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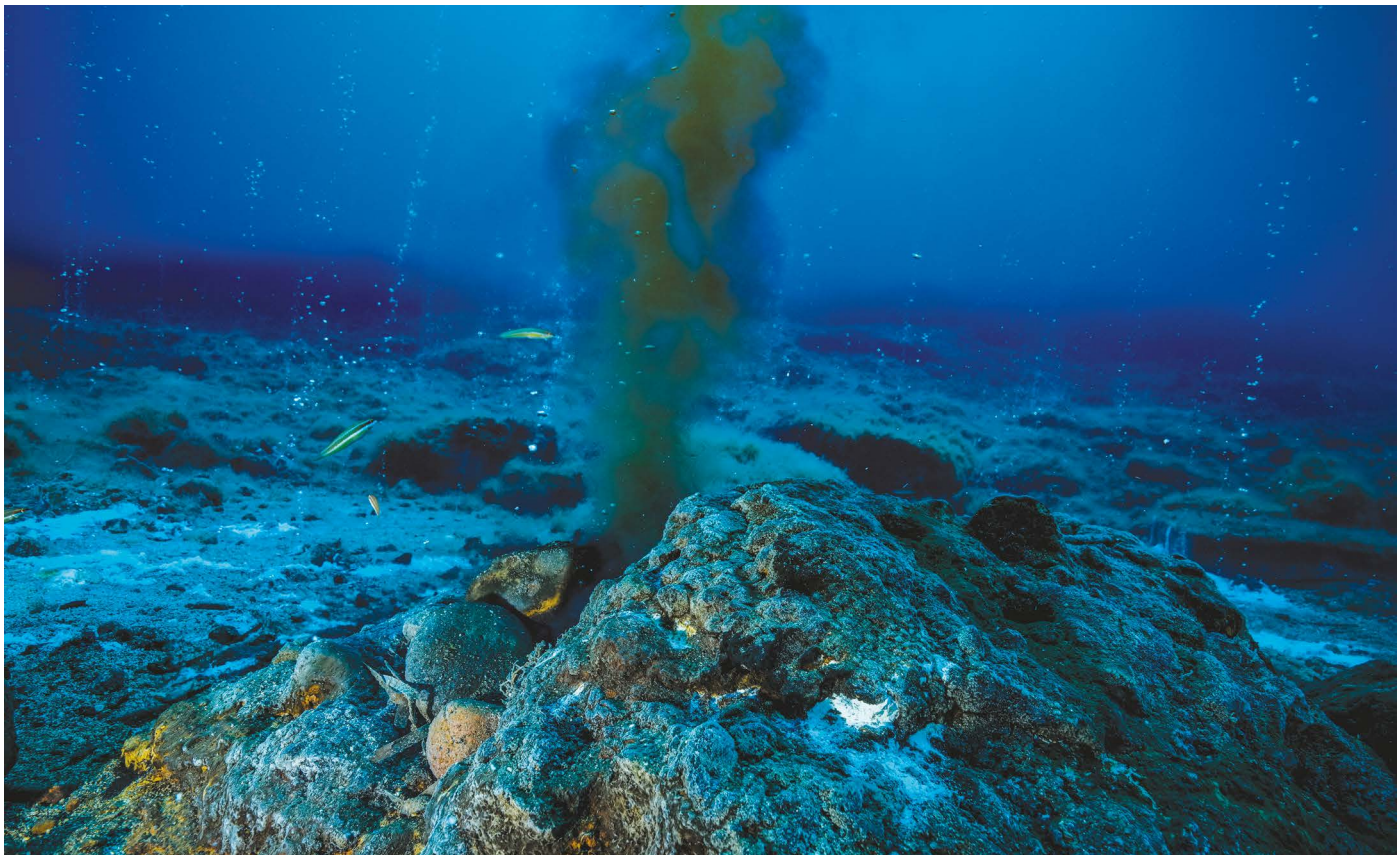

ALEXIS ROSENFELD/GETTY

Figure 1 | A hydrothermal vent.

Microbiology

From marine microbial genomes to biotechnology

A. Murat Eren & Tom O. Delmont

The direct recovery of microbial genomes from complex environments is now routine. Going from environmental genomes to laboratory experiments is rare, but the tide is turning. **See p.371**

In the past few decades, microbiology has revealed the astonishing diversity and dynamism of the microbes that define the boundaries of life on Earth, and that collectively undertake some of the most fundamental biogeochemical processes that maintain the habitability of our planet. As rapidly improving sequencing technologies were combined with molecular and analytical approaches that enabled microbial genomes to be recovered directly from complex environments[1,2], a new era began in life sciences, in which scientists could characterize the gene pool and metabolic potential of environmental microbes without laboriously having to grow them in the laboratory first. On page 371, Chen *et al.*[3] report progress in moving this journey to the next stage of exploration.

One of the most promising applications of this power to peek at the genomic sequences of individual microbes (collectively, the microbiome) is in bioprospecting – the systematic search for natural products with industrial promise, and their genetic origins. Discoveries in this area can advance a wide range of technological needs, ranging from ways to deal with contamination (bioremediation) to drug development, sustainable chemical production and more. Indeed, the potential of marine microbes for bioprospecting is broadly recognized[4,5].

Studies, such as work that charted the biosynthetic potential of the global ocean microbiome[6], show that the majority of previously unknown molecules (molecules that have functional novelty) is accessible only through surveys of environmental genomes. Thus, the need for computational recovery and characterization of environmental genomes is well justified. However, the extent to which these increasingly large genome collections can be effectively used for bioprospecting is rarely explored.

The work by Chen and colleagues joins rare studies that take advantage of the large

number of microbial genomes acquired through detailed surveys of marine metagenomes that emerge from the direct sequencing of DNA molecules in marine samples. The authors first created a catalogue of more than 40,000 such genomes, and mined them for genes that have particular functions. Then the authors used well-established molecular approaches in the laboratory to test the activity and effectiveness of candidate genes for applications such as genome editing, plastic degradation and antimicrobial defence.

In one case, the authors worked with a gene known for its genome-editing capabilities, *cas9*, which they identified in sequences from a bacterial organism of the genus *Staphylococcus* found in the Mediterranean Sea. The authors introduced the gene into a model bacterium in the laboratory, purified the proteins that were expressed and tested their ability to edit the human genome in a cell line derived from embryonic kidney cells. Demonstrating an editing efficiency of 94%, the authors confirmed the feasibility of moving from identifying genes from marine microbes to examining gene products of interest under laboratory conditions to test their biotechnological applications.

In another case, the team used a deep-learning approach to identify 117 candidate antimicrobial peptides, synthesized 63 of them, and examined their activity against five bacterial strains, including some that can act as human pathogens, such as *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Vibrio vulnificus*. The authors found that one of these peptides, derived from a population in the bacterial family Salinibacteraceae, inhibited the growth of all five microbial strains tested at desirably low peptide concentrations.

Finally, in their collection of genomes, the authors identified more than 1,500 genes similar to the gene encoding the bacterial enzyme *Is*PETase. This enzyme, which was originally identified[7] in the bacterium *Ideonella sakaiensis*, can degrade a widely used form of plastic called polyethylene terephthalate (PET), which is a common source of environmental pollution. The authors carried out biochemical characterizations of enzymes they derived from sequences found in microbial genomes recovered from deep sea hydrothermal vent samples (Fig. 1), in the hope of finding a candidate with high stability in extreme conditions. One of these enzymes demonstrated the ability to degrade 'solvent-cast' PET films with an activity that was around two-fold higher compared with the activity of *Is*PETase.

Given the enormous number of microbial enzymes in marine systems and the variety of current problems that society needs biotechnology solutions for, the three independent lines of exploration Chen *et al.* conducted cannot be considered to be exhaustive. Yet, their interdisciplinary work offers a powerful demonstration of the feasibility of using existing tools to deliver some of the promises of microbiology.

The increasingly large number of genomes reported by contemporary microbiology studies surpassed the glamorous mark of one million earlier this year[8]. But the complexity of the vast majority of naturally occurring microbial ecosystems continues to exceed the sophistication of the computational workflows and sequencing chemistry that scientists rely on to characterize the individual microbial residents on a large scale. Thus, a notable fraction of genomes that are recovered from complex environments suffer from non-negligible shortcomings, including excessive DNA fragmentation issues that result in only partial insights into the genomic make-up of many branches of life. Nevertheless, it is safe to say that the ability to generate microbial genomes using state-of-the-art data and tools has already become commonplace in microbiology. Public repositories will continue to grow and advances in sequencing technologies will continuously improve the genome sequences that are obtained.

However, the excitement regarding the ability to recover genomes directly from all of the planet's ecosystems will inevitably taper off, and many scientists will find themselves wondering, 'What now?' We hope that this discontent will inspire greater interdisciplinary collaborations to achieve what reports of genome collections often bill as a 'future direction' for work — the ability to connect genomic observations, however fragmented, with laboratory experiments to propel advances in biotechnology and biomedicine. At this juncture, the work by Chen and colleagues successfully demonstrates the timeliness, feasibility and potential of taking this next step, and reveals the benefits of pushing the boundaries of microbiology through a fusion of its classical and modern means.

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The authors declare no competing interests.
This article was published online on 4 September 2024.

Astronomy

Swirling star bubbles offer a glimpse of Sun's future

Claudia Paladini

A powerful telescope array has imaged the surface of a star called R Doradus. The observations will help astronomers to understand the fluid dynamics of evolved giant stars — a type of star that the Sun will eventually become. **See p.323**

The outermost layer of the Sun, known as the photosphere, is made of bubbling hot gas. It contains millions of granules, each typically with a diameter of about 1,000 kilometres (ref. 1), which are formed through convection. The Sun is set to morph into an evolved giant star in around five billion years, and when that happens, a theory[2] predicts that only a few convective elements will be left in its photosphere. This theory has support from observations[3] of light at near-infrared wavelengths from other evolved giant stars, but images at submillimetre wavelengths can add even more information — namely, the timescale of convection. On page 323, Vlemmings *et al.*[4] report such observations, and use them to track the