IN BRIEF

MICROBIOME

Sublethal antibiotics and a sticky situation

Antibiotic treatment affects commensal bacteria of the gut microbiota, even at sublethal concentrations. Schlomann, Wiles et al. examined the effect of sublethal doses of ciprofloxacin on the dynamics of gut bacterial populations using live imaging of larval zebrafish. They focused on two native zebrafish isolates: fast-growing, planktonic *Vibrio cholerae* ZWU0020 and slow-growing *Enterobacter cloacae* ZOR0014, which forms dense bacterial aggregates. Germ-free fish were colonized with either bacterial strain before ciprofloxacin treatment. The antibiotic enhanced aggregation of bacterial cells, which resulted in their increased expulsion from the gut by the mechanical activity of the intestine. Moreover, the effect was more pronounced for slow-growing bacteria. As low concentrations of the antibiotic are often found in the environment, the findings of this study highlight the possibility of gut microbiota perturbations due to environmental antibiotic contaminants.

ORIGINAL ARTICLE Schlomann, B. H. et al. Sublethal antibiotics collapse gut bacterial populations by enhancing aggregation and expulsion. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1907567116 (2019)

CLINICAL MICROBIOLOGY

Human trial of vaginal microbiome transplantation

Bacterial vaginosis is characterized by changes in the vaginal microbial community, and therapeutic options are limited for persistent or recurrent bacterial vaginosis. Lev-Sagie, Goldman-Wohl, Cohen et al. report the feasibility of vaginal microbiome transplantation (VMT) from healthy donors as treatment for patients suffering from symptomatic, intractable and recurrent bacterial vaginosis. Four of the five treated patients showed full long-term remission and one patient incomplete remission after VMT, which suggests that VMT might be beneficial in treating the condition. Samples from donors and VMT recipients were analysed using shotgun metagenomic sequencing, which revealed that four of five recipients exhibited substantial changes in the microbiome composition, which were more similar to that of the collective donor vaginal microbiome. Randomized, placebo-controlled trials are needed to determine efficacy of VMT and the possible associated risk factors.

ORIGINAL ARTICLE Lev-Sagie, A. et al. Vaginal microbiome transplantation in women with intractable bacterial vaginosis. *Nat. Med.* https://doi.org/10.1038/s41591-019-0600-6 (2019)

ANTIMICROBIALS

Designing phagebodies

Phage therapy is a promising treatment option for multi-drug-resistant infections; however, successful development of phage-based therapies is hampered by the possible acquisition of resistance by bacteria. Lu and colleagues identified regions in the tail fibre of the T3 phage that dictate phage host range, termed host-range-determining regions. They genetically engineered these regions through site-directed mutagenesis in a high-throughput manner. This approach, which is analogous to antibody specificity engineering, led to the generation of synthetic 'phagebodies' with a broadened host range that were able to target naturally occurring phage-resistant bacterial mutants. Bacterial resistance to phagebodies was not observed. Finally, an engineered phagebody cocktail eliminated sensitive bacterial strains in a mouse skin infection model. The findings will enhance the development of phage-based antimicrobials.

ORIGINAL ARTICLE Yehl, K. et al. Engineering phage host-range and suppressing bacterial resistance through phage tail fibre mutagenesis. *Cell* **179**, 459–469 (2019)

MICROBIOME

An apple a day helps *Bacteroides* to stay

Previous studies have shown that the gut microbiota can have a role in protection from obesity, in particular certain *Bacteroides* spp. However, the relationship is complex and involves interactions between different members of the microbiota and dietary components such as fibre. It has been difficult to determine the underlying mechanisms, molecules and pathways and thus to target them specifically. In a new study, Gordon and colleagues use germ-free mice, colonized with defined consortia of gut bacteria, and artificial food particles coated with different fibres to better understand these interactions.

The authors colonized germ-free mice with bacteria isolated from a lean donor and fed them a human diet high in fat and low in fruits and vegetables supplemented with 34 different fibres, including fibres from apples, citrus, peas and other plants. The different fibres had specific effects on the composition of the gut bacterial community; for example, fibre from pea skins increased the abundance of *Bacteroides thetaiotaomicron*, whereas fibres from orange peels increased *Bacteroides cellulosilyticus*.

The next step was to identify the bioactive fibre components and how they were used by community members. Biochemical analyses showed that the fibres contained complex mixtures of different molecular components. The authors used proteomic analysis to demonstrate that *Bacteroides* spp. responding to different types of fibres upregulated enzymes encoded in polysaccharide utilization loci linked to

MICROBIOME

Microbial conductors

The mammalian circadian clock synchronizes physiological processes, such as cellular metabolism, with day–night cycles by controlling rhythmic oscillations in gene expression. Emerging evidence suggests that diurnal host–microbiota interactions also affect host metabolism; however, the molecular mechanisms underlying the crosstalk between the circadian clock and the microbiota and its effect on metabolic gene expression were not well understood. Kuang et al. now link a host factor and the gut microbiota to the circadian regulation of host metabolism.

The authors collected small intestinal epithelial cells (IECs) from wild-type and germ-free mice in a 24-hour period and assessed two acetylation marks associated with transcriptional activity: histone H3 lysine 9 acetylation (H3K9ac) and H3K27ac. Both acetylation marks showed synchronized diurnal oscillations in IECs from wild-type mice, but not in IECs from germ-free mice. Moreover, oscillating histone acetylation marks were enriched at genes encoding proteins involved in metabolic processes, such as nutrient transport and lipid metabolism. The findings suggest a role for both the microbiota and a histone deacetylase (HDAC), and indeed compared to the wild type,