IN BRIEF

BACTERIAL GENETICS

ppGpp triggers the switch

Riboswitches are highly structured, non-coding RNA elements located upstream of the coding region of bacterial mRNAs. They bind cellular ligands via their aptamer domain to regulate gene expression of the adjacent gene or operon through their expression platform domain. Five riboswitch classes have been identified that sense nucleotide-based signalling molecules, including c-di-GMP and c-di-AMP. This study describes a riboswitch class that selectively binds the alarmone guanosine tetraphosphate (ppGpp). Binding of ppGpp to candidate riboswitches induced structural changes in the RNA, and gene expression was regulated via transcription termination. Riboswitches for ppGpp may regulate genes involved in branched-chain amino acid biosynthesis, genes encoding glutamate synthase domains and operons containing ATP-binding cassette transporters.

ORIGINAL ARTICLE Sherlock, M. E., Sudarsan, N. & Breaker, R. R. Riboswitches for the alarmone ppGpp expand the collection of RNA-based signaling systems. *Proc. Natl Acad. Sci.* https://doi.org/10.1073/pnas.1720406115 (2018)

FUNGAL PATHOGENESIS

Breaking barriers

Candida albicans asymptomatically colonizes healthy individuals, but it is also an opportunistic pathogen that can translocate across the intestinal epithelium and cause bloodstream infections. Using in vitro cell culture models, Allert, Förster et al. show that translocation through an intact intestinal barrier is initiated by invasion and followed by cellular damage and loss of epithelial integrity. Translocation occurs mainly via a transcellular route, which causes necrotic epithelial damage. The cytolytic peptide toxin of *C. albicans*, candidalysin, was found to be essential for damage of enterocytes and was a key factor in fungal translocation. However, fungal invasion and low-level translocation can also occur in a candidalysin-independent manner — possibly by passing through intercellular spaces.

ORIGINAL ARTICLE Allert, S. & Förster, T. M. et al. Candida albicans-induced epithelial damage mediates translocation through intestinal barriers. *mBio* **9**, e00915-18 (2018)

SYMBIOSIS

Four is a crowd

Acromyrmex leafcutter ants form a tripartite symbiosis with the fungal cultivar *Leucoagaricus gongylophorus* and *Pseudonocardia* bacteria. Ants provide leaves as growth substrate for the fungus and the fungus provides the sole food source for ant larvae. The bacteria produce molecules that protect the cultivar against pathogens, such as the fungal parasite *Escovopsis weberi*. Two studies show that *E. weberi* produces secondary metabolites during infection of the cultivar that promote the collapse of the fungus garden in leafcutter ant colonies. Heine et al. identified melinacidin IV and the terpene-indole alkaloid shearinine D, both of which kill *Pseudonocardia* species. Ingestion of shearinine D by ants adversely affects their behaviour and results in ant death. Dhodary et al. showed that *E. weberi* produces shearinine L and shearinine M, as well as emodin and cycloarthropsone, which inhibit the growth of *L. gongylophorous*.

ORIGINAL ARTICLES Heine, D. et al. Chemical warfare between leafcutter ant symbionts and a co-evolved pathogen. *Nat. Comms.* **9**, 2208 (2018). | Dhodary, B. et al. Secondary metabolites from *Escovopsis weberi* and their role in attacking the garden fungus of leaf cutting ants. *Chem. Eur. J.* **24**, 4445–4452 (2018)

BIOFILMS

Sharing the burden to build a matrix

Biofilms are structured consortia of bacteria embedded in a self-produced extracellular matrix (ECM) of exopolysaccharides (EPSs), structural proteins and extracellular DNA. As the production of the ECM is metabolically costly, it has been suggested that the overall metabolic cost to the community may be reduced by allocating ECM production to a subpopulation of cells. In a recent study, Dragoš et al. investigate the benefits of division of labour during ECM production and show that both genetic and phenotypic strategies for a division of labour promote biofilm formation.

Using *Bacillus subtilis* pellicle (a floating biofilm at an air-liquid interface) formation as a model system, the authors observed that the two major ECM components — EPSs and TasA — are metabolically costly to produce and are shared amongst the community. Using Δ*eps* and Δ*tasA* mutants in growth competition assays, they observed a significant fitness cost of EPSs and TasA production. In agreement with previous observations, they found that Δ*eps* and Δ*tasA* mutants could not establish biofilms in monoculture, but could when they were co-cultured or if conditioned media from producers was added, indicating that EPSs and TasA can be shared.

The authors hypothesised that phenotypic differentiation into EPS producers and TasA producers could occur within *B. subtilis* pellicles. Using confocal laser scanning microscopy and cells expressing fluorescent markers under the control of the ECM gene promoters, they observed heterogeneity in the expression of *eps* and *tasA* within

BACTERIAL PATHOGENESIS

Falling into your own trap

Staphylococcus aureus is an important bacterial pathogen that can cause serious invasive infections in humans. The first line of defence against invasive *S. aureus* involves the recruitment of neutrophils, which release extracellular traps (termed NETs, which are composed of chromatin, proteases and antimicrobial peptides) that capture microorganisms and enable their elimination by macrophage-mediated phagocytosis. To escape clearance, *S. aureus* degrades NETs, which is associated with the formation of cytotoxic deoxyadenosine (dAdo) by *S. aureus* nuclease and adenosine synthase A. Previous work showed that dAdo induces apoptosis in macrophages and thus promotes persistent infection; however, the underlying mechanism was not clear. This study reports that dAdo-mediated macrophage apoptosis involves a macrophage membrane transporter and kinases of the purine salvage pathway.

The authors used a CRISPR-Cas9 screen in human macrophages and found that cells that lacked genes that encode human equilibrative transporter 1 (hENT1, which mediates uptake of nucleosides and of nucleoside derivatives) and kinases of the purine salvage pathway (adenosine kinase (ADK) and deoxycytidine kinase (DCK)) were resistant to dAdo.

Although dAdo was found in the cytoplasm of control cells, dAdo could not be detected in the cytoplasm of mutant cells that lacked the membrane protein hENT1, which suggests that hENT1 transports dAdo across the plasma membrane. Furthermore, inhibition of ADK and DCK decreased dAdo-mediated apoptosis of macrophages, which is in agreement with a role of those kinases in dAdo intoxication.

Moreover, the authors were able to show that ADK and DCK catalyze the conversion of dAdo to dAMP for the subsequent synthesis of dADP