IN BRIEF

SYMBIOSIS

The root of a new interkingdom interaction

Symbiotic rhizobial bacteria and legumes have evolved complex signal exchange mechanisms that enable bacteria to penetrate the plant root and develop root nodules, where bacteria fix nitrogen. Now, Ren, Wang et al. uncover a new signalling mechanism by which bacteria regulate root nodulation. The authors found that tRNA-derived small RNA fragments (tRFs) from the rhizobium *Bradyrhizobium japonicum* modulate nodule numbers in the soybean *Glycine max* by hijacking the host RNAi machinery and regulating host gene expression. Five host genes involved in root hair and plant development were found to be regulated by tRFs, and silencing the tRFs or overexpressing their targets repressed nodule formation. By contrast, repression of the targets through miRNAs identical to the tRFs or CRISPR–Cas knockout promoted nodulation. These findings provide a new mechanism that could be exploited to enhance nodulation in legumes.

ORIGINAL ARTICLE Ren, B., Wang, X. et al. Rhizobial tRNA-derived small RNAs are signal molecules regulating plant nodulation. *Science* **365**, 919–922 (2019)
RELATED ARTICLE Poole, P., Ramachandran, V. & Terpolilli, J. Rhizobia: from saprophytes to endosymbionts. *Nat. Rev. Microbiol.* **16**, 291–303 (2018)

ANTIMICROBIALS

Metabolic state matters for antibiotic lethality

Bactericidal antibiotics kill pathogens and understanding the mechanisms of antibiotic lethality is important for combatting persistent infections. Both the growth rate and metabolic state of cells affect antibiotic lethality, but they are interrelated as growth affects metabolism and vice versa. Lopatkin et al. investigated the relative contribution of growth and metabolic state to antibiotic lethality by measuring growth rate and metabolism across a range of conditions (nine drugs of different classes, and diverse Gram-positive and Gram-negative bacteria) in which growth and metabolism were coupled and uncoupled (conditions in which only growth is nutrient-limited). The authors found that metabolic state and ATP levels at the time of treatment are more accurate predictors of lethality than growth rate, and determined a critical ATP threshold below which antibiotic lethality is negligible. These findings suggest that antibiotics will kill non-growing bacteria if metabolism is stimulated.

ORIGINAL ARTICLE Lopatkin, A. J. et al. Bacterial metabolic state more accurately predicts antibiotic lethality than growth rate. *Nat. Microbiol.* https://doi.org/10.1038/s41564-019-0536-0 (2019)

VIRAL INFECTION

A close-up of respiratory syncytial virus replication

Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infection in infants and older persons, yet no vaccine is available. Thus, the development of effective RSV inhibitors is an active area of research. An attractive target for antiviral development is the viral RNA polymerase complex consisting of the large protein (L) and the phosphoprotein (P); however, structures of L and P have remained elusive. Now, Gilman et al. report a 3.2 Å cryo-electron microscopy structure of L bound to tetrameric P, providing atomic-level insights into transcription and replication of the RSV genome. For example, the P tetramer binds L in an unusual tentacular arrangement, with each monomer adopting a different conformation. The structure also explains inhibitor escape mutants and mutations that arise in live-attenuated vaccine candidates. Furthermore, it provides a new avenue of exploration for understanding RSV transcription and replication, and should aid in RSV drug development.

ORIGINAL ARTICLE Gilman, M. S. A. et al. Structure of the respiratory syncytial virus polymerase complex. *Cell* https://doi.org/10.1016/j.cell.2019.08.014 (2019)

BACTERIAL PHYSIOLOGY

Commensal defence

Neisseria gonorrhoeae, a sexually transmitted pathogen, is a major global public health concern owing to the rapid emergence of multi-drug resistant strains and the absence of a vaccine. The *Neisseria* genus comprises pathogenic *N. gonorrhoeae* and related non-pathogenic commensal species that colonize human mucosal surfaces. Commensal bacteria can inhibit colonization of pathogens by protein-based mechanisms or nutrient competition. Based on those observations and because *N. gonorrhoeae* infects the same niches as commensal *Neisseria* species, Kim et al. hypothesized that commensal *Neisseria* antagonize *N. gonorrhoeae*. In their study, the authors report that the human commensal *Neisseria elongata* kills *N. gonorrhoeae* through a DNA-mediated mechanism.

First, they showed that *N. elongata* kills *N. gonorrhoeae* when the two species are cultured together, whereas *N. elongata* viability is unaffected by the pathogen. This finding was confirmed in an in vivo mouse model of *N. gonorrhoeae* lower genital tract infection where the presence of *N. elongata* accelerates the clearance of the pathogen. Cell-free supernates of *N. elongata* kill *N. gonorrhoeae*, which indicated that a component released by the commensal is responsible for the killing activity. Further experiments showed that the toxic compound released into the medium is *N. elongata* DNA.

Neisseria species are naturally competent and readily take up DNA. The uptake of DNA involves the type IV pilus-associated protein ComP and the type IV pilus retraction motor PilT. The authors showed that *N. gonorrhoeae comP* and *pilT* deletion mutants are resistant to killing by *N. elongata* DNA. This, together with the finding that *N. elongata* does not accelerate the clearance of *N. gonorrhoeae comP* mutants in the mouse,

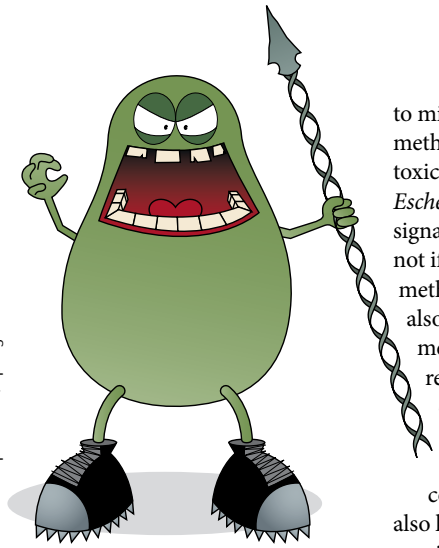
PARASITE DEVELOPMENT

The cat is out the bag about *Toxoplasma* host range

The parasite *Toxoplasma gondii* has a complex life cycle that involves sexual reproduction in the intestine of cats. Although other animals and humans can be infected, they only serve as intermediate hosts in which asexual reproduction occurs, but it can have severe consequences for the host, for example, leading to fetal complications in pregnant women. Little has been known about the factors that restrict sexual reproduction to cats so far; such knowledge could help to develop strategies to prevent shedding of infectious parasites from cats. A new study now finds that *T. gondii* relies on linoleic acid, which is abundant in the cat gut, for sexual development.

When *T. gondii* infects cats, it invades the intestinal epithelium

Credit: Sergey Zaikov / Alamy Stock Photo



Credit: Philip Patenall/Springer Nature Limited

suggests that DNA uptake by the pathogen is required for killing.

The authors could not find any evidence that the DNA contains a toxic locus; however, they observed that *N. elongata* and *N. gonorrhoeae* DNA are methylated differently. Thus, they tested whether this difference in methylation pattern determines the toxicity of the DNA for the pathogen. Indeed, DNA from several commensal *Neisseria* species, which are also methylated differently than *N. gonorrhoeae* DNA, reduces pathogen viability, whereas *N. elongata* DNA modified to mimic the *N. gonorrhoeae* methylation pattern is reduced in toxicity. A DNA fragment with an *Escherichia coli* methylation signature kills the pathogen, but not if it carries the *N. gonorrhoeae* methylation signature. The authors also showed that the killing mechanism involves homologous recombination of the incoming commensal DNA with the pathogen genome. Finally, the authors found that DNA from commensal *Neisseria* species also kills the pathogen *Neisseria meningitidis*.

In sum, the findings suggest that commensal *Neisseria* species antagonize pathogenic *Neisseria* species through their DNA, by a mechanism based on genetic competence and DNA methylation state. The study also suggests that DNA, modified appropriately, may be useful as a preventative against *N. gonorrhoeae* infection.

Andrea Du Toit

ORIGINAL ARTICLE Kim, W. J. et al. Commensal *Neisseria* kill *Neisseria* gonorrhoeae through a DNA-dependent mechanism. *Cell Host Microbe* **26**, 228–239.e8 (2019)

and undergoes sexual reproduction leading to the production of oocysts, which are shed in faeces and then sporulate to produce infectious parasites. Previous work has shown *T. gondii* scavenges fatty acids and, furthermore, one particular fatty acid found in the diet, linoleic acid, has been shown to influence sexual development in fungi. Therefore, the authors set out to test the role of linoleic acid in the sexual development of *T. gondii*. In cat intestinal organoids, *T. gondii* formed merozoites, a pre-sexual stage, macrogametes and, finally, oocysts only in the presence of linoleic acid but not when the control fatty acid oleic acid was added.

Interestingly, cats lack intestinal delta-6-desaturase, which is the first enzyme in the pathway that metabolizes linoleic acid to arachidonic acid. Consequently, cats have much higher levels of linoleic acids than other animals, including mice and humans. The authors thus speculated that this fatty acid is a signal for the parasite to induce sexual development. Indeed, when they treated the mouse intestinal cells with linoleic acid and SC-26196, an inhibitor of delta-6-desaturase, the parasites initiated sexual development. Furthermore, mice receiving high levels of linoleic acid together with the inhibitor also became permissive to sexual development of *T. gondii* and shed similar numbers of oocysts in their faeces as cats. Although mouse-derived oocysts were not as stable as cat-derived ones, they could sporulate and were able to infect recipient mice and form cysts in their brains.

In summary, the study identifies linoleic acid, which accumulates in the cat gut due to absent metabolic conversion of this fatty acid, as a determinant of species-specific sexual reproduction of *T. gondii*. These findings can be used to study sexual parasite development in mice, which is an easier model than cats, and they might also lead to interventions that prevent the development of infectious parasites in cats and thus transmission of *T. gondii*.

Ursula Hofer

ORIGINAL ARTICLE Martorelli Di Genova, B. et al. Intestinal delta-6-desaturase activity determines host range of *Toxoplasma* sexual reproduction. *PLOS Biol.* **17**, e3000364 (2019)

IN BRIEF

ARCHAEAL GENOMICS

Getting your chromosomes organized

The three-dimensional organization of chromatin has an important role in genome functions. In bacteria and eukaryotes, structural maintenance of chromosomes (SMC) protein complexes such as condensin mediate higher-order chromosome organization. However, many archaea do not have condensin, and the establishment and maintenance of archaeal chromosome conformation was not well understood. Takemata, Samson and Bell used chromosome conformation capture to investigate the spatial organization of the chromosomes of *Sulfolobus* species. They found that the chromosomes are organized into two compartments with higher and lower gene expression activities — the A compartment and B compartment, respectively. This non-random chromosome organization was established by coalescin, a novel *Sulfolobus*-encoded SMC protein. Coalescin is enriched in the B compartment and binds to less active genes, thus maintaining the compartmentalization of the archaeal chromosome.

ORIGINAL ARTICLE Takemata, N., Samson, R. Y. & Bell, S. D. Physical and functional compartmentalization of archaeal chromosomes. *Cell* **179**, 165–179.e18 (2019)

MICROBIOME

Establishing the gut microbiota after birth

Following birth, newborn babies are rapidly colonized by microorganisms, and Shao et al. further corroborate that the mode of delivery is a crucial factor that shapes the gut microbiota during the neonatal period, with effects that persist into infancy. Metagenomic analysis of faecal samples from babies delivered vaginally were enriched with commensals (*Bifidobacterium*, *Escherichia*, *Bacteroides* and *Parabacteroides* species), whereas the gut microbiota of babies delivered by caesarean section were depleted of these commensal species and were dominated by opportunistic pathogens associated with the hospital environment (including *Enterococcus*, *Enterobacter* and *Klebsiella* species). Finally, large-scale culturing and whole-genome sequencing of opportunistic pathogens found in the faecal samples identified virulence factors and clinically relevant antimicrobial resistance genes, which suggests that opportunistic pathogen carriage is a risk factor for opportunistic infections.

ORIGINAL ARTICLE Shao, Y. et al. Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth. *Nature* https://doi.org/10.1038/s41586-019-1560-1 (2019)

MICROBIAL ECOLOGY

Core leaf taxa of biofuel crops

Perennial grasses have potential in the production of biofuels, and modulating plant microbiomes may enhance plant growth and productivity, and resilience to environmental stresses. However, our knowledge of the phyllosphere microbiome is limited, in particular for agricultural crops. In this study, Shade and colleagues investigated the assembly and seasonal dynamics of bacterial and archaeal microbiomes of the leaf surfaces and the associated soils of switchgrass and miscanthus across the two growing seasons in 2016 and 2017. They identified core leaf taxa for each crop and season based on abundance and occupancy, including several Proteobacteria (*Methylobacterium* spp., *Sphingomonass* spp. and *Pseudomonas* spp.) and Bacteroidetes (*Hymenobacter* spp.). Further analysis enabled them to identify seasonal trends of the core leaf taxa (that is, early, mid, and late season groups), which might be linked to plant development.

ORIGINAL ARTICLE Grady, K. L. et al. Assembly and seasonality of core phyllosphere microbiota on perennial biofuel crops. *Nat. Commun.* **10**, 4135 (2019)