IN BRIEF

BACTERIAL GENOMICS

Salmonella Enteritidis: chicken or egg?

Salmonella enterica serovar Enteritidis is a major cause of food-borne infections in humans associated with eggs and poultry. The pathogen started spreading globally in the 1980s; however, how the outbreak spread is incompletely understood. Li et al. analysed 30,015 *Salmonella* Enteritidis whole-genome sequences from strains isolated globally between 1949 and 2020 and compared the data with records of the global poultry trade since the 1980s. They found that poultry and egg isolates are less diverse than isolates from other sources and that closely related bacteria occurred in different countries. For example, one isolate from Suriname was almost identical to contemporary US isolates, which might reflect the USA as the main exporter of breeding chicken to Suriname. In support of the important role of breeding stocks spreading the outbreak, egg trading routes and volume were strong predictors of the spread of the global lineage of *Salmonella* Enteritidis and the genomic data suggests that this lineage emerged shortly before chicken breeding became a centralized and globalized industrial operation in the 1980s. Concerningly, the example of export to Suriname occurred in 2016, indicating that *Salmonella* Enteritidis spread via breeding stocks is still a problem today.

ORIGINAL ARTICLE Li, S. et al. Global spread of *Salmonella* Enteritidis via centralized sourcing and international trade of poultry breeding stocks. *Nat. Commun.* **12**, 5109 (2021)

BACTERIAL PHYSIOLOGY

Lassoing OMVs with an LPS receptor

Outer membrane vesicles (OMVs) produced by Gram-negative bacteria have many functions, including delivery of signals and nutrients. Li et al. report a novel tethering mechanism in *Cupriavidus necator*. The authors found that this bacterium, belonging to the Burkholderiales, secretes an effector through its type 6 secretion system (T6SS) that can bind to lipopolysaccharide (LPS) from different bacteria. They termed this effector TeoL for T6SS effector for recruitment of OMVs via LPS, as it binds LPS on the OMV surface and then tethers the OMVs to the cell surface by binding to two outer membrane receptors, both of which are siderophores. Interestingly, this mechanism enables the bacteria to harvest iron from OMVs and to promote plasmid acquisition, providing them with an advantage over competitors and promoting horizontal gene transfer, respectively.

ORIGINAL ARTICLE Li, C. et al. T6SS secretes an LPS-binding effector to recruit OMVs for exploitative competition and horizontal gene transfer. *ISME J.* https://doi.org/10.1038/s41396-021-01093-8 (2021)

VIRAL INFECTION

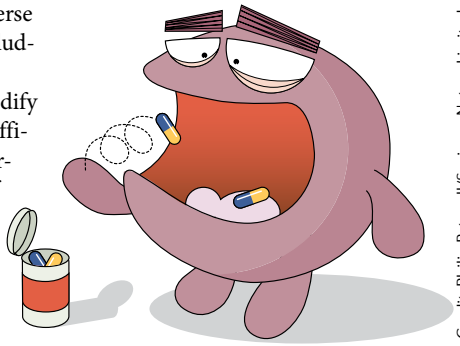
Dose-dependent COVID-19 symptoms

COVID-19 presentation varies widely between individuals, ranging from asymptomatic to life-threatening infection. Several host and viral factors have been shown to influence disease penetrance and severity. In addition, the infectious dose has also been speculated to have a role. Dabisch et al. show in a SARS-CoV-2 challenge study of 16 cynomolgus macaques that the infectious dose indeed influences symptom development and seroconversion. They used aerosolized virus at different concentrations and found that low doses could lead to seroconversion and virus replication in the respiratory tract without symptom development, such as fever, whereas higher doses produced fever, which suggest that low infectious doses might be associated with asymptomatic infection.

ORIGINAL ARTICLE Dabisch, P. A. et al. Seroconversion and fever are dose-dependent in a nonhuman primate model of inhalational COVID-19. *PLoS Pathog.* **17**, e1009865 (2021)

MICROBIOME

Scooping up all the drugs



Credit: Philip Patenall/Springer Nature Limited

The gut microbiota affects diverse aspects of host physiology, including drug metabolism. These bacteria–drug interactions modify drug availability, activity and efficacy, and the chemical transformation (biotransformation) of drugs by microbial members of the gut community has been reported for numerous compounds. Bork, Typas, Patil and colleagues show that gut bacteria also accumulate host-targeted drugs intracellularly, which affects the therapeutic effect of the drug as well as metabolite secretion of the accumulating bacteria, without having much of an impact on bacterial growth.

The authors investigated the interactions between human-targeted drugs and human gut bacterial species representing the healthy microbiota. Testing for drug depletion, they identified 70 bacteria–drug pairs, with 29 of those being previously unknown. Interestingly, for a majority of the newly identified interactions they found that, although the drug was depleted in the supernatant, it could be recovered from the total culture, which indicated drug bioaccumulation; that is, the drug is stored within the bacterial cell without being modified. This finding is in contrast to the previous notion that the only mechanism of drug depletion is microbially mediated biotransformation. To understand the molecular basis for bioaccumulation, the authors focused on duloxetine, an antidepressant that accumulates in several of the tested species/strains. Using a click-chemistry based assay as well as thermal proteome profiling they identified several metabolic enzymes as potential protein targets of the drug in the bacteria. Binding of the drug to the metabolic enzymes indicates a change in cell metabolism. Indeed, using a metabolomics approach, the authors showed that duloxetine induced a shift in the exo-metabolome of bioaccumulators. To test a possible effect on community composition, the authors assembled a community of five gut bacterial species (including *Streptococcus salivarius*, a duloxetine bioaccumulator, and *Eubacterium rectale*, which is directly inhibited by the drug). In the presence of the drug, the community composition changed, with an increased abundance of *E. rectale*. The extent of the increased abundance could not be explained by the decreased duloxetine concentration owing to bioaccumulation in *S. salivarius*. The authors found that the drug modulated metabolite secretion in *S. salivarius*, and this shift enhanced the growth of *E. rectale*. The authors conclude that the human-targeted drug induces changes in microbial community composition indirectly by inducing cross-feeding between species. Finally, the authors tested the effect of duloxetine bioaccumulation on the host response (in this case, movement of *Caenorhabditis elegans*), and they showed that in the presence of a bioaccumulating bacterial strain, host behaviour following drug treatment was modulated compared with animals cultured in the presence of non-bioaccumulating bacteria.

In sum, the study suggests that the bioaccumulation of human-targeted drugs by gut bacteria may be a common mechanism, which results in altered drug availability and bacterial metabolism.

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ORIGINAL ARTICLE Klünemann, M. et al. Bioaccumulation of therapeutic drugs by human gut bacteria. *Nature* https://doi.org/10.1038/s41586-021-03891-8 (2021)