IN BRIEF

MICROBIOME

Feast and famine: the keys to gut engraftment

The efficient use of polysaccharides is one of the main features of successful gut commensals, such as *Bacteroides thetaiotaomicron*, leading to the hypothesis that rapid growth promotes gut engraftment. By contrast, Goodman and colleagues now find that *B. thetaiotaomicron* requires the alarmone (p)ppGpp, which downregulates several biosynthetic pathways in response to starvation, for the colonization of the mouse gut. A strain in which two (p)ppGpp synthases were deleted could not compete with wild type *B. thetaiotaomicron* or with several other gut commensals for gut engraftment. (p)ppGpp halts growth and upregulates the tricarboxylic acid cycle, in particular the production of α-ketoglutarate, which is important to survive starvation. This suggests that gut bacteria face temporary nutrient shortages and other stresses, through which they can persist by inducing the stringent response and arresting growth.

ORIGINAL ARTICLE Schofield, W. B. & Zimmermann-Kogadeeva, M. et al. The stringent response determines the ability of a commensal bacterium to survive starvation and to persist in the gut. *Cell Host Microbe* **24**, 120–132.e6 (2018)
FURTHER READING Fisher, R. A. et al. Persistent bacterial infections and persister cells. *Nat Rev Microbiol.* **15**, 453–464 (2017)

MICROBIAL ECOLOGY

Provoking your enemies to kill each other

Bacteria produce diverse toxins to eliminate their competitors; however, some of these toxins provoke retaliation. Gonzalez et al. now show that an *Escherichia coli* strain, which produces a DNA-damaging toxin, incurs a fitness cost in one-on-one competitions, as DNA damage upregulates toxin production in the competitor. Other toxins that do not affect DNA integrity have no 'provocative' effect. Interestingly, the provoking strain can have a fitness benefit if it faces more than one competitor by increasing their aggression against each other. The benefit occurs if the provoking strain is spatially shielded from or resistant to the toxins of the competitors, both scenarios that are likely to be found in the microbiota or biofilms.

ORIGINAL ARTICLE Gonzalez, D. et al. Costs and benefits of provocation in bacterial warfare. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1801028115 (2018)
FURTHER READING Nadell, C. D., Drescher, K. & Foster, K. R. Spatial structure, cooperation and competition in biofilms. *Nat. Rev. Microbiol.* **14**, 589–600 (2016)

BACTERIAL PATHOGENESIS

Defence countermeasures

During human infection, *Neisseria gonorrhoeae* colonizes mucosal sites, an environment that is enriched in host-derived antimicrobials, including the cell wall-degrading enzyme lysozyme. *N. gonorrhoeae* has developed strategies to counteract lysozyme activity, including maintenance of envelope integrity, peptidoglycan modifications and protein inhibitors of lysozyme. Ragland et al. show that Ng_1063 and a previously described protein, Ng_1981, contribute to full resistance of *N. gonorrhoeae* against lysozyme. Lysozyme interacts with Ng_1063 and Ng_1981, and treatment of *N. gonorrhoeae* with lysozyme increased their protein levels. Both proteins exhibit similar ability to inhibit the lytic activity of lysozyme and were crucial for cell survival in the presence of lysozyme. Finally, Ng_1981 is both released extracellularly and located in the bacterial envelope, whereas Ng_1063 is anchored to the outer membrane and surface-exposed.

ORIGINAL ARTICLE Ragland, S. A. et al. *Neisseria gonorrhoeae* employs two protein inhibitors to evade killing by human lysozyme. *PLOS Pathog.* https://doi.org/10.1371/journal.ppat.1007080 (2018)

ANTIMICROBIALS

Candida tolerates and persists

Persister cells survive antimicrobial drug treatment without being resistant to the drug; instead they develop tolerance. Persisters are intensely studied in bacteria but less so in other microorganisms. Berman and colleagues have now investigated tolerance in the important human fungal pathogen, *Candida albicans*.

Resistant cells can overcome antimicrobial drug treatment through specific mechanisms, such as inactivating the drug or pumping it out of the cell. By contrast, persisters arise through phenotypic heterogeneity, that is, a subpopulation of cells that are otherwise identical to their kin can tolerate the drug, for example by slowing growth, which affects growth-dependent drug targets.

Tolerance or 'trailing growth' has been previously observed in *Candida* spp., but it was unclear how it related to persistence. Berman and colleagues measured the drug resistance and tolerance of 219 clinical *C. albicans* isolates in disk diffusion assays by quantifying the proportion of cells that grew inside the zone of inhibition around the antifungal drug fluconazole; that proportion ranged from 0.1 to 0.85 between isolates.

To identify the mechanisms underlying tolerance, the authors measured intracellular drug levels with a fluorescent azole probe. The average level of tolerance of different isolates correlated inversely with intracellular azole levels. However, how the more tolerant cells achieved lower drug concentrations is unclear, as there was no direct relationship between drug uptake or export and the steady-state azole levels.

Next, the authors tested whether they could eliminate the tolerant cells with adjuvants, such as inhibitors of the calmodulin, calcineurin and heat shock protein 90 pathway, when combined with fluconazole.

MICROBIOME

Delivery of the gut microbiome

The infant gut microbiome has an important role in human physiology and in the establishment of a life-long symbiotic relationship with the host. Extensive microbial colonization of neonates begins postpartum, but the contribution of maternal microbiomes remains unclear. Now, two studies characterize the transmission of the microbiome from mother to infant during the first months of life.

Using high-resolution metagenomic sequencing, both studies assessed transmission patterns longitudinally in mother–infant pairs. In the first study, Ferretti et al. sampled five potential sources of transmission (skin, breast milk, vagina, stool (as a proxy for the gut) and the oral cavity) in 25 women. Stool and the oral cavity of neonates were sampled up to 4 months postpartum. High inter-subject diversity and strain heterogeneity in the composition of infant gut microbiomes on day 1 of birth suggested that seeding is partially stochastic and influenced to varying degrees by different maternal microbiomes, potential microbial acquisition in utero or the environment. This high diversity decreased within the first week of life before steadily increasing again over the following 4 months, which the authors argue is the result of selective forces that maintain a portion of this early diversity. Of the species that were lost after day 1 of life, 80% were shared with at least one body site of the mother, suggesting that they are of maternal origin. Indeed, all infants were enriched with species present in the microbiomes of their mothers and a substantial overlap was also observed on the strain level. The gut microbiome of the mother was found to be the largest donor of infant-acquired strains. The authors