IN BRIEF

ANTIMICROBIALS

A class of its own

The spread of multidrug-resistant (MDR) bacteria poses a great risk to global health, and despite considerable efforts, no new class of antibiotic has been approved for Gram-negative pathogens in recent years. Arylomycins are a class of natural products that exhibit low antibacterial activity. By chemically modifying arylomycin, the authors discovered a synthetic derivative, termed G0775, with potent in vitro and in vivo antibacterial activity against multiple clinically relevant MDR Gram-negative pathogens. G0775 binds to the bacterial signal peptidase LepB, a new antibiotic target, with high affinity and kills bacteria by inhibiting this peptidase. Moreover, G0775 has improved ability to cross the outer membrane through a porin-independent mechanism, and de novo resistance to G0775 occurred at a low frequency. Thus, optimized arylomycin analogues may represent a new class of Gram-negative antibiotics.

ORIGINAL ARTICLE Smith, P. A., Koehler, M. F. T. et al. Optimized arylomycins are a new class of Gram-negative antibiotics. *Nature* https://doi.org/10.1038/s41586-018-0483-6 (2018)

BACTERIAL PHYSIOLOGY

Increasing virulence factors

A previous transcriptome study revealed an increase in antisense transcription and gene expression changes in the absence of the transcription termination factor Rho in *Staphylococcus aureus*. This study assessed the physiological importance of Rho-dependent transcription termination by comparing the *S. aureus* HG001 strain and its isogenic *rho*-deletion mutant. Proteome analysis revealed an increase in the levels of secreted virulence factors that are controlled by the SaeRS two-component system in the absence of Rho in vitro. In addition, inhibition of Rho by the antibiotic bicyclomycin led to increased levels of SaeRS-dependent virulence factors, similar to those observed in the *rho*-deletion mutant. Finally, a *rho*-deletion strain exhibited increased virulence in mice compared to the wild type. These findings identify a link between Rho-dependent transcription termination and virulence regulation in *S. aureus* and suggest that antibiotic treatment can modulate the expression of virulence factors.

ORIGINAL ARTICLE Nagel, A. et al. Inhibition of Rho activity increases expression of saers-dependent virulence factor genes in *Staphylococcus aureus*, showing a link between transcription termination, antibiotic action, and virulence. *mBio* https://doi.org/10.1128/mBio.01332-18 (2018)

VIRAL EVOLUTION

Folding unstable proteins

Adaptive mutations enable influenza viruses to evade host immune responses; however, these adaptive amino acid substitutions are often biophysically deleterious and can affect either protein folding or stability. For example, adaptive mutations in influenza virus nucleoprotein (NP) enables escape from human restriction factors but might render the protein unstable. Thus, viruses must balance the costs of NP folding defects with the benefits of escaping host immunity. The authors tested the hypothesis that viruses hijack host chaperones to promote folding of biophysically defective NP escape variants. A destabilized Pro283 NP variant, which enables evasion of the restriction factor Myxovirus resistance protein A, is not tolerated in chaperone-depleted host cells. This suggests that host chaperones rescue biophysically defective viral protein variants and thus influence the fitness cost of destabilized protein variants.

ORIGINAL ARTICLE Phillips, A. M., Ponomarenko, A. I. et al. Destabilized adaptive influenza variants critical for innate immune system escape are potentiated by host chaperones. *PLOS Biol.* https://doi.org/10.1371/journal.pbio.3000008 (2018)

VIRAL EVOLUTION

HIV-1's fingerprint

Only few people that are infected with HIV-1 develop broadly neutralizing antibodies (bnAbs), which target conserved viral antigens and thus can neutralize diverse viral variants. The factors that determine whether someone will develop bnAbs are not entirely clear; in particular, the contribution of virus characteristics is unknown. Identifying viral determinants of a broadly neutralizing immune response would be very helpful for vaccine development. Kouyos et al. investigated the antibody responses in a large cohort of HIV-1 transmission pairs within the Swiss HIV Cohort Study and found that the HIV-1 strain that someone is infected with determines part of the breadth and strength of the antibody response.

The authors hypothesized that if viral factors determine the quality of the antibody response, individuals with closely related viral strains would have similar neutralization responses. To test this hypothesis, they identified 303 transmission pairs based on the sequence similarity of their HIV-1 polymerase gene. They then tested the ability of the antibody response in these individuals to neutralize 14 different virus strains and to bind 13 antigens, determining what the authors call the 'antibody fingerprint' of the infecting virus. Indeed, transmission pairs had a more similar antibody fingerprint than pairs that were randomly assigned. Specifically, the infecting virus determined 13.2% in the variability of neutralization responses and 7–19% of the IgG reactivity (depending on the IgG class), which confirms that the infecting virus can imprint the neutralization capacity of the ensuing antibody response. Even when taking into account factors that are known to influence bnAb development, such as duration of infection and HIV-1 subtype, the correlation between infecting virus

BACTERIAL PHYSIOLOGY

Surf's up!

Surfing motility is an accelerated form of active surface motility that is dependent on the presence of the glycoprotein mucin. This form of motility was first described when *Pseudomonas aeruginosa* was cultured in cystic fibrosis medium, which is formulated with mucin to mimic cystic fibrosis lung sputum. In *P. aeruginosa* several characteristics of surfing motility have been observed, including rapid surface spread, adaptability to various media viscosities, a dependence on flagella and quorum-sensing systems, and conferring broad-spectrum antibiotic resistance; however, it was unknown whether other mucosa-associated bacteria use this form of motility. Now, Sun et al. report that surfing motility is a conserved yet diverse form of motility in bacteria.

To determine whether other motile bacteria can surf, the authors cultured

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