cell junctions. Each ameloblast develops an asymmetric structure called the Tomes' process. Like the ends of a picket fence, the Tomes' processes protrude without contacting each other. The spaces between them become filled with an amelogenin-rich matrix, a hydrated protein gel without apparent structure. In this matrix, oriented ribbon-like crystallites of enamel mineral assemble and elongate from the dentin-enamel junction to the outer enamel surface. The ribbons thicken and aggregate to form enamel rods, while the amelogenin matrix is degraded and removed. The spaces between the Tomes' processes are thus the closed compartments required in matrix-mediated mineralization. However, it has never been clear how the gel-like matrix provided by the amelogenin might nucleate and direct the oriented crystal growth. This is the aspect addressed by Du *et al.* (*3*).

Amelogenin molecules are mostly hydrophobic but contain a short carboxyl-terminal sequence of hydrophilic amino acids. In the extracellular space (the space surrounding the Tomes' processes) they assemble into nanospheres, each of which contains tens of molecules. Du *et al*. demonstrate (*3*) that in each molecule, the hydrophilic sequence resides on the surface. They also show that during nanosphere assembly, each nanosphere develops an asymmetric charge distribution. The nanospheres further assemble into ordered linear arrays, giving a defined, direction-dependent structure to the gel-like matrix.

The hypothesized colinear arrangement of the hydrophilic sequences of the nanospheres (*3*) could template crystal nucleation and growth in the enamel. This is conceptually similar to the binding of matrix proteins in the gaps between collagen fibrils to nucleate and orient the dentin mineral. The dentin and enamel mineralization systems—mechanistically very different but operating at the same time across the dentin-enamel boundary (see the figure, right panel)—show how the supramolecular organization and properties of the extracellular matrix regulate the nature and organization of the mineral phases.

The study by Du *et al*. further shows that the nanosphere self-assembly process can take place in vitro, without requiring ameloblasts. In vivo, two processes may play a role. First, the Tomes' processes may help to orient and elongate the enamel crystallite aggregates by controlling the orientation of the nanosphere chains. Second, the mineralized dentin, which protrudes into the amelogenin matrix at the dentin-enamel boundary, may orient the first nanospheres.

Others have shown that minerals can develop within protein and synthetic polypeptide gels (*8*, *9*), but a scaffold was necessary to provide long-range order. In contrast, Du *et al*. (*3*) show that the self-assembly of the amelogenin nanospheres, and their further assembly into nanosphere arrays, forms its own scaffold that can direct the alignment of the mineral crystallites. The in vitro self-assembly system of Du *et al.* will be a useful guide to the development of biomimetic structures.

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10. I thank T. G. H. Diekwisch for supplying the electron micrograph shown in the left panel of the figure.

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OCEAN SCIENCE

Lost City Life

Antje Boetius

One of the first underwater scenes in James Cameron's spectacular new IMAX adventure *Aliens of the Deep* stars a truly alien panorama. It is a stunning view of the giant white carbonate chimneys of a submarine hydrothermal vent field called Lost City, which looms like a conglomeration of colossal beehives from outer space. The discovery of the Lost City hydrothermal field in December 2000 was a real fluke (*1*). A team of scientists working with Deborah Kelley came across this new ecosystem during an off-axis camera survey near the Mid-Atlantic Ridge at 30°N. As Kelley *et al.* (*2*) report on page 1428 of this issue, they returned in 2003 for a detailed study of Lost City and discovered a remarkable array of micro- and macro-organisms that reside in this hydrothermal ecosystem, which is fueled by abiotic methane and hydrogen. Their results provide fascinating insights into the nature of life at Lost City. Although Lost City represents a unique vent system, the underlying processes responsible for its formation and geochemical setting are likely to drive many other vent ecosystems. This has important implications for biogeochemical cycles, for ocean exploration, and for understanding microbial habitats on Earth and beyond.

The Lost City vent field is characterized by carbonate towers up to 60 m in height. It is located on 1.5-million-year-old rock that is 15 km away from the spreading center. This implies that hydrothermal venting must be more widespread than previously assumed. In the case of Lost City, venting is the consequence of serpentinization reactions between seawater and fresh peridotite, which lead to formation of heat, hydrogen, and methane (*3*, *4*). Typical for exothermic subsurface reactions with iron-bearing olivine, the hydrothermal fluids of Lost City are characterized by temperatures of 40° to 90°C, high pH (9 to 11), a low concentration of magnesium, and elevated concentrations of hydrogen and methane (*1*). Früh-Green *et al*. (*5*) found that this type of hydrothermal venting may have been present for more than 30,000 years at the Lost City field. This lifetime exceeds that of most of the known black smoker–type hydrothermal vents by at least two orders of magnitude. Considering Lost City's longevity and the active proliferation of methane and hydrogen, it seems odd that not much life was observed at this type of vent system, except for some cryptic microbial mats hidden inside the carbonate towers (*1*, *7*).

Kelley and her collaborators went back to Lost City in 2003 for a month-long field expedition (*2*). With the research vessel Atlantis, the submersible Alvin, and the Autonomous Benthic Explorer (ABE) at their disposal, they were able to conduct detailed mapping of the vent field. This multidisciplinary research adventure is beautifully illustrated at www.lostcity.washington.edu. A principal goal of the expedition was to discern how vent fluids, mineral precipitation, and microbial metabolisms interact to produce this extraordinary hydrothermal ecosystem and its underlying flow of energy and carbon.

The vent fluids of the Lost City system are very different from those of black smokers, white smokers, and other Mid-Atlantic Ridge systems fueled by serpentinization reactions. Seawater-basalt reactions driving volcanically hosted vents produce substantial amounts of CO_2, sulfide in the millimolar range, and low pH (3 to 5), as well as extremely high temperatures (200° to 400°C). In contrast, the Lost City vents lack CO_2 but provide high fluxes of hydrogen and methane at warm temperatures and high pH (see the figure, A). The fluids of other very iron- and magnesium-rich (ultra-

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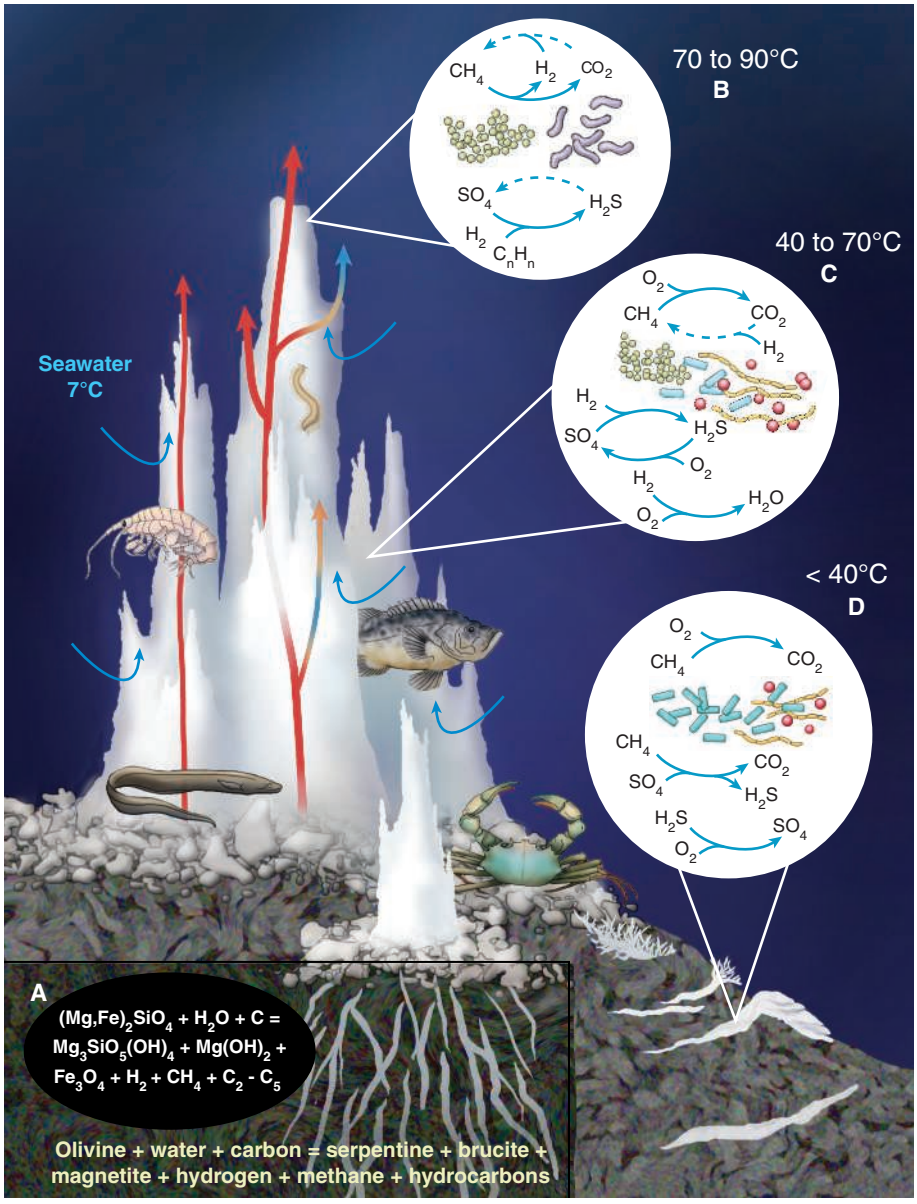

A beehive of activity. Microbial niches in serpentinization-influenced environments at the Lost City hydrothermal field. (**A**) Exothermic serpentinization reactions within the subsurface produce fluids of high pH enriched in methane and hydrogen, as well as some hydrocarbons. (**B**) Environments within the warm interior of carbonate chimneys in contact with end-member hydrothermal fluids host biofilms of *Methanosarcina*-like archaea (green circles). These organisms may play a dominant role in methane production and methane oxidation within the diverse environments present in the chimneys. Bacterial communities within these biotopes are related to the Firmicutes (purple rodlike cells). These organisms may be important for sulfate reduction at high temperature and high pH. (**C**) Moderate-temperature (40° to 70°C) endolithic environments with areas of sustained mixing of hydrothermal fluids and seawater support a diverse microbial community containing *Methanosarcina*-like archaea, ANME-1 (a methane-oxidizing phylotype; blue rectangular cells), and bacteria that include ε- and γ-proteobacteria (yellow filaments and red circles). The oxidation and reduction of sulfur compounds, the consumption and production of methane, and the oxidation of hydrogen most likely dictate the biogeochemistry of these environments. (**D**) In cooler environments (<40°C) associated with carbonate-filled fractures in serpentinized basement rocks, ANME-1 is the predominant archaeal phylotype. The bacterial populations contain aerobic methanotrophs and sulfur-oxidizing phylotypes.

mafic) vent systems at the Mid-Atlantic Ridge, such as at Logatchev and Rainbow, also show substantial methane and hydrogen anomalies but are distinguished by their much higher temperatures, low sulfide flux, and acidic pH (*6*). This difference between Lost City and other vent sites explains the lack of chemoautotrophic symbiotic organisms in Lost City fauna. Most of the reduced energy at the Lost City field is provided by hydrogen. Today, no animals are known to harbor hydrogen oxidizers as symbionts. Kelley *et al*. (*2*) found a high diversity of small invertebrates associated with the active carbonate structures, with a relatively high endemicity of nearly 60%. These invertebrates—snails, bivalves, polychaetes, amphipods, and ostracods—most likely derive some fraction of their energy requirement and carbon source by grazing on vent-associated carbonates and microbial biofilms (*1*).

The carbonate vents hold the key for understanding what is new about the metabolism, diversity, and distribution of microbial life at Lost City. An astonishingly high cell biomass is found inside the cavities and channel systems of the actively venting chimneys. The first analysis of such fluid-filled carbonate channels revealed the presence of archaeal biofilms (*7*). With their systematic study of diverse carbonate samples, Kelley *et al*. (*2*) now show that an almost pure culture of a new type of archaea develops in a specific setting within the chimneys characterized by direct contact with the hot end-member fluids (see the figure, B). The dominant archaea are phylogenetically related to the methanogenic archaea of the order Methanosarcinales. Interestingly, their closest relatives belong to ANME-3, a group of uncultivated anaerobic methanotrophs from cold-seep environments (*8*, *9*). However, lipid biomarker analyses of the Lost City archaeal biofilms show an isotopic enrichment in ^{13}C relative to source methane, indicative of a dominance of methanogenic growth. But the cooler parts of the vented carbonates appear to represent a crossroads between methanogenic and methanotrophic microniches (see the figure, C). This is indicated by the presence of both Methanosarcinales and ANME-1, as well as of functional genes indicative of anaerobic oxidation of methane (*10*, *11*). The anaerobic oxidation of methane is assumed to function as a reversal of methanogenesis. However, no microorganism capable of switching between the two types of metabolism has yet been identified. Perhaps such an organism lives in Lost City. Indeed, physiological experiments with the new group of archaea dominating the Lost City vents may shed light on this question. Within carbonates hosted by basement rocks at ambient temperature (see the figure, D), gene and biomarker lipid analyses point to the coexistence of ANME-1 and sulfate-reducing bacteria, as in other methanotrophic ANME-1/carbonate habitats (*12*). Hence, abiotic and microbial methane production based on serpentinization reactions may be globally very high, but this methane appears to be directly con-

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sumed within neighboring microniches.

Ultramafic rocks favoring serpentinization reactions may have been some of the oldest habitats for microbial life on Earth. With their detailed study of the Lost City vent field, Kelley *et al*. present the first systematic portrayal of this type of subsurface ecosystem, which may still be widespread today. As proposed for early life on Earth and for potential life in outer space, this is an ecosystem in which abiotic methane and hydrogen production is exploited for anaerobic microbial methane and CO_2 fixation as the primary processes for generating biomass. Intriguingly, the resulting biomass of the modern day analog at Lost City has an average isotopic carbon signature that we would not interpret as a signature of life, because it is not different from abiotic carbon sources. Hence, the submarine Lost City hydrothermal field discovered by Kelley and her team is one of the most interesting natural laboratories available to geologists, chemists and biologists, for studying the biogeochemical signatures of ecosystems driven by abiotic methane and hydrogen.

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HIV/AIDS

HIV: Experiencing the Pressures of Modern Life

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No doubt many readers are familiar with the dilemmas posed by multiple competing pressures: each demanding attention that must be allotted from a finite store; each with a more or less strict deadline that must be met; and each extracting some cost to our resources, in terms of both the effort involved in achieving success and the pain derived from failing a given task. For all of us who need to deal with these dynamic and constantly varying pressures, we can now spare a thought for the human immunodeficiency virus (HIV) as it attempts to deal with what is becoming increasingly apparent as a complex and formidably variable immune environment provided by the human host. New findings presented on page 1434 of this issue by Gonzalez and colleagues (*1*) add to our appreciation of host genetic diversity, along with a grudging respect for HIV and its ability to successfully negotiate the challenges it faces on many fronts. This study also provides evidence that the boundary between immunology and virology, in which interactions between host and pathogen are explored at a population and even global level, is a fertile research area.

Many of the barrier and immune surveillance systems that humans use against invading pathogens can be overcome by successful viruses such as HIV, using reasonably stereotypic responses. Indeed, the ability of a virus to establish pandemic levels of infection presupposes that it arrives at its human host with an array of tools designed to foil the immune response. A recent case study is provided by a family of host cytidine deaminases (termed APOBEC proteins) that are capable of introducing lethal editing errors in HIV DNA transcripts (*2*, *3*). This antiviral mechanism, despite its biological elegance, is readily countered by the presence of an accessory HIV protein (Vif) that binds to APOBEC proteins and targets the resulting complex for proteasomal degradation and destruction. Through strategies that are similarly uniform, in which the virus often harnesses itself to indispensable host cellular functions, HIV is able to access the very core of the human immune machinery and establish infection.

There is another layer of complexity, however, to the host response to HIV-1 infection. Highly polymorphic genetic systems of the host can determine an immunological "landscape" that is highly individual-specific, thereby creating challenges that HIV-1 must negotiate in each and every new host (see the figure). In their new work, Gonzalez *et al*. show that chemokine receptor 5 (CCR5), a HIV coreceptor, and its ligand partners (including CCL3L1) form a genetic barrier to HIV infection in certain individuals. The authors demonstrate that the copy number of a segmental duplication encompassing the gene encoding CCL3L1 varies markedly between individuals and between different populations. Those with a high *CCL3L1* gene copy number are more resistant to HIV infection than those with a low copy number, presumably because there is more ligand to compete with HIV during binding to CCR5. In addition, those individuals with a low *CCL3L1* gene copy number combined with a disease-accelerating CCR5 genotype are even more susceptible to HIV infection.

The complexity of the CCR5-CCL3L1 genetic system can be attributed to genetic traits that are both qualitative (dictated by variant alleles that influence protein expression and function) and quantitative (dictated by the number of *CCL3L1* gene copies inherited). CCR5 and CCL3L1 (as well as other CCR5 ligands) thus create a variable barrier to HIV binding to its coreceptor, ultimately modulating disease susceptibility and clinical endpoints such as pretreatment viral load and rate of $CD4^+$ T cell decline. The phenotypic effects of genetic variation within this system suggest that the CCR5 receptor-ligand network serves an important role in HIV pathogenesis that cannot readily be subserved by alternative chemokine receptors (that is, redundancy in this system is low). Accordingly, adaptive responses by HIV-1 such as alternative tropisms (the use of other coreceptors) appear unable to reproduce the disease-accelerating effects of permissive CCR5 variants and low *CCL3L1* gene copy number.

A similar conceptual framework may be applied to the dynamic interaction between HIV-1 and polymorphic host human leukocyte antigen (HLA) molecules (see the figure). Here, the extreme genetic diversity of the HLA system and the importance of these cell surface molecules to the generation of antiviral cytotoxic T lymphocyte (CTL) responses provide a powerful individual-specific host environment for HIV infection. This has been highlighted recently in studies by Goulder and colleagues (*4*, *5*). These investigators demonstrated the importance of the HLA-B gene locus and its numerous allelic variants in shaping the HIV-specific immune response. They also have elegantly mapped the dynamic interplay between host HLA-restricted selection pressure and adaptive HIV escape mutations that subvert this immune recognition system by altering viral epitopes (see the figure). Again, this polymorphic genetic system provides a highly variable barrier to HIV replication

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