

CLIMATE SCIENCE

How Low Can We Go?

Though it is well established that greenhouse gas emissions are causing the world to warm, policy-makers would benefit from further specific information in order to produce legislation that balances the environmental and economic effects of a given emissions reduction strategy. Washington *et al.* use a global coupled climate model to evaluate the consequences of a low-emission scenario developed by the United States Climate Change Science Program (CCSP), and thereby illustrate how aggressive mitigation can limit the rise of the global average tropospheric temperature to 1°C above current value by the year 2100. This temperature target is used because it is thought to represent the maximum at which the consequences of climate warming will remain manageable, before becoming dangerous. The authors also discuss ancillary climate consequences of this mitigation route, in an attempt to provide information relevant for the assessment of a wide range of policy options. — HJS

Geophys. Res. Lett. **36**, L08703 (2009).

HUMAN GENETICS

Expedited Pharmacogenomics

Drug-induced liver injury is one of the most common reasons that approved drugs are recalled from the market and that clinical trials of experimental drugs are terminated early. Susceptibility to liver damage and other adverse drug reactions are in part genetically determined, and a major goal of pharmacogenomics research is to find genetic markers that can be used to identify at-risk individuals in advance of drug treatment. The search for such biomarkers in human populations has proven to be labor-intensive, but a new study suggests that the hunt can be streamlined by using data derived from genetically diverse mouse populations to guide the human studies.

Harrill *et al.* studied 36 inbred strains of mice given large doses of acetaminophen and found that there were large strain-dependent variations in drug-induced liver injury, as assessed by histology and by elevated serum levels of the liver enzyme alanine aminotransferase (ALT). Candidate genes likely to be responsible for the inter-strain differences were identified by whole-genome association analysis, and the human versions of these genes were then sequenced in two small groups of humans. Sequence variants in several of these candidate genes—which, interestingly, encode proteins related to immune function rather than to xenobiotic metabolism—were indeed found to corre-

late with the presence of acetaminophen-induced elevation of serum ALT levels in the humans. — PAK

Genome Res. **19**, 10.1101/gr.090241.108 (2009).

CELL BIOLOGY

Warming Up to Its Host

The fungal pathogen *Candida albicans* responds to increases in temperature by initiating a transition from growing as a single-celled yeast to a multicellular filamentous form, the latter associated with greater virulence. Shapiro *et al.* report that inhibition of heat shock protein 90 (Hsp90) was necessary to promote filamentous growth in response to environmental conditions and was sufficient to promote filamentous growth in cells that would normally grow as the budding yeast form. Filament formation in cells with reduced expression of Hsp90 was more sensitive to increased temperature, and lower doses of a pharmacological inhibitor were required to promote filamentous growth at 37°C than at 30°C. Cells with mutations in the Ras1-PKA pathway [from the GTPase Ras1 to the cAMP-dependent protein kinase A (PKA)] failed to respond to inhibition of Hsp90. Genetic experiments also supported a role of Hsp90 in restraining filamentous differentiation by repressing signaling through the Ras1-PKA pathway, and in a mouse model, genetic depletion of Hsp90 completely cleared the kidney of *C. albicans*. — LBR

Curr. Biol. **19**, 621 (2009).

MICROBIOLOGY

Aeolian Microbes

In their day, Darwin and Pasteur both commented on microbe-bearing dust plumes from Africa. Climate change is exacerbating this phenomenon, and Hervàs *et al.* have investigated the potential for oligotrophic alpine lakes as sentinels for long-distance bacterial dispersal. Using 16S rRNA sequences, they compared the bacterial genera found in Mauritanian soil samples with those in dust plume



samples deposited in the Spanish Pyrenees and also examined the growth of the microbes in alpine lake water. Although the findings revealed the immigration capacity of certain taxa, many of the bacteria that survive passage to the Pyrenees are not spore-forming species. Some of the African soil samples contain organisms that do not survive air transport,

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such as the cosmopolitan *Duganella zoogloeooides*, and pathogens, such as *Sphingomonas*, that have been implicated in coral disease in the Caribbean. — CA

Environ. Microbiol. **11**, 10.1111/j.1462-2920.2009.01926.x (2009).

CHEMISTRY

A Simple Twist

The topologically fascinating Möbius strip exhibits a single face and a single edge; it has no distinguishable back or front. At the molecular scale, Möbius strips intrigue chemists for the additional reason that they change the rules of aromaticity. Ring structures such as benzene and naphthalene have particular electronic stability on account of the atoms along the periphery sharing a certain number of pi-bonded electrons—specifically, even non-multiples of 4. If a twist is introduced into the ring framework, p orbitals overlap in an orientation opposite to that in a flat ring, and aromatic stabilization occurs instead when the pi

electrons sum to multiples of 4. A few molecules exhibiting such Möbius aromaticity have been prepared, but the routes were complex. Tokuji *et al.* found

that simple treatment of a hexaphyrin precursor with acetic acid yields an aromatic Möbius compound directly. The twist, confirmed crystallographically, ensues from the introduction of an oxygen atom that links a pendant perfluorophenyl group to the pyrrole backbone. — JSY

J. Am. Chem. Soc. **131**, 10.1021/ja902836x (2009).

GEOCHEMISTRY

Nanoparticle Coastlines

Mineral nanoparticles are naturally abundant in a wide range of environments, from the oceans to the atmosphere. Despite observations that particle size influences the reactivity of a mineral surface in a number of geochemical reactions, it is still largely unknown why nanoparticles behave differently than larger particles with the same composition. Spagnoli *et al.* show that in aqueous solutions, the size and shape of mineral particles influence the structure of the first few layers of water on their surfaces—an important determinant of reactivity. Using molecular dynamics simulations of the common iron-oxide mineral hematite, they found that water order

and layering around the particle decreased for hematite particles of decreasing size. The residence time of water molecules near the surface was shorter for smaller, less-crystalline nanoparticles than for larger nanoparticles or a bulk hematite surface. Particles with facets or low curvature, however, tended to preferentially stabilize the water network and in some cases caused faceting within the water layer itself. The dynamic nature of the water solvation shell surrounding environmental nanoparticles probably influences the energetics of crystal growth and may help explain why some surface processes—including heterogenous catalysis, bacterial metal respiration, and ion adsorption—show trends that vary with particle size. — NW

Geochim. Cosmochim. Acta **73**, 10.1016/j.gca.2009.04.005 (2009).

HUMAN GENETICS

From AA to ZZ

Not only who we are, but also what diseases we suffer from is probably written somewhere in our DNA. Some genetic diseases

are associated with the aggregation of misfolded mutant proteins that are toxic to cells.

Quality-control mechanisms ensure that incorrectly folded proteins are usually degraded. For example, secretory proteins are folded in the

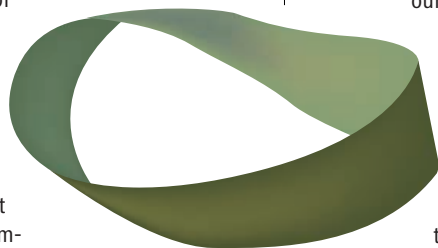
endoplasmic reticulum (ER), and

defective proteins are sorted and targeted for degradation, which is mediated in part by the enzyme ER mannosidase I (ERManI). A mutated version of the gene encoding alpha-1 antitrypsin (AAT) is associated with the accumulation of the misfolded Z variant of AAT in the ER and is a risk factor for the development of end-stage liver disease. However, the age of onset of this disease is variable, and other factors may be involved.

Pan *et al.* have discovered that a single-nucleotide polymorphism (A instead of G) in the 3' untranslated region of the ERManI gene is associated with earlier onset. Individuals carrying two A alleles experience reduced synthesis of ERManI under stress, rendering them more vulnerable to deleterious effects if they should also be homozygous for the Z-variant anti-trypsin. These data provide a molecular mechanism for how a genetic locus can modify the severity of a protein-folding disease by moderating a quality-control checkpoint protein. — HP*

Hepatology **49**, 10.1002/hep.22974 (2009).

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