

IN BRIEF

ANTIMICROBIALS

Strengthening the cell membrane barrier

Vancomycin-resistant enterococci (VRE) are among the most difficult to treat pathogens as some have evolved resistance to all available antimicrobials, including the frontline lipopeptide antibiotic daptomycin, which targets the bacterial cell membrane. Now, Khan et al. found that antimicrobial sensing coupled with cell membrane remodelling mediates resistance to daptomycin and virulence in *Enterococcus faecalis*. Daptomycin resistance involves the activation of the LiaFSR cell membrane stress response, which regulates cell membrane remodelling and phospholipid distribution. The authors found that the extracellular domain of LiaX binds to daptomycin or antimicrobial peptides (AMPs) and activates the stress response, resulting in protective changes in cell membrane phospholipid architecture. *E. faecalis* strains that exhibited LiaX-mediated cell membrane remodelling caused more virulent infections in *Caenorhabditis elegans*, which was dependent on the host's ability to produce AMPs. Targeting this stress response could be a promising strategy for treating VRE infections.

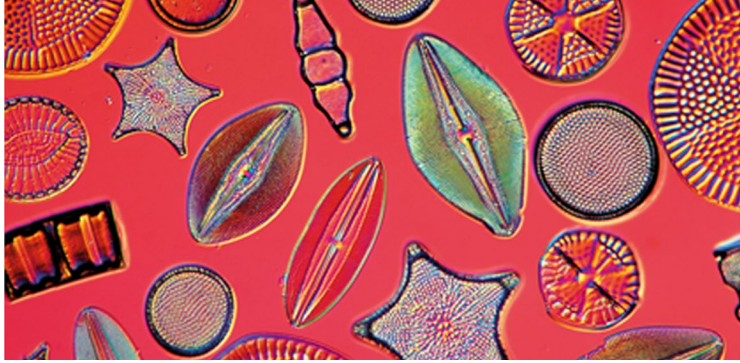
ORIGINAL ARTICLE Khan, A. et al. Antimicrobial sensing coupled with cell membrane remodeling mediates antibiotic resistance and virulence in *Enterococcus faecalis*. *Proc. Natl Acad. Sci. USA* <https://doi.org/10.1073/pnas.1916037116> (2019)

ARCHAEOLOGICAL EVOLUTION

New data for the tree of life

The evolutionary relationship between bacteria, archaea and eukaryotes is a hotly debated topic. Much of the ongoing debate is based on assertions that evolutionary relationships and the topology of the tree of life depend on the quality of data generated in genomics studies and the choice of marker genes and taxa that are included in analyses. Williams et al. evaluated the data and analyses that have led to conflicting views in the field and used phylogenomics and the latest supermatrix, supertree and coalescent methods on an expanded dataset to explore the evolutionary relationships between archaea and eukaryotes. The authors interrogated >3,000 gene families in archaea and eukaryotes and confirmed previous studies that eukaryotes originated from within the archaea. They argue that their analyses provide robust support for a two-domain tree of life and for a close relationship between eukaryotes and Asgard archaea, and they suggest that the phylum Heimdallarchaeota is the current best candidate for the closest relatives of eukaryotes. In another study, Zhu et al. investigated the evolutionary proximity between the different domains within the tree of life. The authors constructed a reference phylogeny of 10,575 bacterial and archaeal genomes based on 381 marker genes using a statistical approach that maximized the covered biodiversity. The authors argue that their tree provides a high resolution view of the basal relationships between microbial clades. Remarkably, the tree indicated a closer evolutionary proximity between bacteria and archaea than expected, owing to previous analyses being limited to a few core genes. The authors posit that this observation is supported using multiple tree-building methods and after considering several variables (for example, taxon and site sampling, amino acid substitution heterogeneity and saturation, and non-vertical evolution). Although the debate continues, these studies highlight that new data and tools provide further opportunities to understand the tree of life.

ORIGINAL ARTICLES Williams, T. A. et al. Phylogenomics provides robust support for a two-domain tree of life. *Nat. Ecol. Evol.* <https://doi.org/10.1038/s41559-019-1040-x> (2019) | Zhu, Q. et al. Phylogenomics of 10,575 genomes reveals evolutionary proximity between domains Bacteria and Archaea. *Nat. Commun.* **10**, 5477 (2019)
RELATED ARTICLE Eme, L. et al. Archaea and the origin of eukaryotes. *Nat. Rev. Microbiol.* **15**, 711–723 (2017)



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dead or dying cells, or smothered the nucleus of the host to assume a parasitic or saprophytic life style. In addition, some NCLC1 cells also associated with the surface of diatom hosts, potentially in a wider symbiotic relationship.

Up to 70% of all NCLC1 cells were free-living cells and had an ovoid or round shape, which might represent spore or cyst-like life-cycle stages. Rarely, NCLC1 assumed a multi-nucleate structure, which might be a short-lived replicative stage, as seen in other microbial eukaryotes.

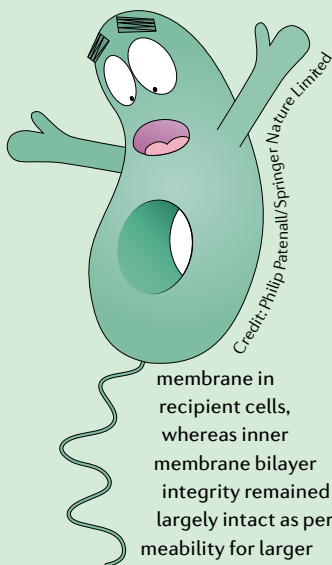
Notably, the authors found NCLC1 cells in samples both from 1 m below the surface of the sea and from the deep chlorophyll maximum, where phytoplankton (including diatoms) are particularly

abundant. In a different study, NCLC1 sequences were detected in sediments, where dead or dying cells are buried. These observations, combined with the detection of NCLC1 inside potentially necrotic host cells, open the possibility that these microorganisms might influence nutrient cycling and drawdown by diatoms. As the NCLC1 hosts also included bloom-forming diatoms, such an interaction could have substantial consequences for nutrient fluxes, including the marine carbon pump.

Ursula Hofer

ORIGINAL ARTICLE Chambouvet A. et al. Intracellular infection of diverse diatoms by an evolutionary distinct relative of the Fungi. *Curr. Biol.* **29**, 1–9 (2019)

RELATED ARTICLE Grossart, H.-P. et al. Fungi in aquatic ecosystems. *Nat. Rev. Microbiol.* **17**, 339–354 (2019)



membrane in recipient cells, whereas inner membrane bilayer integrity remained largely intact as permeability for larger compounds was not

increased. This suggested that Ssp6 does not induce the formation of large, unspecific pores, but instead that the membrane potential is disrupted by the formation of ion-selective pores that lead to ion leakage. To test this, the authors incorporated Ssp6 into artificial membranes and found that incorporation generated a

current, indicative of the formation of ion-conducting channels. Further experiments showed that the Ssp6-dependent pores were most selective for monovalent cations. Moreover, the authors also found that Ssp6 intoxication increased the permeability of the outer membrane of target cells. Interestingly, Sip6 was localized to the outer membrane, which suggests that the immunity protein might avoid Ssp6-mediated damage to the outer membrane and/or sequester incoming Ssp6 away from the inner membrane to prevent pore formation.

Finally, the authors reported that genes encoding Ssp6-like effectors are widespread in Enterobacteriaceae and are located within T6SS gene clusters.

In summary, this study identifies a new family of T6SS-delivered ion-selective pore-forming toxins that is distinct from previously described T6SS effectors.

Andrea Du Toit

ORIGINAL ARTICLE Mariano, G. et al. A family of Type VI secretion system effector proteins that form ion-selective pores. *Nat. Commun.* **10**, 5484 (2019)