf phages. Pf4 in particular had been linked to pathogenesis through modulation of the host response and antibiotic tolerance. However, the mechanisms that underlie the inhibition of antibiotic action by Pf4 are incompletely understood. Tarafder et al. now purified Pf4 from *P. aeruginosa*



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ANTIMICROBIAL RESISTANCE

Stop that plasmid

Plasmids are one of the key ways by which antimicrobial resistance can spread between bacteria. Plasmids can disseminate resistance determinants such as extended-spectrum β-lactamases (ESBLs) and carbapenemases, which inactivate antibiotics, and inhibiting their spread or replication can help to eliminate them from bacterial populations. Buckner et al. have now developed a medium-throughput screen for compounds that inhibit plasmid spread and identify two antiretroviral drugs used to treat HIV infection as promising plasmid inhibitors.

A few compounds that inhibit plasmid spread have been identified previously, but identifying hits has so far mostly relied on low-throughput plating experiments. To enable screening of a large library of compounds, the authors developed a flow-cytometry based assay to track plasmid transfer between bacteria. The plasmids in donor bacteria