In This Issue

Methane-rich groundwater contributes to emissions from Arctic lakes

Arctic lakes emit methane into the atmosphere that mainly originates from the action of microbes in the water column and sediments. Previous studies have documented methane emission rates from Arctic lakes, but few have examined whether methane transported to the lake by seasonally thawed groundwater influences the overall lake methane budget. To address this question, Adina Paytan et al. (pp. 3636–3640) tracked methane concentrations in Toolik Lake, Alaska, concurrently with naturally occurring radon and radium levels as tracers for groundwater. The authors' measurements reveal that methane-rich water flows

At Lake Toolik, Alaska, exogenous methane in groundwater affects the overall lake methane budget.

from the seasonally thawed, active melt layer into Toolik Lake, constituting a potentially important and currently unrecognized conduit for methane transport and emissions from Arctic lakes. Furthermore, the authors suggest that future warming in the Arctic might expand the active layer and increase groundwater discharge, which would in turn increase methane fluxes to lakes, and from the lakes into the atmosphere. The findings highlight the need for additional studies to identify and quantify the processes that control methane transport out of the active layer, particularly in the context of greenhouse gas-driven climate warming, according to the authors. — T.J.

Genetic ancestry of 17th-century slaves

Despite extensive historical knowledge about the African slave trade, including trends in the volume and demographics of the roughly 12 million people shipped from West and West Central

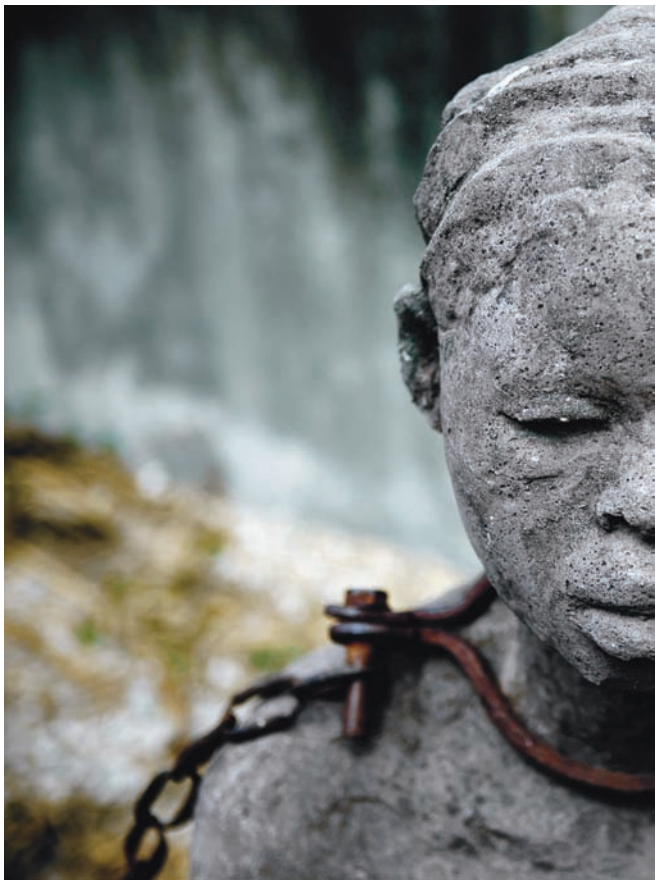


Image courtesy of Eric Lafforgue (photographer).

Detail of slavery memorial in Stone Town, Zanzibar.

Africa to the New World between 1500 and 1850, details about the slaves' ethnic and geographic origins remain elusive. Hannes Schroeder et al. (pp. 3669–3673) performed a genome-wide analysis on DNA extracted from the tooth roots of three enslaved Africans buried in the Zoutsteeg area of Philipsburg on the Caribbean island of Saint Martin during the 17th century. Previous reports suggest that the "Zoutsteeg Three," including one adult female and two adult males, were likely born in Africa as opposed to the New World. But the authors further investigated the Africans' genetic origins, enriching the poorly preserved DNA using a technique known as whole-genome capture. The authors compared the genomes with a reference panel of genotype data from 11 West African populations, tracing the three Africans to Bantu-speaking groups from northern Cameroon and non-Bantu speakers living in present-day Nigeria and Ghana. According to the authors, the findings demonstrate that genomic data can be used to trace the genetic ancestry of long-dead and poorly preserved individuals. — A.G.

Prophylactic vaccine candidate against *Staphylococcus aureus*

Developing an efficacious prophylactic vaccine against *Staphylococcus aureus*, a human pathogen with emerging drug-resistant strains, has proved challenging, partly because of the lack of evidence of natural immunity against the pathogen, which produces

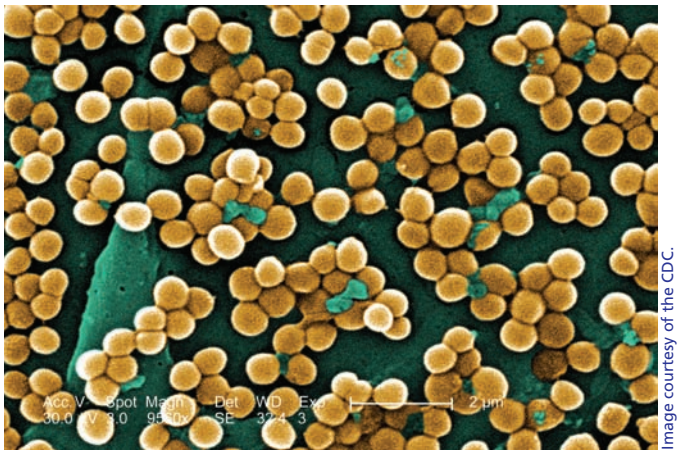


Image courtesy of the CDC.

SEM of clumps of methicillin-resistant *Staphylococcus aureus*.

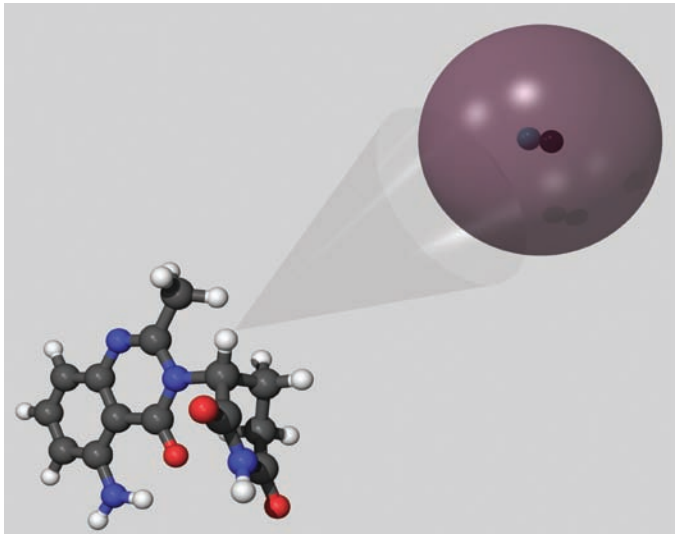
several immune evasion factors. Fabio Bagnoli et al. (pp. 3680–3685) developed a vaccine candidate based on five *S. aureus* antigens—FhuD2, Csa1A, Hla, EsxA, and EsxB—implicated in pathogenesis. Formulated with alum adjuvant, the combination vaccine, named 4C-Staph, reduced bacterial load to a greater extent than did single antigens in immunized mice challenged with clinical strains of *S. aureus*. Further, 4C-Staph conferred greater protection against genetically distinct pathogen strains in mouse models of pathogen-induced peritonitis and pneumonia, compared with a single antigen previously tested in trials. Serum from rabbits immunized with 4C-Staph reduced bacterial load and improved survival when administered to mice challenged with *S. aureus*, indicating a role for protective antibodies in passive immunization with the vaccine. Coupling the vaccine with an immune-activating molecule that targets the Toll-like receptor 7 boosted the vaccine's efficacy, enhancing protective antibody levels, triggering a characteristic helper T-cell response, and improving survival in mice exposed to lethal doses of *S. aureus*. According to the authors, effective adjuvants and cell-mediated immunity may be crucial to the success of prophylactic *S. aureus* vaccines. — P.N.

Potential drug target for schizophrenia

Patients with schizophrenia suffer from cognitive deficits that are largely resistant to current therapeutic strategies. Previous studies have suggested that a brain chemical called dopamine likely plays a role in some disabling aspects of the disease. Using a schizophrenia mouse model that displays learning, memory, and motivational deficits, Sabine Krabbe et al. (pp. E1498–E1506) found that these symptoms could arise from abnormalities in dopamine-releasing neurons in a brain region called the ventral tegmental area (VTA). The authors genetically engineered mice to express a greater-than-normal number of dopamine D2 neuronal receptors (D2Rs) in a brain region called the striatum, which sends signals to the VTA. Compared with normal mice, genetically engineered mice showed reduced activity of dopamine-releasing VTA neurons. Neuronal firing patterns in a brain region called the substantia nigra, which receives input from the striatum, were unaffected by the excess of D2Rs in genetically engineered mice, suggesting that not all dopamine pathways are similarly affected in schizophrenia. Moreover, dopamine-releasing VTA neurons in genetically engineered mice showed abnormalities in NMDA receptors, providing a possible explanation for the altered activity of these neurons. According to the authors, selective pharmacological manipulation of NMDA receptor activity in the VTA might provide a potential treatment target for schizophrenia. — J.W.

Improving drug safety and efficacy

Many drugs currently in use are chiral compounds, which exist in two nonsuperimposable mirror-image forms called enantiomers. Drugs consisting of a single enantiomer have improved therapeutic properties compared with racemates, which are mixtures of left- and right-handed enantiomers. However, many chiral drugs are sold as racemates because of the difficulty of developing chirally pure drug molecules and assessing the properties of individual enantiomers. Vincent Jacques et al. (pp. E1471–E1479) report the stabilization and testing of individual enantiomers by replacing a key hydrogen atom with deuterium, a stable isotope of hydrogen. The authors synthesized a deuterium-containing version of CC-122—a chiral compound currently in clinical trials for blood cancers—and separately tested the two deuterium-stabilized enantiomers. One of the enantiomers was 20 times more potent than the other at inhibiting the production of the tumor-promoting protein tumor necrosis factor alpha in human blood cells. In a mouse model of blood cancer, the more potent CC-122 enantiomer significantly inhibited tumor growth, compared with the less potent CC-122 enantiomer, suggesting that the efficacy of the compound is almost due to a single enantiomer. According to the authors, using hydrogen–deuterium substitution to stabilize and differentiate enantiomers could pave the way for the development of safe and effective therapeutics. — J.W.



Rendering of a deuterium atom and the (*S*)-enantiomer of a racemic thalidomide analog currently in clinical trials.