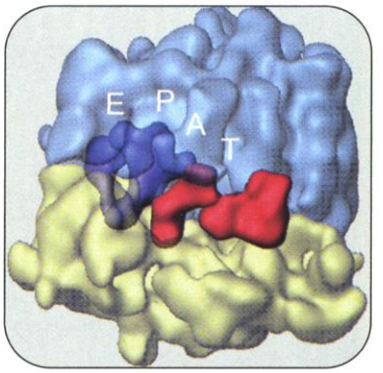
EDITORS' CHOICE

edited by Gilbert Chin

BIOCHEMISTRY

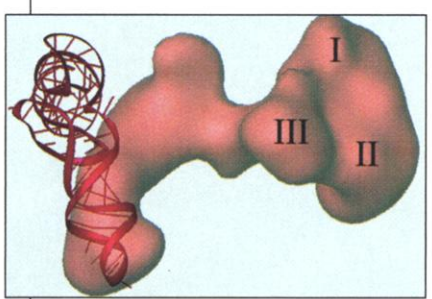
A Fitting Accommodation



The elongation factor Tu (EF-Tu) delivers amino acids in the form of aminoacyl transfer RNAs (aa-tRNAs) to the ribosome, which couples the amino acids together to form proteins. The choice of aa-tRNA (and thus the choice of amino acid) is dictated by the matching of the codon (on the messenger RNA) and the anticodon (at one end of the tRNA). Proper matching triggers a movement that results in hydrolysis of the EF-Tu–bound guanosine triphosphatase (GTP), releasing the aa-tRNA, which is bound less tightly by the GDP form of EF-Tu.

Valle *et al.* present a detailed analysis of the conformational changes that occur upon aa-tRNA delivery by fitting the crystal structures of the isolated components into a cryoelectron microscopic map of the entire ribosome captured in a state with the aa-tRNA–EF-Tu complex in the act of delivery. The remarkable result is that the tRNA inserts first the anticodon end into the decoding center on the small subunit of the ribosome and then the amino acid–carrying end into the peptidyl transferase center on the large subunit by swiveling one end and then the other into place. A twist in the middle or elbow region of the L-shaped tRNA apparently serves as the sign that the codon-anticodon match is perfect, telling EF-Tu to hydrolyze GTP and to let go of the other end of the tRNA, which then can slide into position. The proposed flexibility brings to mind previous studies and raises the possibility that the fidelity of interactions at the decoding center is signaled generally by tRNA arm movements. — GJC

EMBO J. **21**, 3557 (2002).



An overview of the ribosome (right), with tRNA and EF-Tu in red, and a close-up (above), with the final position of the delivered tRNA overlaid.

CHEMISTRY

Touchy-Feely Drug Design

The active agent produced by *Vibrio cholerae* is cholera toxin, which contains five identical subunits arranged in the form of a pentagon. The toxin pentamer has been the target of studies aimed at designing prophylactic drugs for cholera. It can also serve as a model system for the design of inhibitor molecules that bind to several sites at the same time. If such multivalent inhibitors are optimized for interaction with the pentamer, they should exhibit higher affinity for the toxin than univalent or randomly oriented multivalent molecules.

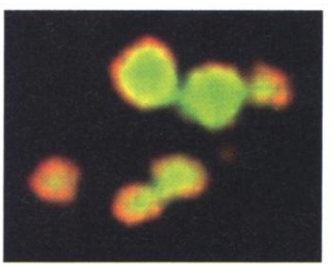
Earlier, Merritt *et al.* had described a modular design strategy for synthesizing star-shaped inhibitor molecules consisting of a core, five linkers, and five "fingers" that touch the five binding sites of the toxin. These pentavalent inhibitors did display a higher affinity for the toxin than the corresponding single-site inhibitors. The authors now show that the affinity gain can be increased further through the use of better-fitting fingers, and they also find that the toxins form 1:1 complexes with the inhibitor in solution. The crystal structure of the complex provides more opportunities for improving inhibitor design, especially by tinkering with linkers. — JU

J. Am. Chem. Soc., 10.1021/ja0203560 (2002).

CELL BIOLOGY

Recruitment Centers

A variety of neurodegenerative disorders involve the misfolding and aggregation of proteins carrying tracts of polyglutamine. Using fluorescent imaging in living cells, Chai *et al.* studied the dynamic properties of polyglutamine proteins. Different proteins exhibited very different mobilities and propensities to form mixed aggregates. For example, ataxin-3 (the mutated protein in spinocerebellar ataxia type 3) formed aggregated nuclear inclusions, which could recruit the cAMP response element binding protein (CBP). Similarly, huntingtin (mutated in Huntington's disease) formed common aggregates with CBP in the nucleus. However, cells expressing another polyglutamine protein, ataxin-1, did not recruit CBP to immobile protein aggregates. A variety of components of the nuclear transcription machinery may therefore be differentially recruited to nuclear inclusions in different diseases, presumably accounting for some of the distinct pathologies observed. — SMH



Nuclear inclusions contain both CBP (green) and ataxin-3 (red).

Proc. Natl. Acad. Sci. U.S.A. **99**, 9310 (2002).

ECOLOGY/EVOLUTION

Invader Profiling

An aggressively invasive strain of the tropical alga *Caulerpa taxifolia* was first reported from the Mediterranean coast of France in the mid-1980s. Since then, it has dispersed and expanded to cover more than 13,000 hectares of Mediterranean seabed; more recently, it has also been reported from the coast of California, USA. The invasive strain, which is widely thought to have been introduced accidentally from aquarium waste, is cold-tolerant, hence its survival in these unaccustomed waters. Successful eradication of such invaders can depend on early and correct identification. Famà *et al.* have developed a genetic assay, based on the presence or absence of a 735–base pair intron (noncoding region) in the *rbcL* gene of the *Caulerpa* chloroplast DNA. Unlike other strains, the invasive strain lacks the intron; the PCR-based assay rapidly distinguishes the invasive strain from other strains of the alga. Such techniques, which have also been used successfully in the case of other aquatic invaders such as the zebra mussel, may help coastal environment managers to halt the spread of the invader. — AMS

J. Evol. Biol. **15**, 618 (2002).

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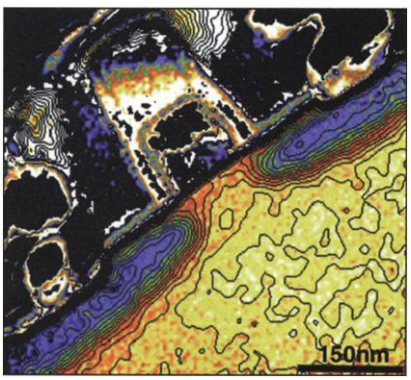
CREDITS: (TOP IMAGES) VALLE *ET AL. EMBO J.* **21**, 3557 (2002); (BOTTOM) CHAI *ET AL., PROC. NATL. ACAD. SCI. U.S.A.* **99**, 9310 (2002)

PHYSICS

Electron Holography in Microelectronics

During the fabrication of microelectronic devices, the ion implantation and annealing processes lead to the diffusion of the dopant atoms. Although secondary ion mass spectrometry and detailed process simulations have been used to characterize and monitor the depth of the dopant distribution in the devices, little is known about the lateral diffusion of dopants. As device dimensions get smaller, monitoring this lateral diffusion and the subsequent distribution of electric field throughout the device will become an increasingly important issue.



The two-dimensional distribution of electrostatic field due to the diffusion of implanted dopant atoms.

Addressing this point, Gribelyuk *et al.* show that electron holography can be used to provide a two-dimensional map of the electrostatic potential in submicrometer devices, revealing the extent of both the depth and lateral diffusion of the dopant atoms. With a resolution of 6 nanometers, it should prove a powerful characterization technique in the microelectronics field. — ISO

Phys. Rev. Lett. **89**, 025502 (2002).

GEOPHYSICS

Still Waiting After All These Years

Six successive magnitude 6 earthquakes had occurred at Parkfield, California, on the San Andreas fault, regularly every 21 to 24 years from the middle of the 19th century to 1966. It thus seemed a perfect place to collect detailed data toward understanding how earthquakes happen, and the region was instrumented in 1985 in anticipation of the next big one.

The expected earthquake has not taken place, however. Toda and Stein provide an explanation for at least part of the long delay: Earthquakes in 1983 near Coalinga, east of the San Andreas fault, were oriented so that they reduced the stress on the Parkfield part of the San Andreas fault. The predicted stress reduction can account for a delay of the Parkfield earthquake by about 10 years and for increases in activity on other parts of the San Andreas fault that were loaded by these earthquakes. This model explains why the Parkfield quake did not occur in the 1980s, but why it hasn't occurred by now is unclear. Still, seismicity has increased at Parkfield over the past several years, so it may be returning to its normal cycle. — BH

J. Geophys. Res. **107**, 10.1029/2001JB000172 (2002).

HIGHLIGHTED IN *SCIENCE*'S SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

Science's stke www.stke.org

Synaptic Communication

Cadherins are transmembrane adhesion proteins whose cytoplasmic domains bind to β-catenin, which in turn binds to α-catenin, which interacts with the actin cytoskeleton. The interaction between cadherin and β-catenin is regulated by phosphorylation, with a decreased interaction between the two when β-catenin is phosphorylated. Togashi *et al.* disrupted cadherin-cadherin interactions in cultured hippocampal neurons with a dominant negative form of *N*-cadherin, lacking the extracellular domain but still able to bind β-catenin. Postsynaptic dendritic spines became thinner and longer as compared to the usual mushroom shape. Presynaptic activity decreased (as reflected in less vesicle cycling), and postsynaptic proteins were more diffuse than in control cultures. Murase *et al.* show that depolarization or treatment of hippocampal neurons with a tyrosine kinase inhibitor shifted β-catenin into dendritic spines and promoted its interaction with cadherin. These changes could be mimicked by mutation: Y654F (corresponding to the unphosphorylated state) accumulated in spines, and these synapses displayed increased spontaneous neurotransmitter release. Thus, changes in dendritic morphology and the postsynaptic cadherin-catenin complex occur in concert with presynaptic activity. — NG

Neuron **35**, 77; 91 (2002).

CREDIT: GRIBELYUK *ET AL.*, *PHYS. REV. LETT.* **89**, 025502 (2002)