Epidemiology

Sewer biofilms and SARS-CoV-2

Wastewater surveillance of SARS-CoV-2 can be useful in providing information about the prevalence and the possible emergence of new variants in a community. Although wastewater-based approaches have been implemented globally to monitor the virus, there remain various challenges and knowledge gaps that make it difficult to fully and reliably interpret the data obtained; for example, the fate of SARS-CoV-2 in sewer systems is not well understood. In this study, Li and colleagues used a sewer reactor to analyse sorption, stability and persistence of SARS-CoV-2 RNA in sewers. The authors found that SARS-CoV-2 RNA accumulated on solid compartments and biofilms in sewers, which offered more niches and sorption sites. In addition, they also reported that biofilms may facilitate the decay of the virus and/or its genetic fragments in sewers, which might lead to the loss of the RNA signal and could thus affect the analysis, particularly in low-case settings. Moreover, the results also suggest that biofilms are a reservoir for viral RNA that accumulate, retain and subsequently release RNA fragments back into wastewater, which would have an impact on the interpretation of surveillance data. In sum, the results of this study could aid in advancing the efforts in wastewater surveillance.

Andrea Du Toit

Original article: Li, J. et al. Impact of sewer biofilms on fate of SARS-CoV-2 RNA and wastewater surveillance. *Nat. Water* https://doi.org/10.1038/s44221-023-00033-4 (2023)

Bacterial physiology

Fluid flow stress

Bacteria experience varying environmental conditions such as fluid flow, which are often not fully replicated under laboratory conditions. Previous studies have suggested that fluid flow has an impact on biofilm formation, virulence and gene expression. In this new study, Sanfilippo and colleagues used microfluidics to study how fluid flow is linked to changes in gene expression in bacterial pathogens. They report that flow generates stress and triggers a transcriptional response in *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Hydrogen peroxide (H_2O_2) diffuses into bacterial cells, and to protect themselves from oxidative damage, cells scavenge it using catalases and NADH peroxidases, thus depleting H_2O_2 in the environment. In their model, the authors propose that increased shear rates replenish H_2O_2 levels, which leads to increased levels of H_2O_2 within the cells. The increased H_2O_2 levels are sensed by the cells, which leads to the activation of cellular stress responses involved in H_2O_2 scavenging. The authors note that bacteria in flow are sensitive to H_2O_2 concentrations that are lower than those used in the laboratory, and that the levels more resemble those that are found in natural environments such as blood. The data suggest that flow sensitizes bacteria to chemical stress in natural environments.

Andrea Du Toit

Original article: Padron, G. C. et al. Shear rate sensitizes bacterial pathogens to H_2O_2 stress. *Proc. Natl Acad. Sci. USA* **120**, e2216774120 (2023)

Antimicrobials

Heat up the antibiotics

Antimicrobial resistance is a global threat to human health, and therefore the need to develop new antimicrobial molecules or to potentiate the efficacy of existing antibiotics has become imperative. In this study, Lv et al. present evidence showing that thermal treatment can augment the bactericidal efficacy of aminoglycoside antibiotics against several multi-drug resistant bacteria. The authors show that sublethal heat shock combined with aminoglycosides effectively killed Gram-negative pathogens like *Escherichia coli*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*. The authors further investigated the mechanism of heat potentiation and showed that heat shock increased the bacterial uptake of aminoglycosides, and promoted irreversible protein aggregation and production of reactive oxygen species, thus boosting aminoglycoside bactericidal activity. In vivo, the authors showed that thermal treatments (for example, infrared irradiation or photothermal nanosphere delivery) enhanced the activity of aminoglycosides against *Pseudomonas aeruginosa* in a mouse acute skin wound model. In sum, these results point at a promising use of thermal therapy to enhance the efficacy of antibiotics for the treatment of infections caused by multi-drug resistant and persistent pathogenic bacteria.

Agustina Taglialegna

Original article: Lv, B. et al. Heat shock potentiates aminoglycosides against gram-negative bacteria by enhancing antibiotic uptake, protein aggregation, and ROS. *Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.2217254120 (2023)

Vaccines

Chimeric protection to dengue

There are four serotypes of Dengue virus (DENV1 to 4) that circulate in the world and can cause asymptomatic or symptomatic infections with a range of mild to severe manifestations. In cases where individuals experience primary infection with a serotype and secondary infection with another serotype, cross-reactive and non-neutralizing antibodies can either be protective, or can enhance viral replication and lead to more severe disease. For this reason, the development of dengue vaccines is challenging. The most advanced DENV vaccines are tetravalent live virus vaccines that contain representative strains from each serotype. Although this vaccine has proven effective in seropositive individuals, inducing a balanced protective immune response against all four serotypes in naïve individuals has been difficult. In this study, Young et al. developed a simplified recombinant DENV vaccine, for which the domain II (EDII) of the DENV2 envelope glycoprotein was replaced with the EDII from the DENV4 serotype. The authors showed that this chimeric DENV2/4EDII virus replicated efficiently in vitro and in vivo, and induced type-specific neutralizing antibodies to DENV2 and DENV4 in macaques. These results demonstrate the potential to design simplified bivalent live dengue vaccines to induce immunity against multiple serotypes.

Agustina Taglialegna

Original article: Young, E. et al. A live dengue virus vaccine carrying a chimeric envelope glycoprotein elicits dual DENV2-DENV4 serotype-specific immunity. *Nat. Commun.* **14**, 1371 (2023)