IN BRIEF

VIRAL INFECTION

The right place at the right time

Conventional models of the HIV-1 replication cycle have considered that reverse transcription and disassembly of the viral core are cytoplasmic events. In this study, Campbell and colleagues set out to explore the spatio-temporal staging of reverse transcription and capsid disassembly. They used an inducible nuclear pore complex blockade to inhibit HIV-1 infection at the nuclear entry stage and determined nuclear import kinetics of infectious HIV-1 particles. Surprisingly, the data suggest that HIV-1 nuclear import occurs hours before the completion of reverse transcription. In addition, they found that uncoating is also completed in the nucleus. Finally, the authors provide evidence that HIV-1 can use distinct nuclear import pathways during infection. In the future, this experimental system may provide insights into cytoplasmic and nuclear events during infection by other viruses.

ORIGINAL ARTICLE Dharan, A. et al. Nuclear pore blockade reveals that HIV-1 completes reverse transcription and uncoating in the nucleus. *Nat. Microbiol.* https://doi.org/10.1038/s41564-020-0735-8 (2020)

APPLIED MICROBIOLOGY

Targeted microbiome depletion

The selective depletion of specific bacteria from complex microbial communities may provide an alternative to broadly acting antibacterials; however, the development of such targeted approaches has been slow. Bacterial-mediated contact-dependent killing via the type VI secretion system (T6SS) may be a feasible strategy, yet the T6SS targets cells indiscriminately. To overcome this limitation, Ting et al. developed programmed inhibitor cells (PICs) that express nanobodies on their surface that mediate cell–cell adhesion via antigen recognition. The authors showed that targeting a unique natural cell surface antigen resulted in the selective killing of target cells in a complex community in liquid medium. Finally, resistance to PIC-mediated killing seems to emerge slowly, which is encouraging for the development of PICs for medical applications.

ORIGINAL ARTICLE Ting, S.-Y. et al. Targeted depletion of bacteria from mixed populations by programmable adhesion with antagonistic competitor cells. *Cell Host Microbe* https://doi.org/10.1016/j.chom.2020.05.006 (2020)

STRUCTURAL BIOLOGY

Taking a closer look

Neisseria gonorrhoeae causes the sexually transmitted disease gonorrhoea and shows high levels of antibiotic resistance. Multidrug efflux mediated by the multiple transferrable resistance tripartite efflux pump (encoded by the *mtrCDE* locus) is one of the causes of treatment failure. It was previously shown that gonococci with mosaic-like sequences within *mtrD* exhibit enhanced transport function and drug resistance. In this study, Lyu et al. present the cryo-electron microscopy structures of the antibiotic-bound MtrD multidrug efflux pump and found that ampicillin and erythromycin bind to an overlapping multidrug-binding site in the periplasmic domain of the transporter. Moreover, they identified that amino acid changes at MtrD positions 714 or 823 (residues that are part of the substrate-binding site and possibly have a role in drug recognition) might be important for enhanced drug resistance, informing structure-guided drug design.

ORIGINAL ARTICLE Lyu, M. et al. Cryo-EM structures of a gonococcal multidrug efflux pump illuminate a mechanism of drug recognition and resistance. *mBio* https://doi.org/10.1128/mBio.00996-20 (2020)

BACTERIAL PHYSIOLOGY

T6SS: shoot and scrub

The type 6 secretion system (T6SS) is a molecular syringe that bacteria use to inject toxic effectors into competitor or host cells. Although directly injecting effectors into target cells ensures that they indeed are delivered, it limits the efficacy of T6SS-mediated killing to neighbouring cells. Smith, Vettiger et al. now show that the efficacy of the T6SS can be greatly increased if injected toxins not only kill but also lead to quick lysis of competitor cells.

To study the fitness effects of T6SS use, the authors simulated competition between an 'attacker' strain with a T6SS and a susceptible strain, varying the rate of T6SS firing. The null hypothesis was that increased firing rates would lead to more killing. However, in opposition of this hypothesis, the computer simulations predicted that higher firing rates do not guarantee that more competing cells will be killed. The problem was that a protective 'corpse barrier' of dead victims formed around the attacker, which absorbed T6SS attacks and protected susceptible cells. The simulations showed that this effect could be mitigated if attackers injected a toxin that causes rapid lysis of killed cells, thus leaving 'fresh' susceptible cells in the firing range.

> a protective 'corpse barrier' of dead victims formed around the attacker

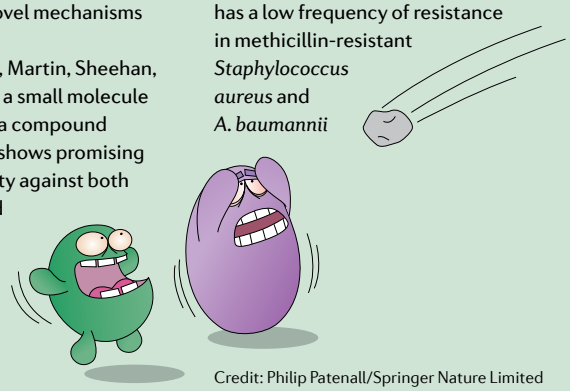
The authors confirmed the effect of the 'corpse barrier' in microfluidic and plating experiments, using two strains of *Acinetobacter baylyi* attackers and susceptible *Escherichia coli* cells. *A. baylyi* usually expresses

ANTIMICROBIALS

Two birds with one stone

Since the 1960s, there has been a decline in the discovery of new antibiotics, particularly against Gram-negative bacteria. Increases in antibiotic resistance calls for an urgent need to identify suitable candidates for broad-spectrum antibiotics with novel mechanisms of action (MoA).

In a recent study, Martin, Sheehan, Bratton et al. used a small molecule screen to identify a compound (SCH-79797) that shows promising bactericidal activity against both Gram-positive and Gram-negative bacteria. After confirming antibiotic activity against a variety of pathogens in vitro, the authors showed that SCH-79797 is effective against a lethal dose of *Acinetobacter baumannii* in the wax worm *Galleria mellonella*, prolonging survival without any noticeable toxicity. The authors found that SCH-79797 has a low frequency of resistance in methicillin-resistant *Staphylococcus aureus* and *A. baumannii*



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