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# The Atacama Desert: Technical Resources and the Growing Importance of Novel Microbial Diversity

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## Abstract

The Atacama Desert of northern Chile is the oldest and most arid non-polar environment on Earth. It is a coastal desert covering approximately 180,000 km<sup>2</sup>, and together with the greater Atacama region it comprises a dramatically wide range of ecological niches. Long known and exploited for its mineral resources, the Atacama Desert harbors a rich microbial diversity that has only recently been discovered; the great majority of it has not yet been recovered in culture or even taxonomically identified. This review traces the progress of microbiology research in the Atacama and dispels the popular view that this region is virtually devoid of life. We examine reasons for such research activity and demonstrate that microbial life is the latest recognized and least explored resource in this inspiring biome.

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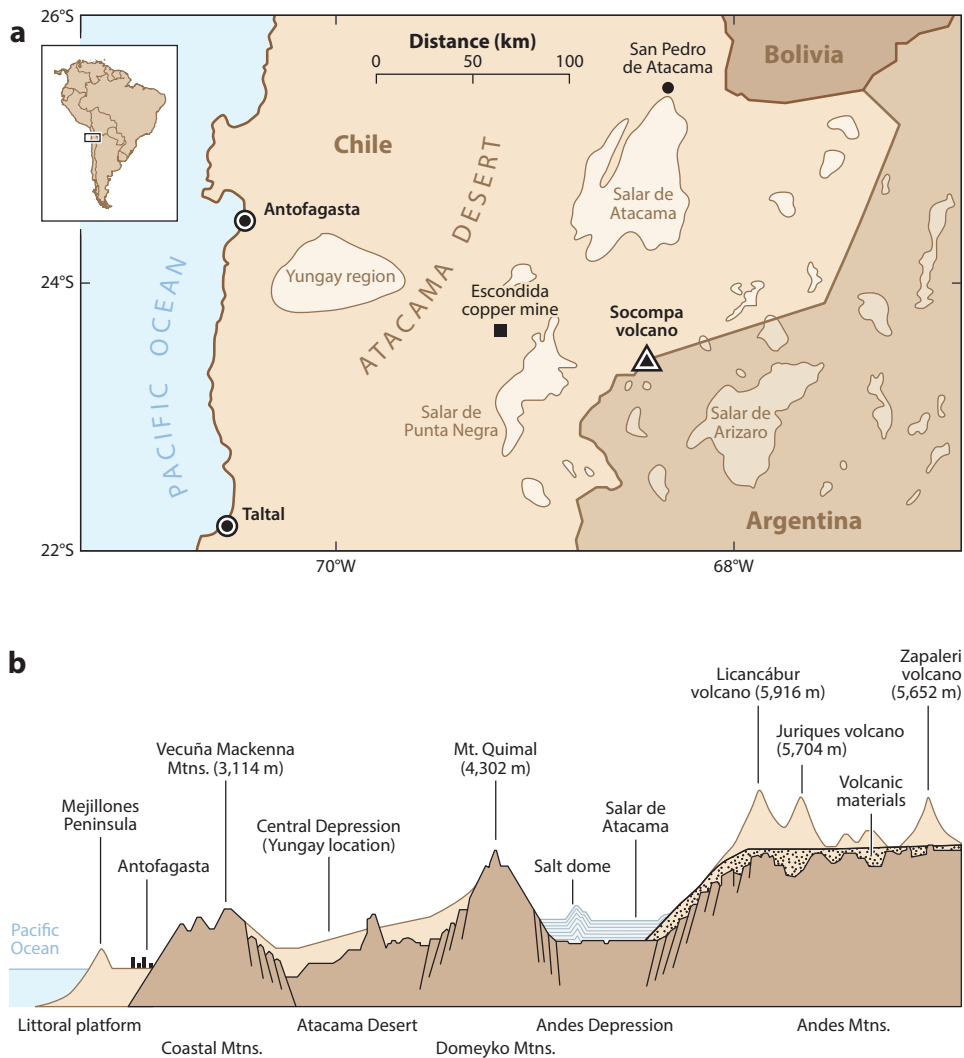
## INTRODUCTION

### Background

The Atacama Desert is located in the Norte Grande natural region of Chile bordering Peru in the north and extending to the Copiapó River in the south. It is considered the oldest and continuously driest nonpolar desert on Earth, being arid since the Jurassic period, 150 million years ago, and evolving to hyperaridity during the Miocene period, 135 million years later (69). This temperate desert extends for 1,000 km, from north to south, approximately between latitudes 19°S and 30°S and from the Coastal Cordillera in the west to the Andean Cordillera in the east. Its elevation ranges between sea level and about 3,500 meters above. Its hyperarid region is in the valley bounded by the coastal mountains and the medial Cordillera de Domeyko (**Figure 1**). The hyperaridity is due to a combination of a subtropical center of high pressure and the cold coastal Humbolt current that creates a constant temperature inversion, offshore winds, and the Andean rain shadow effect that restrict moisture advection from east of the Cordillera (26, 75). Hyperarid conditions exist when the ratio of mean annual rainfall to mean annual evaporation is less than 0.05; when it is less than 0.002, extreme hyperarid conditions exist (73).

Almost without exception, moisture in these arid environments is limited to fog (4) and water adsorbed on soil (17) and other surfaces, including spider webs (5). The organic carbon content of the soil is extremely low, approximately 2–50 µg of carbon in 1 g of soil (59, 126). The geochemistry of the Atacama Desert and adjacent Altiplano environments is diverse and similarly imposes extreme conditions for life. Halite, nitrate, sulfate, and perchlorate salts are prevalent in much of the land, whereas brines may be enriched with lithium, boron, and potassium in salt flats (74). Concentrations of arsenic, of both geochemical and anthropogenic origins, in brines and sediments of the Atacama Desert are among the highest reported worldwide (49).

Apart from the hyperarid and extreme hyperarid environments at the core of the desert *sensu stricto*, the region comprises salt flats; the Altiplano, which, at an elevation greater than 3,500 m, is significantly more humid and supports vegetation that includes *bofedales*, unique peatlands comprising “extremely fragile water features sensitive to climate changes and human disturbances”



**Figure 1**

(a) Map and (b) topographical cross section of the Atacama Desert. The hyperarid core of the desert is located between approximately 22°S and 26°S. Panel a redrawn with permission of the American Society for Microbiology; panel b adapted from Gómez-Silva (59).

(122); geyser fields; high plateaus; cave systems in the coastal mountains; and occasional river and salt flat feeder streams. Human occupation of the Atacama Desert, though sparse, is evidenced by pre-Columbian *pujarías* (fortified communities) and by more recent but abandoned saltpeter-mining settlements.

## Resource Exploitation

The Atacama Desert is resource rich with respect to minerals. The first notable development occurred in the nineteenth century with the mining of the world's largest deposit of sodium

nitrate. Such deposits are unusual and reflect an absence of removal mechanisms owing to the lack of water, and hence microbial denitrification. Introduction of the Haber-Bosch process in 1909 severely curtailed the saltpeter industry. Only one operating works remains, in María Elena, and the once impressive Humberstone-Santa Laura works has been declared a World Heritage Site. The Atacama Desert is the center of copper mining in Chile and also has commercial gold and silver mines. Owing to recent demands for lithium, mining also extends to the salt-rich brines, which are the world's second-largest reserve.

Seawater desalination is required to extract these minerals and consumes high levels of energy. The high irradiance levels in the Atacama Desert make solar energy the ideal solution; thus, a 110-MW concentrated solar power plant using molten salt technology is being developed at María Elena and is expected to begin operations in 2017.

## **Purpose of This Review**

A little over a decade ago the hyperarid core of the Atacama Desert was considered to represent “the dry limit of microbial life” (91). However, subsequent investigations made in the same hyperarid core demonstrated that several kinds of cultivable microorganisms can be recovered from this harsh environment. Thus, the whole of the Atacama region, including its areas of environmental extremes, provides another and perhaps unexpected resource—microbiological diversity.

The microbiology of extreme environments has progressed substantially over the last two decades (72), but as Gould commented, “Bacteria dwell in virtually every spot that can sustain any form of life . . . we have underestimated their global number because we, as members of a kingdom far more restricted in potential habitation, never appreciated the full range of places that might be searched” (63). Whereas attention has long focused on deep-sea, hyperthermal, and permanently cold environments, research on hyperarid deserts is more recent and understanding of their microbiology fragmentary.

The earliest records of bacteria in the Atacama Desert soils came from the Jet Propulsion Laboratory in Pasadena, California, in the 1960s (18). At about the same time, Opfell & Zebal (97) performed important microbiological analyses of salt flats and sand dunes near Antofagasta. However, not until two decades later did a (first slow) flow of publications begin. In this review we trace the growth of microbiological investigations in the world's oldest, driest desert and analyze the drivers of and changing trends in research; we conclude by identifying aspects of desert microbiology that merit greater attention and argue why the Atacama Desert has prime relevance in this context.

## **ATACAMA MICROBIOLOGY**

### **The Catalyst for Microbiology Studies**

A small cluster of studies published in the 1960s was catalyzed by the development of life detection systems in preparation for NASA's (i.e., the US National Aeronautics and Space Administration's) Viking Mission in 1975. The prevailing conditions in the Atacama Desert were thought to “represent in several respects the closest approach to the Martian environment that is available on earth” (97). These early studies are exemplary in their planning and execution and emphasize the importance of intelligent site selection, aseptic sampling, comprehensive site and sample descriptions, isolation procedures, selective media, and—not least—long incubation times needed to isolate particular groups of microorganisms. These all remain essential features of contemporary desert microbiology. However, after six years of data collection by Viking Lander no conclusive signs of

life had been detected; consequently, interest in the microbiology of Mars-like environments on Earth waned. However, one finding from the Viking mission suggested that organic material from a labeled-release experiment was consumed, a result explained in terms of inorganic oxidants in Martian soil and one that reignited interest in the Atacama. Research targeted the extreme hyper-arid core of the desert at the University of Antofagasta/NASA Yungay Station, and because of the extreme dryness, very low organic matter content, and apparent lack of bacteria, it was posited that these soils were beyond the threshold for life. This hypothesis was presented in two papers (83, 91) reporting that extremely low concentrations of cultivable bacteria—but no DNA—had been recovered from soil. A Viking-type labeled-release experiment (91) revealed active decomposition of organic species in the Yungay soils by nonbiological processes, thus confirming the presence of oxidants in Atacama Desert soils.

Atacama Desert microbiology was regenerated by two pioneering Chilean scientists, Victoriano Campos in Valparaíso and Benito Gómez-Silva in Antofagasta, who initiated studies on halotolerant and halophilic bacteria in the Salar de Atacama (106) and microalgae of athallassohaline lakes (60), respectively. These studies provided an early indication of potential biotechnology applications (e.g.,  $\beta$ -carotene from *Dunaliella* species; 2) and of the prevalence of cyanobacteria in Atacama Desert habitats (19, 58). The few additional topics to excite interest during the final years of the twentieth century included limnology–paleohydrology–climate change studies of Altiplano lakes (66, 67, 87); lichen diversity (55); and aspects of the paleopathology (53, 68, 82) of early Atacama human communities.

## The Blossoming of Microbiology Research

The annual output of research publications on Atacama microbiology increased tenfold during the last decade, reflecting the substantial widening of interests in both fundamental and applied topics (Table 1). Major areas were microbial diversity, ecology, biogeochemistry, and the Mars analog projects.

The strong interest in the microbial diversity of the Atacama, especially its hyperarid core (29, 45, 78, 92), is unsurprising given that the descriptive biology of this biome is still sparse. Increased research on two bacterial phyla is noteworthy: *Cyanobacteria*, well-known pioneer organisms still being studied in the context of environmental stress resistance and in capacity as primary colonizers, and *Actinobacteria*. The detection and frequent dominant position of the members of the latter phylum were also mentioned in early publications, but only in the mid-2000s did directed research on actinobacteria begin, first on their numbers, diversity, and distribution in hyperarid and extreme hyperarid soils (94), and subsequently on the capacity of novel isolates to produce new bioactive compounds (12). New areas of eukaryotic microbial diversity were also being explored—notably, the myxomycetes (136) and nonlichenized fungi (28).

Our designation of biogeochemistry encompasses several topics: biomineralization related to carbonates (113) and gypsum evaporites (50), bioleaching, and arsenic mobilization. Similarly, the literature relating to ecology is broad and encompasses relationships of microorganisms to each other and to their biologic and abiotic environments. Opfell & Zebal (97) noted that the factors defining ecological niches and relationships in Atacama soils were largely unknown, and to a large extent functional ecology (the mechanistic understanding of ecological patterns and processes) remained in its infancy. Reports pertaining to ecology are dominated by descriptions of microbial consortia associated with various desert substrata and habitats, but more recently attempts have been made to reveal the underlying determinants of spatial and temporal changes in microbial communities. For example, spatial landscape studies of phototroph patchiness on translucent rocks concluded that patchiness was the result of nonrandom factors, including rock

**Table 1** Topics of Atacama microbiology publications, 1966–2015

Topic	1966–2015	2006–2015
Microbial diversity	115	83
Cyanobacteria	30	28
Actinobacteria	20	20
Microalgae	15	9
Fungi/lichens	14	9
Archaea	12	10
Myxomycetes	6	6
Other	18	1
Molecular biology	43	40
Phylogenetic analysis	21	18
Culture-independent surveys/pyrosequencing	10	7
Whole-genome sequencing	2	2
Other	10	13
Biogeochemistry	39	38
Method developments and applications <sup>a</sup>	25	21
Biomass measurement/viability testing	11	8
Applications of Raman and mass spectroscopy	9	8
Application of molecular chip and array technology	4	4
Robotic mapping	3	3
Endolithic/hypolithic colonization	24	21
Mars-like soils/Mars analogue studies	23	20
Ecology, environment related	19	16
Systematics	19	15
Biotechnology <sup>a</sup>	15	12
Bioleaching	15	13
Bioactive natural products	7	7
Stress tolerance/desiccation response/UV effects	8	6
Climate/climate change	7	5
Hygrosopy/limits of life conditions	6	3
Human paleopathology	6	4

<sup>a</sup>The sums of the subcategories exceed those in this row because the topic is common to individual publications.

size and orientation, water availability, and organism dispersal (132, 133). In a very different Atacama ecosystem, the hypersaline Lake Tebenquiche, groundwater affects salinity and controls the spatial heterogeneity of populations, whereas seasonal changes have little effect (37). In yet another Atacama ecosystem, gypsum evaporite domes, distinct winter and summer microbial communities develop in the submerged part of the dome (107).

An exciting development that opens up functional ecology per se in the Atacama Desert relates to the mineralogical generation of water. Mineral deliquescence had been proposed as a source of water for endolithic communities (33, 135), but definitive evidence for this appeared in a groundbreaking study by Parro et al. (102; see below). Subsequently Davila et al. (34) showed that cyanobacterial photosynthesis can be sustained within halite crystals by deliquescence events, while even halite samples from the Yungay region, the driest part of the desert, contain carbon

from modern atmospheric CO<sub>2</sub> (138), confirming that active microbial life is possible in this extreme environment.

The majority of the publications about endolithic/hypolithic colonization in **Table 1** could be categorized under ecology, but they stand out because of the distinctive geomorphology of the Atacama Desert and the variety of adaptive strategies that have evolved there. The contributions made by microorganisms to geomorphological processes have been relatively neglected (127); consequently, this aspect of Atacama microbiology deserves emphasis. An increasing number of reports are analyses of the endolithic and hypolithic colonization of halite (rock salt), gypsum (calcium sulfate dehydrate), carbonates, quartz, pyroclastic volcanic rock such as ignimbrite, and rock varnish. Hypersaline halite and perchlorate deposits, some of which have remained unaltered for millions of years (e.g., Permian halite), have been found to preserve biomolecules (52, 65). These findings could make saline materials a prime target in the search for evidence of life on Mars.

Atacama Desert microbiology has benefitted from new technologies. These have included methods to estimate soil microbial biomass (e.g., sublimation of adenine; 56), developments in spectroscopy to detect and identify endolithic phototrophs and epilithic lichens (114, 128–131), robotic biosignature mapping (134), and high-throughput molecular detection technologies.

## CHANGING TRENDS—FROM FUNDAMENTAL SCIENCE TO MICROBIAL TECHNOLOGY

### Molecular Biology

The impact of molecular biology has spanned several areas of Atacama microbiology, including biotechnology, community analysis, functional ecology, genomics, and systematics. Taxonomic studies have focused on cyanobacteria—where polyphasic methods have led to the characterization of new, including cryptic, species (88, 89, 100)—and actinobacteria (12). *Actinobacteria* are a dominant taxon in many Atacama Desert habitats, and new species have been reported regularly in recent years based on polyphasic approaches (15, 16, 94, 95, 115–117). Putatively novel species of rare and poorly studied taxa, notably *Actinomadura*, *Blastococcus*, *Geodermatophilus*, *Modestobacter*, *Pseudonocardia*, and *Saccharothrix*, have been detected in extensive 16S rRNA gene–sequencing studies (14). Other notable taxonomic-physiological reports refer to novel psychrotolerant, acidophilic *Acidithiobacillus ferrivorans* (8), and *Pseudomonas arsenicoxydans* sp. nov. (22).

Metagenomic analyses of Atacama microbial communities have been taxon- and habitat-oriented. The former have emphasized cyanobacteria (41, 103), but research has extended to archaea (36, 43, 64) that, in the case of certain high-altitude athalassohaline lakes, may be the dominant prokaryotic population (42) and also to fungi. In pioneering high-altitude studies, Schmidt et al. (118) described very low-diversity fungal communities dominated by basidiomycete yeasts in soils collected between 6,000 m and 7,000 m from the Socompa and Llullaillaco volcanoes.

Habitat-oriented studies have focused on an almost full range of Atacama environments, including bioleaching heaps (39). Profiling using denaturing gradient gel electrophoresis revealed the presence of archaea, cyanobacteria, and heterotrophic bacteria in halite evaporate communities (35), whereas 454 pyrosequencing studies have shown that hyperarid soils from in and around the Yungay region are dominated by actinobacteria (32).

The work comparing high-altitude fumarolic and nonfumarolic communities on Socompa (31) is remarkable both for its cryospheric nature and sample collection. Standard 16S rRNA gene amplifications and phylogenetic analyses showed that nonfumarolic soil communities were

dominated by actinobacteria and fungi, in contrast to fumarolic sites, where photoautotrophic phylotypes, including green algal lineages, were dominant. These latter sites contained increased moisture and nutrient contents compared to the nonfumarolic soils that had the characteristics of the most extreme Atacama Desert soils.

Functional microbial ecology studies of the Atacama Desert have been initiated in the last few years. Aspects of nitrogen cycling at Altiplano and arid desert sites suggest metabolic activity; enrichment culture and culture-independent approaches indicate the genetic potential for this. Dorador and colleagues (40), in exploring nitrification activity in athalassohaline lake habitats, identified ammonia-oxidizing bacteria from 16S rDNA and *amoA* gene sequence analyses. Similar observations were made in soils affected by ephemeral desert bloom events in the southern limit of the desert (98). Nitrogen loss has been investigated via denitrification of nitrogen-limited desert soil (99). Use of functional gene markers for bacterial denitrifier communities (*nirK*, *nirS*) allowed detection of only *nirK*-type denitrifier genotypes, and it was concluded that these genotypes are predominantly dormant and stable over long periods but may become active when conditions become favorable for denitrification. Schmidt's group recently obtained convincing metagenomic evidence for the assimilation of atmospheric gases in high-altitude mineral soils (81). Approximately 98% of the metagenome of the debris field on the volcano Llullaillaco (80) was from actinobacterial lineages; the most abundant genome belonged to the genus *Pseudonocardia*, which includes well-known carboxydobacteria. Analysis of the metabolic pathways encoded by this genome revealed capacities to assimilate CO<sub>2</sub>, trace gases (CO, H<sub>2</sub>), and other C1 compounds, suggesting that the "community structure and various functional genes have undergone strong selection in the nutrient poor desert mineral soils and high-elevation atmospheric conditions" (80). Other targets for functional ecological investigations have included tolerance of high-altitude acidic saline lake systems (48), desiccation (77), and UV (104). The heterotrophic phylotypes common to all hypoliths examined were associated largely with desiccation-tolerant actinobacteria and deinococci. Another innovative application of molecular biology has been used to determine photobiont selectivity in populations of the lichen *Caloplaca* spp. in an isolated, fog-sustained oasis in the Atacama Desert (23).

An astrobiological field laboratory at a mountain apron site was designed to study the geomicrobiology of the Atacama subsurface (102). A range of molecular biology-based instruments, including a life detector chip comprising antibodies to detect prokaryotes and a broad selection of biomarkers, were used to gather a comprehensive data set that in several cases enabled immediate analysis of samples in the field. These data when combined with those from extensive geochemical analyses enabled the definition of a 2-m subsurface microbial ecosystem sustained by mineral deliquescence and fueled by nonphototrophic primary production. This ecosystem comprised abundant hygroscopic salts, including halite and perchlorate, within which deliquescence occurred even at low relative humidity. The resultant thin liquid water films would be sufficient to permit microorganisms to proliferate by using detected organic acids such as acetate and formate as electron donors and sulfate, nitrate, and/or perchlorate as electron acceptors. Thus the critical zone, defined as the "near surface environment in which complex interactions involving rock, soil, water, air, and living organisms regulate the natural habitat and determine the availability of life-sustaining resources" in deserts, may extend deep below the surface rather than "just at, on or in the top few centimeters of rock or soil surfaces," as proposed by Pointing & Belnap (105).

## Biotechnology Developments

The exploration of microbial life in extreme environments and surge of interest in biotechnology occurred more or less simultaneously, and it was "not surprising that extremophiles and



extremotrophs became prime targets in search and discovery programs” (72). Interests in the Atacama Desert have centered mainly on aspects of biohydrometallurgy, bioremediation, and bioactive natural products, although other activities based on harvesting renewable resources of the desert have been explored. Low-cost cultivation of algae has demonstrated the possibilities for producing  $\beta$ -carotene (2) or hydrocarbon-rich biomass (9) and takes advantage of year-round high solar radiation. Attention is turning to enzymes that have commercially attractive properties, such as the capacity to catalyze reactions at low water activities or in the presence of toxic metals. These enzymes and the organisms that produce them might have applications in bioremediation technology (86).

Bioremediation may also be able to utilize the arsenic that is found extensively in parts of the Atacama Desert. Campos and colleagues (20, 47) initiated arsenic mobilization studies, isolating bacteria tolerant of very high concentrations of the especially toxic arsenite [As (III)] species and capable of oxidizing it to arsenate [As (V); (21)]. Subsequently, arsenic-stress-related genes have been mapped that code for oxidation, reduction, and extrusion in bacterial communities isolated from salt deposits, geyser fields, and feeder rivers to the Salar de Atacama (49), and the draft genome sequence of a *Nitricola* strain isolated from the Salar de Ascotán (125) includes arsenic resistance and arsenic metabolism genes. Reverse osmosis and nanofiltration technologies for removing arsenic from drinking water, though effective, are costly, and chemical oxidation of As (III) to As (V) is slow and contaminate the environment. Consequently, efforts to develop cleaner biotreatment options merit consideration.

**Copper bioleaching.** The declining copper content of Chilean ores has heightened interest in bioleaching technologies. An early indication of the impact of bacteria in this context came from a study of supergene enrichment of copper-rich sulfide deposits at several Chilean copper mines (121), a process previously believed to be abiotic. Subsequently a series of papers have described aspects of heap leaching at the Escondida mine. A test heap of marginal copper ore was first built in 2006 has been extended during intervening years to become a commercial bioleaching operation. Quantitative analysis of microbial community dynamics revealed that variables such as pH and the  $\text{Fe}^{3+}:\text{Fe}^{2+}$  ratio were the principal regulating factors (111) and enabled the bioleaching cycle to be defined as a succession of five stages (38). As the height of the heap increased, temperatures up to 50°C were generated and the microbial community changed from mesophilic to one comprising moderate thermophiles and thermotolerant organisms (1); because of the high diversity of the initial populations, reinoculation of the maturing heap was not necessary.

Copper bioleaching technology also is being investigated by the Santiago-based BioSigma group, who argue that continuous inoculation with specifically adapted microorganisms substantially reduces the time for the indigenous ore microbiota to become established and thus increases bioleaching rates. A large-scale airlift bioreactor has been developed for producing either iron- or sulfur-oxidizing bacteria, and inoculations of bioleaching heaps and dumps have been successful (101). Genomic studies of native chemolithotrophic bacteria have provided insight into bacterial adhesion and the identity of a single lipoprotein (licanantase) that enhanced the bioleaching rate of chalcopyrite (51). The genome of *Acidithiobacillus thiooxidans* (124), the first obtained from an industrial bioleaching process, contains strain-specific genes related to heavy metal tolerances and mineral attachment, several of which were located close to genetic mobility elements, suggesting the existence of genomic islands resulting from horizontal gene transfer in bioleaching environments. Analysis of copper homeostasis in a strain of *Acidithiobacillus ferrooxidans* showed that 9% of genes were upregulated by copper (including copper efflux and sulfur metabolism genes), whereas iron transport genes were repressed.

Metabolic models have been constructed for several of the key bioleaching bacteria. These include bioleaching flux analysis of *A. ferrooxidans* (71); ferrous iron oxidation and nitrogen and CO<sub>2</sub> assimilation by *Leptospirillum ferrooxidans* (84); metabolic reconstruction of mixed populations of dominant leaching bacteria in Chilean operations (85); and modeling of the bacterial biomass at the mineral surface (96).

**Bioactive compounds.** Deserts have often been overlooked in the search for bioactive, natural products, and the focus on the Atacama Desert is very recent in this regard. The success of bioprospecting is dependent upon a number of critical elements, particularly chemical, environmental, and taxonomic space from which we have argued that there is a high probability of isolating novel organisms that present novel chemistry from extreme environments (11, 62).

A variety of methods are available for detecting novel natural products, a common approach being bioassay-guided isolation of active compounds followed by structure determination. This strategy led to the discovery of new types of aminobenzoquinones (abenquines) that contain rare combinations of benzoquinones and a range of amino acids (119). These compounds were produced by a streptomycete isolated from soil sampled at the Salar de Tara (4,500 meters above sea level); they present weak antibacterial and antifungal activities but also inhibitory activity against type 4 phosphodiesterase (PDE4b) that might be explored in the context of inflammatory diseases. The group led by Bull and Goodfellow and their scientific partners in Chile is generating extensive information on bioactive metabolites produced by Atacama Desert actinobacteria (12). The first report from this group (90) described a new family of 22-membered macrolactone (atacamycin) antibiotics from a *Streptomyces leeuwenhoekii* strain isolated from lake sediment. Atacamycins A, B, and C exhibited moderate inhibitory activities against type 4 phosphodiesterase (PDE-4b2), and atacamycin A showed moderate antiproliferative activity against adenocarcinoma and breast carcinoma cells. The OSMAC (one strain–many compounds) approach, which seeks to maximize the productivity of a given microorganism through expression of silent or cryptic biosynthetic genes, was successfully applied to a strain of *S. leeuwenhoekii* to isolate three new metabolites (chaxalactins) of the rare class of 22-membered macrolactone polyketides (110) by varying the composition of the fermentation medium. These compounds showed strong activities against gram-positive bacteria. A new lasso peptide (chaxapeptin) is produced by another member of the *S. leeuwenhoekii* 16S rRNA gene clade, strain C58 (46). These rare peptides have a topology that resembles a threaded lasso and exhibit a range of potentially therapeutic characteristics, including antimicrobial activity, receptor antagonism, and enzyme inhibition. Chaxapeptin has inhibitory activity in cell invasion assays with human lung cancer cells.

Coculture screening has been applied successfully using an Atacama Desert actinobacterium. The induction of biosynthetic pathways in *Aspergillus fumigatus* in response to a strain of *Streptomyces bullii* (117) led to the isolation of ergosterol, seven metabolites belonging to the diketopiperazine class of alkaloids, and two metabolites from the rare class of pseurotins (108). None of these compounds were observed in pure independent cultures of the fungus or bacterium.

In contrast to bioassay-guided and chemical profiling approaches, genome mining (“translating secondary metabolite-encoding gene sequence data into purified molecules”; 7) has the potential to eliminate chance from bioprospecting, and now that whole-genome sequencing is fast and inexpensive it seems sure to become the screening method of choice. In this context *S. leeuwenhoekii* DSM 42122<sup>T</sup> (15) has the hallmarks of a key model organism for the study of actinobacterial natural products. Prior to its taxonomic characterization and genome sequencing, an in silico genome-mining strategy was used to discover four new ansamycin-type polyketides produced by this strain. Amino-hydroxybenzoic acid (AHBA) synthetase provides an excellent target in genetic screening for novel compounds including ansamycin antibiotics related to rifamycin. Thus genome mining

was used successfully to target the gene encoding rifamycin-specific AHBA synthase and led to the discovery of chaxamycins (109). Chaxamycin D was active against clinical isolates of methicillin-resistant *Staphylococcus aureus*, whereas chaxamycins A, B, and C had inhibitory activity against the intrinsic ATPase of the human Hsp90 heat shock protein, indicating putative antitumor activities. The draft genome sequence of *S. leeuwenhoekii* DSM 42122<sup>T</sup> (15) revealed strong potential for the synthesis of natural products. Subsequently, next-generation DNA sequencing technologies yielded a greatly refined, nonfragmented genome sequence for this strain (57) that contains 38 gene clusters for specialized metabolites.

Development of genetic tools to manipulate *S. leeuwenhoekii* DSM 42122<sup>T</sup> has continued; thus, the 80.2-kb chaxamycin biosynthetic gene cluster was identified and partially characterized by mutational analysis in the natural producer organism and by heterologous expression in *Streptomyces coelicolor* A3(2) strain M1152. Restoration of chaxamycin production in a nonproducing  $\Delta ccmK$  mutant (*ccmK* encodes AHBA synthase) was achieved by supplementing the growth medium with AHBA, showing that mutasynthesis may be a viable approach for the generation of novel chaxamycin derivatives (24).

**Actinobacterial diversity.** Bioprospecting ambitions to date have centered on a single actinobacterial genus and, moreover, the single clade of *Streptomyces leeuwenhoekii*. The reality of actinobacterial diversity in the Atacama Desert is quite different. A recent study by our group (H. Idris, A.T. Bull, M. Goodfellow, unpublished manuscript) illustrates this dramatically. Environmental DNA recovered from over 23 sites in the Atacama was surveyed for actinobacteria by pyrosequencing and filtering of sequence artifacts; rarefaction analyses indicated good coverage at nearly all sites. The results revealed a remarkable and unexpected taxonomic diversity at order, family, and genus ranks. A total of 391 genera were detected, about 66% of which were unidentified, putatively novel taxa, facts that emphasize the scale of this untapped actinobacterial “dark matter.” It is notable that members of less than 10% of these genera have yet been cultivated. Nevertheless this metagenomics approach opens the way for identity, isolation, and expression of biosynthetic gene clusters in heterologous hosts: “Metagenomics has the potential to provide a complete toolkit for bringing biosynthetic diversity from the environment into drug discovery pipelines” (25). Moreover, the biodiscovery armamentarium can be complemented by in silico data mining programs such as ChEMBL (10) to predict bioactivities and assess in vivo properties. We are left with the exciting conclusion that there appear to be no conceptual barriers to exploiting the richness of the Atacama Desert microbiome for biotechnology discoveries.

## UNIQUENESS OF THE ATACAMA DESERT AND FUTURE PRIORITIES

Other great nonpolar deserts have attracted the interest of microbiologists, but the majority of studies refer to semi- rather than hyperarid deserts, and plant-associated communities are frequently the focus. The uniqueness of the Atacama Desert lies in its amazing diversity of ecological niches, its geology and geochemistry, its elevation and topography, and the intensity of radiation. Meteorological data collected at Yungay Station revealed Atacama Desert aridity to be greater than that of the Gobi, Negev, and Mojave Deserts—as much as 50 times drier than the latter (61). Although the Yungay region of the desert has been considered the paradigm of the driest sites on Earth, a recent survey reported that other locations in this desert are even drier and still yield viable populations of bacteria, most notably actinobacteria (3). Subsurface geochemistry at various locations provides a unique ecological niche where deliquescence can occur even at low relative humidity, while other geochemical features (e.g., arsenic enrichment) select for specialist microbial communities. Finally, the highest levels of UV radiation on Earth’s surface have been

recorded recently at the Paranal Observatory (2,635 meters above sea level) and the Chajnantor Plateau (5,000 meters above sea level) (30). UV radiation in itself is not an extreme stressor for life in the Atacama Desert; rather, its synergy with desiccation is (6, 44). Thus, although extreme desiccation and ambient UV flux may render rock surfaces sterile, millimeter-thick mineral coatings can protect microorganisms (27), a finding consistent with the observed patterns of lithotrophic colonization in the Atacama Desert.

### **Microbial Diversity and the Rare Biosphere**

The Atacama's array of ecological niches recommends it as a major region for microbial diversity initiatives that might address a complete inventory of prokaryotes, for example, and for scrutinizing the everything-is-everywhere concept. Several complementary issues arise here. First, the advantages and disadvantages of open format and closed format molecular detection technologies must be considered before selecting one for diversity surveys (137). Second, high-throughput sequencing technologies have revealed the spectacular biosphere of rare microbial taxa (79), which constitutes <0.1% of any community. Striking examples of such rare actinobacterial biospheres exist in the Atacama Desert and typically show low taxonomic evenness; i.e., high-ranking taxa show much higher abundances than low-ranking taxa (H. Idris, A.T. Bull, M. Goodfellow, unpublished manuscript). The ecological roles of these rare actinobacteria remain to be determined, but as reservoirs of genetic and functional diversity in extreme environments they are likely very important. Third is the failure to cultivate a more diverse group of species, given the diversity identified by metagenomics. While determined efforts are being made to invigorate microbial cultivation methods (e.g., 93, 123) and to accurately quantify low-density populations in desert soils (54), other emerging approaches undoubtedly will contribute to a more complete understanding of the Atacama Desert's microbial dark matter. Single-cell genomics has started to uncover a dramatic range of new candidate prokaryotic phyla that, particularly in the context of desert microbiology, promise to provide further insights into extremophiles and microbes that tolerate extreme conditions (70, 112).

Returning briefly to the microbial ecology of the Atacama, several options warrant consideration. First, reverse ecology employs genomics to study organism-habitat interactions without prior knowledge of the organisms per se. To this end Shapiro et al. (120) advocate sequencing clusters of closely related genomes from the same environmental sample, in the form of either isolates or single-cell genomes, searching for genes of potential ecological relevance, and then forming testable hypotheses of environmental differentiation. Thus some indication of a community's ecological niche can be established and correlations made with biotic and abiotic environmental data. Such an approach must consider the minute scale of microbial habitats and interactions. Second, the well-established technique of DNA stable-isotope probing provides a means of identifying specific functional groups of microorganisms in a habitat without cultivating them. This technique has not been utilized in desert ecology, but its potential was demonstrated by a study to trace autotrophically fixed  $^{13}\text{C}$  into phospholipid fatty acids of fungi and bacteria in Mojave Desert soils (76). Community characteristics in these desert soils have shifted in response to long-term exposure to increased atmospheric  $\text{CO}_2$ , a conclusion that resonates with early studies of climate change in the Atacama Desert over geologic time.

### **EPILOGUE**

In 1994 the University of Antofagasta and NASA established a research station in the Atacama's hyperarid core at Yungay to study the Atacama as a model of the Mars surface. Now abandoned,

this initiative rekindles thoughts of an Atacama Desert network—or even a global network—of observatories loosely modeled on successful ocean observatory projects. Such observatories could provide a basis for desert microbiology to engage more effectively in functional ecology; establish quasi-real-time monitoring, including that of anthropogenic disturbance; develop and evaluate sampling strategies; and prioritize habitat conservation. This would require a substantial financial commitment; thus, an alternative would be to mount field campaigns similar to AtacaMars2009 (102). Collaboration also promotes adherence to the terms of the Convention on Biological Diversity, not the least of which is the 2010 Nagoya Protocol. It is of some concern that a substantial proportion of publications on Atacama Desert microbiology lack a Chilean coauthor or do not indicate that samples were collected with permission.

Nearly 25 years ago in this journal, the *Annual Review of Microbiology*, we first discussed microbial diversity as a resource for innovations in biotechnology (13). We opine that the conclusions reached and recommendations made at that time remain valid, and we trust that the wonders of the Atacama Desert will awe and inspire future generations of microbiologists to study a biome that is teeming with unexplored life.

## DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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## LITERATURE CITED

1. Acosta M, Galleguillos P, Ghorbani Y, Tapia P, Contador Y, et al. 2014. Variation in microbial community from predominantly mesophilic to thermotolerant and moderately thermophilic species in an industrial copper heap bioleaching operation. *Hydrometall.* 150:281–89
2. Araneda P, Jimenez C, Gómez-Silva B. 1992. Microalgae from Northern Chile. III. Growth and beta-carotene content of three isolates of *Dunaliella salina* from the Atacama Desert. *Rev. Biol. Mar. Oceanogr.* 27:157–62
3. Azua-Bustos A, Caro-Lara L, Vicuña R. 2015. Discovery and microbial content of the driest site of the hyperarid Atacama Desert, Chile. *Environ. Microbiol. Rep.* 7:388–94
4. Azua-Bustos A, González-Silva C, Mancilla RA, Salas L, Gómez-Silva B, et al. 2011. Hypolithic cyanobacteria supported mainly by fog in the coastal range of the Atacama Desert. *Microb. Ecol.* 61:568–81
5. Azua-Bustos A, González-Silva C, Salas L, Palma RE, Vicuña R. 2010. A novel subaerial *Dunaliella* species growing on cave spider webs in the Atacama Desert. *Extremophiles* 14:443–52
6. Azua-Bustos A, Zuniga J, Arenas-Fajardo C. 2014. *Gloeocapsopsis* AAB1, an extremely desiccation-tolerant cyanobacterium isolated from the Atacama Desert. *Extremophiles* 18:61–74
7. Bachmann BO, Van Lanen SG, Baltz RH. 2014. Microbial genome mining for accelerated natural products discovery: Is a renaissance in the making? *J. Ind. Microbiol. Biotechnol.* 41:175–84

8. Barahona S, Dorador C, Zhang Z, Aguilar P, Sand W, et al. 2014. Isolation and characterization of a novel *Acidithiobacillus ferrivorans* strain from the Chilean Altiplano: attachment and biofilm formation on pyrite at low temperature. *Res. Microbiol.* 165:782–93
9. Bazaes J, Sepulveda C, Acien FG, Morales F, Gonzales L. 2012. Outdoor pilot-scale production of *Botryococcus braunii* in panel reactors. *J. Appl. Phycol.* 24:1353–60
10. Bento AP, Gaulton A, Hersey A, Bellis LJ, Chambers J, et al. 2014. The ChEMBL bioactivity database: an update. *Nucleic Acids Res.* 42:D1083–90
11. Bull AT. 2004. How to look, where to look. In *Microbial Diversity and Bioprospecting*, ed. AT Bull, pp. 71–79. Washington, DC: ASM
12. Bull AT, Asenjo JA. 2013. Microbiology of hyper-arid environments: recent insights from the Atacama Desert, Chile. *Antonie van Leeuwenhoek* 103:1173–79
13. Bull AT, Goodfellow M, Slater JH. 1992. Biodiversity as a source of innovation in biotechnology. *Annu. Rev. Microbiol.* 6:219–52
14. Busarakam K. 2014. *Novel actinobacterial diversity in arid Atacama Desert soils as a source of new drug leads*. PhD Thesis, Newcastle Univ., UK
15. Busarakam K, Bull AT, Girard G, Labeda DP, van Wezel GP, Goodfellow M. 2014. *Streptomyces leeuwenhoekii* sp. nov., the producer of chaxalactins and chaxamycins, forms a distinct branch in *Streptomyces* gene trees. *Antonie van Leeuwenhoek* 105:849–61
16. Busarakam K, Bull AT, Trujillo ME, Riesco R, Sangal V, et al. 2016. *Modestobacter caceresii* sp. nov., novel actinobacteria with an insight into their adaptive mechanisms for survival in extreme hyper-arid Atacama Desert soils. *Syst. Appl. Microbiol.* 39:243–51. doi: 10.1016/j.syapm.2016.03.007
17. Cáceres L, Gómez-Silva B, Garró XB, Rodríguez V, Monardes V, McKay CP. 2007. Relative humidity patterns and fog water precipitation in the Atacama Desert and biological implications. *J. Geophys. Res.* 112:G054S14
18. Cameron RE, Gensel DR, Blank CB. 1966. Soil studies—desert microflora. XII. Abundance of microflora in soil samples from the Chile Atacama Desert. In *Supporting Research and Advanced Developments, Space Programs Summary* No. 37–38, Vol. IV, pp. 140–147. Pasadena, CA: Jet Propulsion Lab.
19. Campos V. 1997. Microorganismos de ambientes extremos: Salar de Atacama, Chile. In *El Altiplano: Ciencia y Conciencia de los Andes*, ed. C González, pp. 143–47. Santiago: Editor. Artega
20. Campos VL, Escalante G, Yañez J, Zaror CA, Mondaca MA, et al. 2009. Isolation of arsenite-oxidizing bacteria from a natural biofilm associated to volcanic rocks of Atacama Desert, Chile. *J. Basic Microbiol.* 49:S93–97
21. Campos VL, León C, Mondaca MA, Yañez J, Zaror C. 2011. Arsenic mobilization by epilithic bacterial communities associated with volcanic rocks from Camarones River, Atacama Desert, northern Chile. *Arch. Environ. Contamin. Toxicol.* 61:185–92
22. Campos VL, Valenzuela C, Yarla P, Kämpfer P, Vidal R, et al. 2010. *Pseudomonas arsenicoxydans* sp nov., an arsenite-oxidizing strain isolated from the Atacama Desert. *Syst. Appl. Microbiol.* 33:193–97
23. Castillo RG, Beck A. 2012. Photobiont selectivity and specificity in *Caloplaca* species in a fog-induced community in the Atacama Desert, northern Chile. *Fungal Biol.* 116:665–76
24. Castro JF, Razmilic V, Gomez-Escribano JP, Andrews BA, Asenjo JA, et al. 2015. Identification and heterologous expression of the chaxamycin biosynthetic gene cluster from *Streptomyces leeuwenhoekii*. *Appl. Environ. Microbiol.* 81:5820–31
25. Charlop-Powers Z, Milshteyn A, Brady SF. 2014. Metagenomic small molecule discovery methods. *Curr. Opin. Microbiol.* 19:70–75
26. Clarke DA. 2006. Antiquity of aridity in the Chilean Atacama Desert. *Geomorphology* 73:101–14
27. Cockell CS, McKay CP, Warren-Rhodes K, Homeck G. 2008. Ultraviolet radiation-induced limitation to epilithic microbial growth in arid deserts—dosimetric experiments in the hyperarid core of the Atacama Desert. *J. Photochem. Photobiol. B* 90:79–87
28. Conley CA, Ishkhanova G, McKay CP, Cullings K. 2006. A preliminary survey of non-lichenized fungi cultured from the hyperarid Atacama Desert of Chile. *Astrobiology* 6:521–26
29. Connon SA, Lester ED, Shafaat HS, Obenhuber DC, Ponce A. 2007. Bacterial diversity in hyperarid Atacama Desert soils. *J. Geophys. Res.* 112:G04S17

30. Cordero RR, Seckmeyer G, Riechelmann S, Damiai A, Labbe F, Larose D. 2014. The world's highest levels of surface UV. *Photochem. Photobiol. Sci.* 13:70–81
31. Costello EK, Halloy SRP, Reed SC, Sasha C, Sowell O, Schmidt SK. 2009. Fumarole-supported islands of biodiversity within a hyperarid, high-elevation landscape on Socompa Volcano, Puna de Atacama, Andes. *Environ. Microbiol.* 75:735–47
32. Crits-Christoph A, Robinson CK, Barnum T, Fricke WF, Davila AF. 2013. Colonization patterns of soil microbial communities in the Atacama Desert. *Microbiome* 1:28
33. Davila AF, Gómez-Silva B, de los Ríos A, Ascaso C, Olivares H. 2008. Facilitation of endolithic microbial survival in the hyperarid core of the Atacama Desert by mineral deliquescence. *J. Geophys. Res. Biogeosci.* 113:G01028
34. Davila AF, Hawes I, Ascaso C, Wierzycheros J. 2013. Salt deliquescence drives photosynthesis in the hyperarid Atacama Desert. *Environ. Microbiol. Rep.* 5:583–87
35. de los Ríos A, Valea S, Ascaso C, Davila A, Kastovsky J, et al. 2010. Comparative analysis of the microbial communities inhabiting halite evaporites of the Atacama Desert. *Int. Microbiol.* 13:79–89
36. Demergasso CS, Casamayor EO, Chong G, Galleguillos P, Escudero L, Pedrós-Alió C. 2004. Distribution of prokaryotic genetic diversity in athalassohaline lakes of the Atacama Desert, northern Chile. *FEMS Microbiol. Ecol.* 48:57–69
37. Demergasso CS, Escudero L, Casamayor EO, Chong G, Balagué V, Pedrós-Alió C. 2008. Novelty and spatio-temporal heterogeneity in the bacterial diversity of hypersaline Lake Tebenquiche (Salar de Atacama). *Extremophiles* 12:491–504
38. Demergasso CS, Galleguillos F, Soto P, Serón M, Iturriaga V. 2010. Microbial succession during a heap bioleaching cycle of low grade copper sulfides: Does this knowledge mean a real input for industrial process design and control? *Hydrometall.* 104:382–90
39. Demergasso CS, Galleguillos PA, Escudero LVG, Victot J, Zapeda A, et al. 2005. Molecular characterization of microbial populations in a low-grade copper ore bioleaching test heap. *Hydrometallurgy* 80:241–53
40. Dorador C, Busekow A, Vila I, Imhoff JF, Witzel KP. 2008. Molecular analysis of enrichment cultures of ammonia oxidizers from the Salar de Huasco, a high altitude saline wetland in northern Chile. *Extremophiles* 12:405–14
41. Dorador C, Vila I, Imhoff JF, Witzel KP. 2008. Cyanobacterial diversity in Salar de Huasco, a high altitude saline wetland in northern Chile: an example of geographical dispersion? *FEMS Microbiol. Ecol.* 64:419–32
42. Dorador C, Vila I, Remonsellez F, Imhoff JF, Witzel KP. 2010. Unique clusters of archaea in Salar de Huasco, an athalassohaline evaporitic basin of the Chilean Altiplano. *FEMS Microbiol. Ecol.* 73:291–302
43. Dorador C, Vila I, Witzel K-P, Imhoff JF. 2013. Bacterial and archaeal diversity in high altitude wetlands of the Chilean Altiplano. *Fund. Appl. Limnol.* 182:135–59
44. Dose K, Bieger-Dose A, Ernst B, Feister V, Gómez-Silva B, et al. 2001. Survival of microorganisms under the extreme conditions of the Atacama Desert. *Orig. Life Evol. Biosph.* 31:287–303
45. Drees KP, Neilson JW, Betancourt JI, Quade J, Henderson DA, et al. 2006. Bacterial community structure in the hyperarid core of the Atacama Desert, Chile. *Appl. Environ. Microbiol.* 72:7902–8
46. Elsayed S, Trusch F, Deng H, Raab A, Prokes I, et al. 2015. Chaxapeptin, a lasso peptide from the extremotolerant *Streptomyces leeuwenhoekii* strain C58 from the hyper-arid Atacama Desert. *J. Org. Chem.* 80:10252–60
47. Escalante G, Campos VL, Valenzuela C, Yañez J, Zaror C, Mondaca MA. 2009. Arsenic resistant bacteria isolated from arsenic contaminated river in the Atacama Desert (Chile). *Bull. Environ. Contam. Toxicol.* 83:657–61
48. Escudero LV, Bijman J, Chong G, Pueyo JJ, Demergasso CS. 2013. Geochemistry and microbiology in an acidic, high altitude (4,000 m) salt flat, high Andes, northern Chile. In *Integration of Scientific and Industrial Knowledge on Biobiohydrometallurgy*, Vol. 825, ed. N Guiliani, C Demergasso, R Quatrini, F Remonsellez, C Davis-Belmar, et al. pp. 28–32. Zurich: Trans. Tech. Publ.

49. Escudero LV, Casamayor EO, Chong G. 2013. Distribution of microbial arsenic reduction, oxidation and extrusion genes along a wide range of environmental arsenic concentrations. *PLOS ONE* 8:e78890
50. Farias ME, Contreras M, Rasuk MC, Kurth D, Flores MR, et al. 2014. Characterization of bacterial diversity associated with microbial mats gypsum evaporites and carbonate microbialites in thalassic wetlands: Tebenquiche and La Brava, Salar de Atacama, Chile. *Extremophiles* 18:311–29
51. Fazzini RAB, Levican G, Parada P. 2011. *Acidithiobacillus thiooxidans* secretome containing a newly described lipoprotein Licanantase enhances chalcopyrite bioleaching rate. *Appl. Microbiol. Biotechnol.* 89:771–80
52. Fernandez-Remolar DC, Chong-Diaz G, Ruiz-Bermejo M, Harir M, Schmitt-Kopplin P, et al. 2013. Molecular preservation in halite- and perchlorate-rich hypersaline subsurface deposits in the Salar Grande basin (Atacama Desert, Chile): implications for the search for molecular biomarkers on Mars. *J. Geophys. Res. Biogeosci.* 118:922–39
53. Ferreira LF, Britto MA, Fernandes CO, Reinhard K, Araújo A. 2000. Paleoparasitology of Chagas disease revealed by infected tissues from Chilean mummies. *Acta Trop.* 75:79–84
54. Fletcher LE, Conley, CA, Valdivia-Silva JE, et al. 2011. Determination of low bacterial concentrations in hyperarid Atacama soils: comparison of biochemical and microscopy methods with real-time quantitative PCR. *Can. J. Microbiol.* 57:953–63
55. Follmann G. 1995. On the impoverishment of the lichen flora and the retrogression of the lichen vegetation in coastal central and northern Chile during the last decades. *Cryptogam Bot.* 5:224–31
56. Glavin DP, Cleaves HJ, Schubert M, Aubrey A, Bada JL. 2004. New method for estimating bacterial cell abundances in natural samples by use of sublimation. *Appl. Environ. Microbiol.* 70:5923–28
57. Gomez-Escribano JP, Castro JF, Razmilic V, Chandra B, Andrews B, et al. 2015. The *Streptomyces leeuwenhoekii* genome: de novo sequencing and assembly in single contigs of the chromosome, circular plasmid pSLE1 and linear plasmid pSLE2. *BMC Genomics* 16:485
58. Gómez-Silva B. 1994. Adaptación cromática complementaria en dos cianobacterias del género *Nostoc*, nativas del norte de Chile. *Anal. Microbiol.* 2:22–24
59. Gómez-Silva B. 2010. On the limits imposed to life by the hyperarid Atacama Desert in Northern Chile. In *Astrobiology: Emergence, Search and Detection of Life*, ed. VA Basiuk, pp. 199–213. Los Angeles: Am. Sci. Publ.
60. Gómez-Silva B, Olivares J, Rodríguez L. 1990. Microalgae from northern Chile. I. La Rinconada, a hypersaline aquatic habitat in the Atacama Desert. *Estud. Oceanol.* 9:73–76
61. Gómez-Silva B, Rainey FA, Warren-Rhodes KA. 2008. Atacama Desert soil microbiology. In *Microbiology of Extreme Soils*, ed. P Dion, CS Nutiya, pp. 117–32. Berlin: Springer-Verlag
62. Goodfellow M. 2013. Actinobacterial diversity as a source of new drugs. *Microbiologist* 14:8–12
63. Gould SJ. 1996. Planet of the bacteria. *Wash. Post Horiz.* 119:344
64. Gramain A, Chong-Diaz G, Guillermo D, Demergasso C, Lowenstein TK, McGenity TJ. 2011. Archaeal diversity along a subterranean salt core from the Salar Grande (Chile). *Environ. Microbiol.* 13:2105–21
65. Griffith JD, Wilcox S, Powers DW, Nelson R, Baxter BK. 2008. Discovery of abundant cellulose microfibrils encased in 250 Ma Permian halite: a macromolecular target in the search for life on other planets. *Astrobiology* 8:215–28
66. Grosjean M. 1994. Paleohydrology of the Laguna Lejia (north Chilean altiplano) and climatic implications for late-glacial times. *Palaeogeogr. Palaeoclimatol. Palaeoecol.* 109:89–100
67. Grosjean M, van Leeuwen JFN, van der Knaap WO, Geyh MA, Ammann B. 2001. A 22,000 <sup>14</sup>C year BP sediment and pollen record of climate change from Laguna Miscanti (23°S), northern Chile. *Glob. Planet. Change* 28:35–51
68. Guhl F, Jaramillo C, Yockteng R, Vallejo, GA, Cárdenas-Arroyo F. 1997. *Trypanosoma cruzi* DNA in human mummies. *Lancet* 349:1370
69. Hartley AJ, Chong G, Houston J, Mather A. 2005. 150 million years of climatic stability: evidence from the Atacama Desert, Northern Chile. *J. Geol. Soc.* 162:421–24
70. Hedlund BP, Dodsworth JA, Murugapiran SK, Rinke C, Woyke T. 2014. Impact of single-cell genomics and metagenomics on the emerging view of extremophile “microbial dark matter.” *Extremophiles* 18:865–75

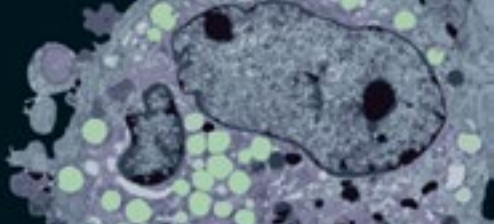


71. Hold C, Andrews BA, Asenjo JA. 2009. A stoichiometric model of *Acidithiobacillus ferrooxidans* ATTC 23270 for metabolic flux analysis. *Biotechnol. Bioeng.* 102:1448–59
72. Horikoshi K, Bull AT. 2011. Prologue: Definition, categories, distribution, origin, evolution and pioneering studies, and emerging fields of extremophiles. In *Extremophiles Handbook*, Vol. 1, ed. K Horikoshi, G Antranikian, AT Bull, F Robb, K Stetter, pp. 3–15. Tokyo: Springer Verlag
73. Houston J. 2006. Evaporation in the Atacama Desert: an empirical study of spatio-temporal variations and their causes. *J. Hydrol.* 330:402–12
74. Houston J, Butcher A, Ehren P. 2011. The evaluation of brine prospects and the requirements for modifications to filing standards. *Econ. Geol.* 106:1225–39
75. Houston J, Hartley J. 2003. The central Andean west-slope rainshadow and its potential contribution to the origin of hyper-aridity in the Atacama Desert. *Int. J. Clim.* 23:1453–64
76. Jin VL, Evans RD. 2010. Microbial <sup>13</sup>C utilization patterns via stable isotope probing of phospholipid biomarkers in Mojave Desert soils exposed to ambient and elevated atmospheric CO<sub>2</sub>. *Glob. Change Biol.* 16:2334–44
77. Lacap DC, Warren-Rhodes KA, McKay CP, Pointing SB. 2011. Cyanobacteria and chloroflexi-dominated hypolithic colonization of quartz at the hyper-arid core of the Atacama Desert, Chile. *Extremophiles* 15:31–38
78. Lester ED, Satomi M, Ponce A. 2007. Microflora of extreme arid Atacama Desert soils. *Soil Biol. Biochem.* 39:704–8
79. Lynch MDJ, Neufeld JD. 2015. Ecology and exploration of the rare biosphere. *Nat. Rev. Microbiol.* 13:217–29
80. Lynch RC, Darcy JL, Kane NC, Nemergut DR, Schmidt SK. 2014. Metagenomic evidence for metabolism of trace atmospheric gases by high-elevation desert *Actinobacteria*. *Front. Microbiol.* 5:698
81. Lynch RC, King AJ, Fariás ME, Sowell P, Vitry C, Schmidt SK. 2012. The potential for microbial life in the highest-elevation (>6000 m.a.s.l.) mineral soils of the Atacama region. *J. Geophys. Res. Biogeosci.* 117:G02028
82. Marsteller SJ, Torres-Rouff C, Knudson K. 2011. Pre-Columbian Andean sickness ideology and the social experience of leishmaniasis: a contextualized analysis of bioarchaeological and paleopathological data from San Pedro de Atacama, Chile. *Int. J. Paleopathol.* 1:24–34
83. McKay CP, Friedmann EI, Gómez-Silva B, Cáceres-Villanueva L, Anderson DT, Landheim R. 2003. Temperature and moisture conditions for life in the extreme arid region of the Atacama Desert: four years of observations including the El Niño of 1997–1998. *Astrobiology* 3:393–403
84. Merino MP, Andrews BA, Asenjo JA. 2010. Stoichiometric model and metabolic flux analysis for *Leptospirillum ferrooxidans*. *Biotechnol. Bioeng.* 107:696–706
85. Merino MP, Andrews BA, Asenjo JA. 2015. Stoichiometric model and flux balance analysis for a mixed culture of *Leptospirillum ferriphilum* and *Ferroplasma acidiphilum*. *Biotechnol. Prog.* 31:307–15
86. Moreno ML, Piubeli F, Bonfa MRL, Garcia MT, Durrant LR, Mellado E. 2012. Analysis and characterization of cultivable extremophilic hydrolytic bacterial community in heavy-metal-contaminated soils from the Atacama Desert and their biotechnological potentials. *J. Appl. Microbiol.* 113:550–59
87. Mühlhauser HA, Hrepic N, Mladinic P, Montecino V, Cabrera S. 1995. Water quality and limnological features of a high altitude Andean lake, Chungará, in northern Chile. *Rev. Chil. Hist. Nat.* 68:341–49
88. Mühlsteinová R, Johansen JR, Pietrasiak N, Martin MP. 2014. Polyphasic characterization of *Kastovskya adunca* gen. nov. et comb. nov. (Cyanobacteria: Oscillatoriales), from desert soils of the Atacama Desert, Chile. *Phytotaxa* 163:216–28
89. Mühlsteinová R, Johansen JR, Pietrasiak N, Martin MP. 2014. Polyphasic characterization of *Trichocoleus desertorum* sp. nov. (Pseudanabaenales, Cyanobacteria) from desert soils and phylogenetic placement of the genus *Trichocoleus*. *Phytotaxa* 163:241–61
90. Nachtigall J, Kulik A, Helaly S, Bull AT, Goodfellow M, Asenjo JA, et al. 2011. Atacamycins A–C, 22-membered antitumor macrolactones produced by *Streptomyces* sp. C38. *J. Antibiot.* 64:775–80
91. Navarro-González R, Rainey FA, Molina P, Bagaley DR, Hollen B, et al. 2003. Mars-like soils in the Atacama Desert, Chile, and the dry limit to microbial life. *Science* 302:16089–94

92. Neilson JW, Quade J, Ortiz M, Nelson WM, Legatzki A, et al. 2012. Life at the hyperarid margin: novel bacterial diversity in arid soils of the Atacama Desert, Chile. *Extremophiles* 16:553–66
93. Nichols D, Cahoon N, Trakhtenberg EM, Pham L, Mehta A, et al. 2011. Use of Ichip for high-throughput in situ cultivation of “uncultivable” microbial species. *Appl. Environ. Microbiol.* 76:2445–50
94. Okoro CK, Brown R, Jones AL, Andrews BA, Asenjo JA, et al. 2009. Diversity of culturable actinomycetes in hyper-arid soils of the Atacama Desert, Chile. *Antonie van Leeuwenhoek* 95:121–33
95. Okoro CK, Bull AT, Mutreja A, Rong X, Huang Y, Goodfellow M. 2010. *Lechevalieria atacamensis* sp. nov., *Lechevalieria deserti* sp. nov and *Lechevalieria roselyniae* sp. nov., isolated from hyperarid soils. *Int. J. Syst. Evol. Microbiol.* 60:296–300
96. Olivera-Nappa A, Picioareanu P, Asenjo JA. 2010. Non-homogeneous biofilm modeling applied to bioleaching processes. *Biotechnol. Bioeng.* 106:660–76
97. Opfell JB, Zebal GP. 1967. Ecological patterns of micro-organisms in desert soils. *Life Sci. Space Res.* 5:187–203
98. Orlando J, Alfaro M, Bravo L, Guevera R, Carú M. 2010. Bacterial diversity and occurrence of ammonia-oxidizing bacteria in the Atacama Desert soil during a “desert bloom” event. *Soil Biol. Biochem.* 42:1183–88
99. Orlando J, Carú M, Pommerenke B, Braker G. 2012. Diversity and activity of denitrifiers of Chilean arid soil ecosystems. *Front. Microbiol.* 3:101
100. Osorio-Santos K, Pietrasiak N, Bohunicka M, Misco LH, Kováčik L, et al. 2014. Seven new species of *Oculatella* (Pseudanabaenales, Cyanobacteria): taxonomically recognizing cryptic diversification. *Eur. J. Phycol.* 49:450–70
101. Parada P, Morales P, Collao R, Bobadilla R, Badilla R. 2013. Biomass production and inoculation of industrial bioleaching processes. *Integration of Scientific and Industrial Knowledge on Biohydrometallurgy*, Vol. 825, ed. N Guiliani, C Demergasso, R Quatrini, F Remonsellez, C Davis-Belmar, et al. pp. 296–300. Zurich: Trans. Tech. Publ.
102. Parro V, de Diego-Castilla G, Moreno-Paz M, Blanco Y, Cruz-Gille P, et al. 2011. A microbial oasis in the hypersaline Atacama subsurface discovered by a life detector chip: implications for the search for life on Mars. *Astrobiology* 11:969–96
103. Patzelt DJ, Hodac L, Friedl T, Pietrasiak N, Johansen JR. 2014. Biodiversity of soil cyanobacteria in the hyper-arid Atacama Desert, Chile. *J. Phycol.* 50:698–710
104. Paulino-Lima IG, Azua-Bustos A, Vicuna R, González-Silva C, Salas L, et al. 2013. Isolation of UVC-tolerant bacteria from the hyperarid Atacama Desert, Chile. *Microb. Ecol.* 65:325–35
105. Pointing SB, Belnap J. 2012. Microbial colonization and controls in dryland systems. *Nat. Rev. Microbiol.* 10:551–62
106. Prado B, Delmoral A, Quesada E, Rios R, Montechiva-Sanchez M, Campos V. 1991. Numerical taxonomy of moderately halophilic gram-negative rods isolated from the Salar-de-Atacama, Chile. *Syst. Appl. Microbiol.* 14:275–81
107. Rasuk MC, Kurth D, Flores MR, Contreras M, Novoa F, et al. 2014. Microbial characterization of microbial ecosystems associated to evaporites domes of gypsum in Salar de Llamara in Atacama Desert. *Microb. Ecol.* 68:483–94
108. Rateb ME, Hallyburton I, Houssen WE, Bull AT, Goodfellow M, et al. 2013. Induction of diverse secondary metabolites in *Aspergillus fumigatus* by microbial co-culture. *RSC Adv.* 3:14444–50
109. Rateb ME, Houssen WE, Arnold M, Abdelrahman MH, Deng H, et al. 2011. Chaxamycins A–D, bioactive ansamycins from a hyper-arid desert *Streptomyces* sp. *J. Nat. Prod.* 74:1491–99
110. Rateb ME, Houssen WE, Harrison WTA, Deng H, Okoro CK, et al. 2011. Diverse metabolic profiles of a *Streptomyces* strain isolated from a hyper-arid environment. *J. Nat. Prod.* 74:1965–71
111. Remonsellez F, Galleguillos F, Moreno-Paz M, Parra V, Acosta M, Demergasso C. 2009. Dynamic of active microorganisms inhabiting a bioleaching industrial heap of low-grade copper sulfide ore monitored by real-time PCR and oligonucleotide prokaryotic acidophile microarray. *Microb. Biotechnol.* 2:613–24
112. Rinke C, Schwientek P, Sczyrba A, Ivanova NN, Anderson IJ, et al. 2013. Insights into the phylogeny and coding potential of microbial dark matter. *Nature* 499:431–37
113. Rivadeneyra MA, Delgado G, Soriano Raamos-Cormenzana A, Delgado R. 1999. Biomineralization of carbonates by *Marinococcus albus* and *Marinococcus halophilus* isolated from the Salar de Atacama (Chile). *Curr. Microbiol.* 39:53–7

114. Roldan M, Ascaso C, Wierzchos J. 2014. Fluorescent fingerprints of endolithic phototrophic cyanobacteria living within halite rocks in the Atacama Desert. *Appl. Environ. Microbiol.* 80:2998–3006
115. Santhanam R, Okoro CK, Rong X, Huang Y, Bull AT. 2012. *Streptomyces atacamensis* sp. nov., isolated from an extreme hyper-arid soil of the Atacama Desert, Chile. *Int. J. Syst. Evol. Microbiol.* 62:2680–84
116. Santhanam R, Okoro CK, Rong X, Huang Y, Bull AT, Goodfellow M. 2012. *Streptomyces deserti* sp. nov., isolated from hyper-arid Atacama Desert soil. *Antonie van Leeuwenboek* 101:575–81
117. Santhanam R, Rong X, Huang Y, Andrews BA, Asenjo JA, Goodfellow M. 2012. *Streptomyces bullii* sp. nov., isolated from a hyper-arid Atacama Desert soil. *Antonie van Leeuwenboek* 103:367–73
118. Schmidt SK, Naff CS, Lynch RC. 2012. Fungal communities at the edge: ecological lessons from high alpine fungi. *Fungal Ecol.* 5:443–52
119. Schulz D, Beese P, Ohlendorf B, Erhard A, Zinecker J, et al. 2011. Abenquines A–D: aminoquinone derivatives produced by *Streptomyces* sp. strain DB634. *J. Antibiot.* 64:763–68
120. Shapiro B, Polz J, Martin F. 2014. Ordering microbial diversity into ecologically and genetically cohesive units. *Trends Microbiol.* 22:235–47
121. Sillitoe RH, Folk RL, Saric N. 1996. Bacteria as mediators of copper sulfide enrichment during weathering. *Science* 272:1153–55
122. Squeo F, Warner BR, Aravena D, Espinoza D. 2006. Bofedales: high altitude peatlands of the central Andes. *Rev. Chil. Hist. Nat.* 79:245–55
123. Thaker MN, Waglechner N, Wright GD. 2014. Antibiotic resistance-mediated isolation of scaffold-specific natural products. *Nat. Protoc.* 9:1469–76
124. Travisany D, Cortéz MP, Latorre M, Genova AD, Budinich M, et al. 2014. A new genome of *Acidithiobacillus thiooxidans* provides insights into adaptation to a bioleaching environment. *Res. Microbiol.* 165:743–52
125. Valdes N, Rivera-Aray J, Bijman B, Escudero L, Demergasso C, et al. 2014. Draft genome sequence of *Nitrimicola* sp. strain A-D6, an arsenic-resistant gammaproteobacterium isolated from a salt flat. *Genome Announc.* 2:6
126. Valdivia-Silva JE, Navarro-González R, Fletcher L, Perez-Montaña S, Condori-Apaza R, McKay CP. 2012. Soil carbon distribution and site characteristics in hyper-arid soils of the Atacama Desert: a site with Mars-like soils. *Adv. Space Res.* 50:108–22
127. Viles HA. 2012. Microbial geomorphology: a neglected link between life and landscape. *Geomorphology* 157–158:6–16
128. Villar JSE, Edwards HGM, Seaward MRD. 2005. Raman spectroscopy of hot desert, high altitude epilithic lichens. *Analyst* 130:730–37
129. Vitek P, Camara-Gallego B, Edwards HGM, Jehlicka J, Ascaso C, Wierzchos J. 2013. Phototrophic community in gypsum crust from the Atacama Desert studied by Raman spectroscopy and microscopic imaging. *Geomicrobiol. J.* 30:399–410
130. Vitek P, Edwards HGM, Jehlicka J, Ascaso C, de los Rios A, et al. 2010. Microbial colonization of halite from the hyper-arid Atacama Desert studied by Raman spectroscopy. *Phil. Trans. R. Soc. A* 368:3205–21
131. Vitek P, Jehlicka J, Edwards HGM, Hutchinson I, Ascaso C, Wierzchos J. 2012. The miniaturized Raman system and detection of traces of life in halite from the Atacama Desert: some considerations for the search for life signatures on Mars. *Astrobiology* 12:1095–99
132. Warren-Rhodes KA, Dungan JL, Piatek J, Stubbs K, Gómez-Silva B, et al. 2007. Ecology and spatial pattern of cyanobacterial community island patches in the Atacama Desert, Chile. *J. Geophys. Res. Biogeosci.* 112:G04S15
133. Warren-Rhodes KA, Rhodes KL, Pointing SB, Ewing SA, Lacap DC, et al. 2006. Hypolithic cyanobacteria, dry limit of photosynthesis, and microbial ecology in the hyperarid Atacama Desert. *Microb. Ecol.* 52:389–98
134. Warren-Rhodes K, Weinstein S, Dohm J, Piatek J, Minkley E, et al. 2007. Searching for microbial life remotely: satellite-to-rover habitat mapping in the Atacama Desert, Chile. *J. Res. Geophys. Res. Biogeosci.* 112:G04S05
135. Wierzchos J, Ascaso C, McKay CP. 2006. Endolithic cyanobacteria in halite rocks from the hyperarid core of the Atacama Desert. *Astrobiology* 6:415–22

136. Wrigley de Basanta D, Lado C, Estrada-Torres A, Stephenson SL. 2009. Description and life cycle of a new *Didymium* (Myxomycetes) from arid areas of Argentina and Chile. *Mycologia* 101:707–16
137. Zhou J, He Z, Yang Y, Deng Y, Triage SF, Alvarez-Cohen L. 2015. High-throughput metagenomic technologies for complex microbial community analysis: open and closed formats. *mBio* 6(1):e02288-14
138. Ziolkowski LA, Wierzchos J, Davila AF, Slater GF. 2013. Radiocarbon evidence for active endolithic microbial communities in the hyperarid core of the Atacama Desert. *Astrobiology* 13:607–16



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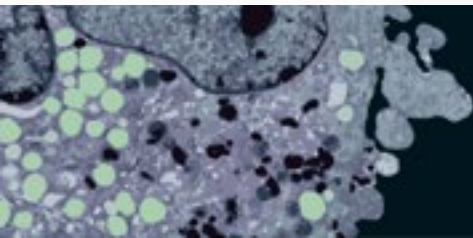
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