IN BRIEF

MICROBIOME

Modifying the gut to treat liver diseases

The gut microbiota produces urease, which transforms urea into ammonia and carbon dioxide. Ammonia has several beneficial roles in host metabolism, but patients with liver disease are unable to process ammonia in the liver, which results in an increase in the systemic levels of ammonia; this leads to neurotoxicity and results in hepatic encephalopathy. Shen *et al.* engineered the microbiota of mice to express low levels of urease by depleting the endogenous microbiota via the use of antibiotics and polyethylene glycol, followed by gavage of a defined consortium of eight bacterial strains with reduced capacity to produce urease, termed altered Schaedler flora (ASF). This strategy resulted in the establishment of a persistent gut microbiota that displayed reduced levels of ammonia production for up to 80 days. Notably, in murine models of liver injury, ASF transplantation resulted in reduced levels of ammonia, improved cognitive performance and reduced mortality.

ORIGINAL RESEARCH PAPER Shen, T.-C. D. *et al.* Engineering the gut microbiota to treat hyperammonemia. *J. Clin. Invest.* **125,** 2841–2850 (2015)

BACTERIAL EVOLUTION

Plague starts with Pla

Yersinia pestis, the causative agent of pneumonic plague, evolved from the mild enteric pathogen *Yersinia pseudotuberculosis*. To understand how *Y. pestis* evolved to cause plague, Zimbler *et al.* used a mouse model to compare ancestral and modern strains of *Y. pestis*. Ancestral strains were capable of causing pneumonic plague, but only if they contained the gene encoding the Pla protease, which is present in all modern strains. Notably, introduction of *pla* into an ancestral strain naturally lacking the gene conferred the ability to cause pneumonic plague, indicating that Pla acquisition was sufficient for ancestral *Y. pestis* to cause severe respiratory disease. Furthermore, modern *Y. pestis* strains also acquired a single amino acid substitution in Pla that increased bacterial invasion of other organs — a characteristic of bubonic plague — indicating that *Y. pestis* evolved to cause pneumonic plague before adapting to cause bubonic plague.

ORIGINAL RESEARCH PAPER Zimbler, D. L. *et al.* Early emergence of *Yersinia pestis* as a severe respiratory pathogen. *Nat. Commun.* http://dx.doi.org/10.1038/ncomms8487 (2015)

VIRAL INFECTION

TRIMming immune responses to dengue

Dengue virus (DENV) outbreaks can occur when new DENV strains emerge and replace endemic strains, as during a 1994 epidemic when a foreign dominant (PR-2B) replaced the endemic (PR-1) viral clade. To understand the changes that resulted in the increased fitness of PR-2B, Manokaran *et al.* compared the two viral sequences and identified mutations that resulted in the increased production of subgenomic flavivirus non-coding RNAs (sfRNAs) by the PR-2B strain. These PR-2B sfRNAs were capable of binding to host TRIM25 and prevented its deubiquitylation, which is crucial for activation of RIG-I, a cytosolic sensor that recognizes viral nucleic acids and induces the expression of antiviral type I interferons by infected cells. These data demonstrate that DENV sfRNAs can bind to host proteins to promote viral evasion of innate immunity and increase viral fitness.

ORIGINAL RESEARCH PAPER Manokaran, G. *et al.* Dengue subgenomic RNA binds TRIM25 to inhibit interferon expression for epidemiological fitness. *Science* http://dx.doi.org/10.1126/science.aab3369 (2015)