EDITORS' CHOICE

edited by Stella Hurtley

GEOPHYSICS

Mixed Up

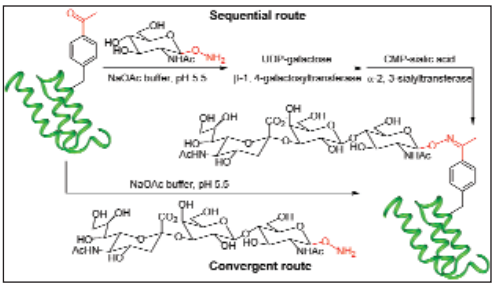
Diapycnal mixing in the ocean —mixing between two adjacent water masses of different densities across the surface that separates them— occurs at scales too small to be resolved in numerical models of ocean circulation. Improvement of these models depends in part on better parameterization of this type of mixing, which mixes both heat and salt, the two major determinants of seawater density. This is because slight differences in mixing coefficients for heat and salt can have important consequences for the thermohaline circulation. It is usually assumed that the eddy diffusivities of heat and salt are equal, but some work suggests that those two quantities diffuse at different rates in stratified turbulence such as that generated by breaking internal waves, a process which is thought to cause most of the mixing in the ocean interior. Hebert and Ruddick measured in the laboratory the vertical fluxes and diffusivities of two tracers with different molecular diffusivities for a wide range of breaking internal wave activity. They found that there is likely to be differential mixing in the ocean interior due to breaking internal waves because the ratio of the diffusivities of salt and heat is slightly less than unity. A more precise estimate of this ratio, and its impact on ocean circulation models, will require more work both in the laboratory and at sea. — HJS

Geophys. Res. Lett. **30**, 1042, 10.1029/2002GL016250 (2003).

BIOCHEMISTRY

Making Proteins Sweeter

Many natural proteins are glycosylated, that is, they possess covalently bound sugar groups that can modify their stability, activity, and interactions with other biomolecules. The sugar groups can be highly variable even for the same protein, making it difficult to study their effects. To generate and study glycoprotein mimics, chemists have used the amino acid cysteine, which can be easily and selectively coupled to sugar groups. However, this method can become problematic if more than one cysteine is present in the target protein.



Scheme for producing glycoprotein mimics

Two papers now show how the selective glycosylation of proteins can be facilitated through the use of an unnatural amino acid. Using a recently reported method for directly synthesizing unnatural amino acids in living cells, Wang *et al.* incorporated an amino acid containing a keto group (which is not present in natural amino acids) into proteins. Liu *et al.* then coupled sugar groups to the keto group in these proteins. The method yields homogeneous glycoprotein mimics with well-defined sugar groups and should be applicable to most proteins that can be expressed in *Escherichia coli*. — JFU

Proc. Natl. Acad. Sci. U.S.A. **100**, 56 (2003); *J. Am. Chem. Soc.* **125**, 1702 (2003).

BIOMEDICINE

Blocking MS

In multiple sclerosis (MS), lymphocytes and monocytes gain access to the central nervous system by breaking through the blood-brain barrier at sites of inflammation. The transendothelial migration and activation of these immune cells depends on the cell surface integrin $\alpha_4\beta_1$/VLA-4. Administration of antibodies against α_4 integrins suppresses disease progression in a mouse model of MS. Miller *et al.* have extended this promising finding by treating patients suffering from relapsing MS with a humanized monoclonal antibody against α_4 integrins, called natalizumab. In a small, placebo-controlled study, patients treated with this integrin antagonist for 6 months showed a 90% reduction in brain lesion formation and progression.

In an independent study, Cannella *et al.* tested a synthetic small-molecule antagonist of $\alpha_4\beta_1$/VLA-4 called TBC 3486 in the mouse model of MS. Mice given this compound before disease onset showed delayed and reduced demyelination and production of proinflammatory cytokines. Even when treatment was terminated, disease severity was reduced for several weeks.

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Polyura jalysus **(Charaxinae) (top) occurs in rainforest gaps, whereas** ***Mycalesis kina*** **(Satyrinae) (right) prefers the shade.**

ECOLOGY/EVOLUTION

Diversity Under Logging

The role that natural disturbances—especially treefalls—play in maintaining biodiversity has produced a large ecological literature in recent decades. At the other extreme, the role of clear-felling of tropical forest in reducing or extinguishing this diversity has also become depressingly familiar. The fate of many tropical forests, however, may lie between these extremes, because the forest is selectively logged for the timber of relatively few species and so the consequences for biodiversity are less well understood.

Hamer *et al.* studied the response of butterflies to selective logging in Borneo by comparing butterfly species assemblages in intact forest and forest that had been logged a decade earlier. Overall butterfly diversity in the two habitats was similar, but the composition of the assemblages differed. Selective logging resulted in a structurally less heterogeneous habitat with fewer open gaps and less dense shade than intact forest. Shade-preferring species with narrow geographic distributions were adversely affected in logged forest, as were widely distributed species that preferred open gaps. Thus, careful management of selective logging to maintain the structural heterogeneity of the forest could be a tool to alleviate potential losses of diversity. — AMS

J. Appl. Ecol. **40**, 150 (2003).

However, the drug had little effect when given during the chronic phase of the disease, suggesting that once inflammation and lesions are established, other adhesion molecules may be involved in disease progression.

Thus, immune cells bearing the α_4 integrins are likely to be important in MS pathogenesis, and selective inhibition of α_4 integrins may be effective in the clinic. — LC

N. Engl. J. Med. **348**,15 (2003); *J. Neurosci. Res.* **71**, 407 (2003).

PHYSICS

Proton Production with Lasers

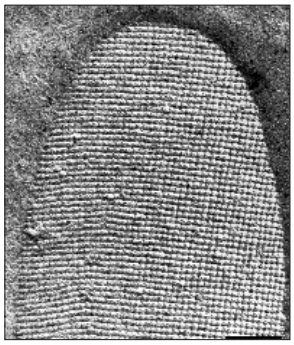
Owing to the large electric fields that can be sustained in a plasma, the production of ions, electrons, protons, and other particles during the interaction between high-powered lasers and matter is currently being pursued for future particle accelerators. However, the broad range of energies with which these particles are produced prevents a clear picture of the acceleration mechanism(s) involved. Zepf *et al*. performed a series of systematic experiments looking at proton production during the impact of high-powered laser pulses on thin foils of varied thickness possessing controlled hydrocarbon surface layers. Three distinct proton populations that contribute to the overall signal were distinguished, thereby providing a handle on the various acceleration mechanisms at play and suggesting possible opportunities for controlling the distribution of the protons produced. — ISO

Phys. Rev. Lett. **90**, 064801 (2003).

MICROBIOLOGY

Anthrax Regulation

Bacillus anthracis is distinguished from its more benign relations among the bacilli by the possession of plasmids containing virulence genes. The virulence genes are transcribed in response to elevated environmental temperature and carbon dioxide levels—key host signals. The plasmid pXO1 carries the anthrax toxin gene and its regulating genes. Mignot *et al*. have discovered that the toxin gene regulator AtxA on the plasmid also regulates the expression of cell surface proteins of the semicrystalline S-layer, via the PagR transcription factor. In the presence of carbon dioxide only one of the S-layer genes is expressed. The S-layer genes are on the bacterial chromosome, so AtxA appears to be a master regulator on the plasmid coordinating the expression of many genes throughout the genome, leading to successful infection. The need for *B. anthracis* to shift S-layer type in vivo may relate to structural constraints on toxin secretion. So, plasmids alone do not a pathogen make. — CA



Electron micrograph of an S-layer.

Mol. Microbiol. **47**, 917 (2003).

HIGHLIGHTED IN *SCIENCE*'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

Science's stke www.stke.org

Live Larger, Live Longer

Control of metabolism and body size are key molecular mechanisms involved in controlling life-span. Hirose *et al*. screened for mutants in *Caenorhabditis elegans* that were larger than normal. Several mutations occurred in the gene *egl-4*, which encodes a guanosine 3′,5′-monophosphate (cGMP)–dependent protein kinase. Phenotypically the worms were 50 to 100% larger, lived 50% longer, and had delayed egg laying and decreased brood size compared to wild-type worms. The larger size was due to increased cell volume, not cell number. Mutations in the genes of the insulin signaling pathway also increase life-span, and when the gene *daf-16*, which encodes a putative transcription factor, was also knocked out, life-span extension was eliminated. Double knockout of *egl-4* and *sma-6* or *dbl-1*, which encode components of the transforming growth factor β pathway, suppressed the size phenotype of *egl-4*. Thus, a cGMP-dependent protein kinase appears to be part of the network of signaling processes regulating cell size and organism longevity. — NG

Development **130**, 1089 (2003).

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Anthrax Regulation

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