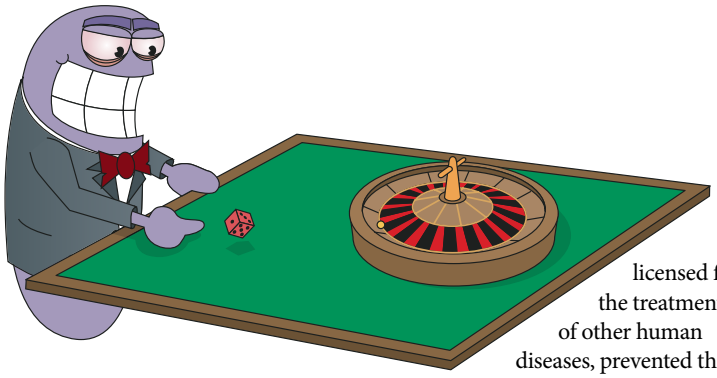

Credit: Philip Patenall/Springer Nature Limited

stress response. Thus, almost 90% of the resistance mutations originated from the σˢ-high cells. Notably, the high mutation rate was transient, as recovered resistant strains had normal σˢ levels and mutation rates. This led the authors to conclude that the low-dose antibiotic treatment leads to the transient differentiation of a hypermutable subpopulation, which they called "gamblers" and which enables *E. coli* to evolve drug resistance without risking mutagenesis in the whole population.

Based on this scenario, blocking the emergence of gambler cells could be a way to prevent the evolution of antibiotic resistance. Indeed, treatment of cultures with edaravone, which is a ROS-reducing drug that is licensed for the treatment of other human diseases, prevented the development of σˢ-high cells and of most resistance mutations. Of note, the drug did not affect high-dose killing by ciprofloxacin, although ROS are known to promote killing.

In summary, the study by Rosenberg and colleagues identified a stress response pathway that contributes to the evolution of resistance in a subpopulation of antibiotic-treated cells and showed in a proof-of-principle experiment that targeting this pathway might be an option to reduce resistance development during antibiotic treatment.

Ursula Hofer

ORIGINAL ARTICLE Pribis, J. P. et al. Gamblers: an antibiotic-induced evolvable cell subpopulation differentiated by reactive-oxygen-induced general stress response. *Mol. Cell* **74**, 1–16 (2019)

P. aeruginosa is often found in biofilms, especially in environments with flow. Indeed, biofilms that formed in microchannels of the microfluidic device showed YFP expression, confirming the existence of rheosensing within a multicellular community.

Next, the authors quantitatively characterized rheosensing by investigating *fro* expression in response to varying shear rates (that is, the kinematic component of flow), and found that induction of *fro* is not binary, but rather expression is tuned by the shear rate.

To investigate the regulation of rheosensing, the authors knocked out an upstream putative sigma factor (FroR), which eliminated *fro* expression, whereas knockout of an upstream anti-sigma factor (FroI) increased *fro* expression. Overexpression of *froR* and *froI* increased and eliminated *fro* expression, respectively. Furthermore, pili and flagella that are involved in surface sensing were not required for *fro* expression, as evidenced by mutants lacking pilins and flagella. Expression was not triggered by surface association alone and was not affected by increased surface adhesion. These observations suggest that rheosensing involves signalling through FroR, which is antagonized by FroI, and that sensing does not depend on surface sensors.

To directly test whether rheosensing measures force, two parameters that contribute to shear stress (the force-related component of flow) — shear rate and viscosity — were altered and *fro* expression was measured. Rheosensing was affected by the shear rate, but, remarkably, increasing the viscosity had no effect. Altogether, these results suggest that rheosensing is a force-independent form of mechanosensing, acting as an intrinsic speedometer. A potential benefit of force-independent rheosensing is the ability to measure the speed of flow across a range of fluids, such as water, blood and sputum.

Ashley York

ORIGINAL ARTICLE Sanfilippo, J. E. & Lorestani, A. et al. Microfluidic-based transcriptomics reveal force-independent bacterial rheosensing. *Nat. Microbiol.* https://doi.org/10.1038/s41564-019-0455-0 (2019)

IN BRIEF

EPIDEMIOLOGY

Undetectable equals untransmittable

Timely identification of HIV-infected individuals and early treatment is a promising strategy for tackling the HIV/AIDS epidemic. There is less available data to estimate HIV-1 transmission risk in serodifferent gay partnerships (in which the HIV-positive partner is taking antiretroviral therapy (ART)) than data on transmission risk in heterosexual couples. Now, an observational study of 782 gay couples across Europe between 2010 and 2018 reports that men whose HIV-1 infection was fully suppressed by ART had zero chance of infecting their partner. The authors monitored sexual behaviour, HIV-1 status of HIV-negative partners and the viral load of HIV-positive partners, which provided results over 1,593 couple-years of follow-up, including 76,088 cases of condomless anal intercourse. No cases of within-couple HIV-1 transmission were detected, which suggests that individuals who achieve and maintain an undetectable viral load cannot sexually transmit HIV.

ORIGINAL ARTICLE Rodger, A. J. et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *Lancet* https://doi.org/10.1016/S0140-6736(19)30418-0 (2019)

CLINICAL MICROBIOLOGY

A phage cocktail for drug-resistant mycobacteria

Non-tuberculous mycobacteria (NTM) cause chronic pulmonary infections in individuals with cystic fibrosis, and antibiotic-resistant NTM (for example, *Mycobacterium abscessus*) is widespread. The use of phages to treat drug-resistant bacterial infections is a potential alternative strategy. Dedrick et al. report the use of a three-phage cocktail in the treatment of disseminated drug-resistant *M. abscessus*. After an uncomplicated bilateral lung transplant in a 15-year-old patient with cystic fibrosis, the patient was diagnosed with a disseminated drug-resistant *M. abscessus* subsp. *massiliense* infection, necessitating an alternative treatment strategy. The authors used screening, genome engineering and forward genetics to develop a cocktail of three lytic phage derivatives that efficiently kill the infectious *M. abscessus* strain. Intravenous administration of the cocktail was well-tolerated and resulted in clinical improvements — sternal wound closure, improved liver function and substantial resolution of infected skin lesions.

ORIGINAL ARTICLE Dedrick, R. M. et al. Engineered bacteriophages for treatment of a patient with a disseminated drug-resistant *Mycobacterium abscessus*. *Nat. Med.* https://doi.org/10.1038/s41591-019-0437-z (2019)

MICROBIOME

Skin microbiome relieves an itch

Disease severity in atopic dermatitis is associated with *Staphylococcus aureus* skin colonization; however, how dysbiosis of the skin microbiome may influence atopic dermatitis pathophysiology is unknown. Williams et al. show that proteases and phenol-soluble modulin-α (PSMα) secreted by *S. aureus* cause epidermal proteolysis and skin barrier damage in mice, thus promoting inflammation. Coagulase-negative staphylococci (CoNS) that are found on human skin were shown to secrete autoinducing peptides that inhibit accessory gene regulator quorum sensing in *S. aureus*, thus reducing PSMα expression. These autoinducers also reduced *S. aureus*-induced dermatitis in mice. Skin microbiome analyses of individuals with atopic dermatitis suggested that the ratio of CoNS to *S. aureus* has a role in atopic dermatitis pathogenesis.

ORIGINAL ARTICLE Williams, M. R. et al. Quorum sensing between bacterial species on the skin protects against epidermal injury in atopic dermatitis. *Sci. Transl Med.* **11**, eaat8329 (2019)