

Klotho for Eternal Youth?

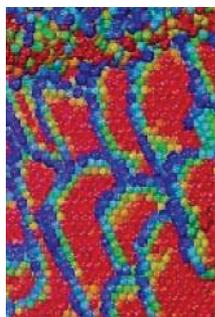
A defect in Klotho gene expression in mice leads to a syndrome resembling aging. **Kurosu *et al.*** (p. 1829, published online 25 August 2005; see the 26 August news story by **Couzin**) now find that Klotho overexpression extends life span in mice. Klotho protein functions as a circulating hormone that binds to a cell-surface receptor and suppresses insulin and insulin-like growth factor-1 (IGF-1) signaling in an evolutionarily conserved mechanism for extending life span in worms, flies, and mice. Furthermore, perturbing insulin/IGF-1 signaling slows aging in Klotho-deficient mice. Thus, it appears that Klotho protein may function as an antiaging hormone.

Right After the Burst

Apart from the Big Bang, gamma-ray bursts are the most powerful explosions in the universe and are thought to be massive stars collapsing to form black holes. Such events are followed by an extended afterglow over a range of wavelengths from x-rays down to radio frequencies. In the past, the afterglows were only detected several hours after the event, which resulted in missed opportunities to study this important phase of the burst. **Burrows *et al.*** (p. 1833, published online 18 August 2005) report their detection of energetic x-ray flares in the afterglows of recent gamma-ray bursts with the Swift x-ray telescope. The flares appear to be evidence of strong shock waves and extended activity in the central region of the burst.

Stronger Under Pressure

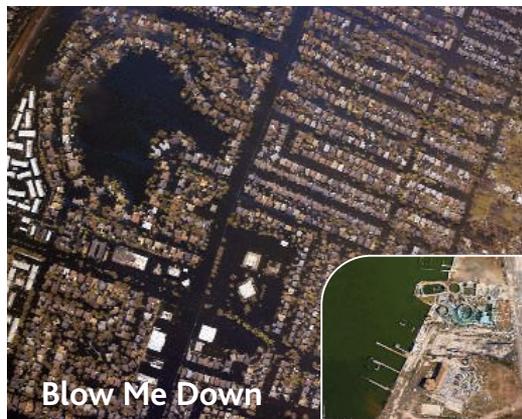
For certain applications, materials need to be designed to sustain extreme shocks, as might be experienced, for example, at national ignition facilities; some nanocrystalline materials are showing promise. **Bringa *et al.*** (p. 1838) report molecular dynamics simulations on nanocrystalline copper subjected to shock loading. At high pressures, the active deformation mechanisms change from those that are thermally activated to those that are pressure mediated. The results show that the copper strengthens because grain boundary sliding is suppressed by the pressure. Experiments on nanocrystalline nickel confirm the behavior seen in the simulations.



Adaptive Immunity in Insects?

Refined and complex genetic mechanisms generate huge levels of diversity in the B cell and T cell receptors of the adaptive immune system, but this diversity generation has been thought to be restricted to some higher vertebrates. **Watson *et al.*** (p. 1874, published online 18 August 2005; see the Perspective by **Du Pasquier**) now describe a mechanism of alternative splicing

of *Dscam*, a single gene locus in insects, that has the potential to generate an exceptional level of protein diversity. Originally identified as a neuronal receptor, splice products of this gene were also found in various immune tissues of *Drosophila*. Functional studies suggest that some isotypes of *Dscam* could assist in the phagocytosis of bacteria, pointing to a direct and adaptable form of insect immunity.



Blow Me Down

It has been suggested that global warming could lead to an increase in the general level of storminess. Evidence that such an effect is occurring has been elusive, however, and the links between increasing atmospheric and sea surface temperatures and hurricane activity have been debated. **Webster *et al.*** (p. 1844; see news story by **Kerr**) examine the frequency and strength of tropical storms and hurricanes worldwide during the past 35 years. Although there has not been an increase in the number or frequency of events, the proportion of hurricanes reaching the most energetic categories increased significantly, particularly in the Pacific and Indian Oceans.



Rings of Uranium

The actinide elements are well known for their nuclear instability, which leads to radioactivity and atomic energy applications. However, they also engage in unusual chemical bonding, resulting from their occupied f-orbitals and the relativistic effects of their high nuclear charge, allowing unusual compounds to be formed and studied. **Evans *et al.*** (p. 1835; see the Perspective by **Burns**) have isolated and characterized a ring of eight uranium atoms connected through alternating nitride and azide (N_3) groups. Prepared by mixing an organo-uranium precursor with sodium azide in solution, the compound sheds light on molecular uranium-nitride bonding and also models the electronics of extended lattice uranium nitride materials.

Connecting Craters

The record of impact cratering observed on the Moon and Mars, calibrated with age determinations from Apollo samples, is the primary means for dating surfaces on the terrestrial planets. **Strom *et al.*** (p. 1847; see news story by **Kerr**) have reexamined the distribution of sizes of craters, inferred the sizes of causative asteroids, and show that an older population of craters, before about 3.8 billion years ago, has the same distribution as observed asteroids in the main asteroid belt. Younger craters seem to be caused by near-Earth asteroids. These data imply that a process early in the history of the solar system, perhaps outward migration of the giant planets, ejected asteroids from the main belt, but that this process ceased about 3.8 billion years ago.

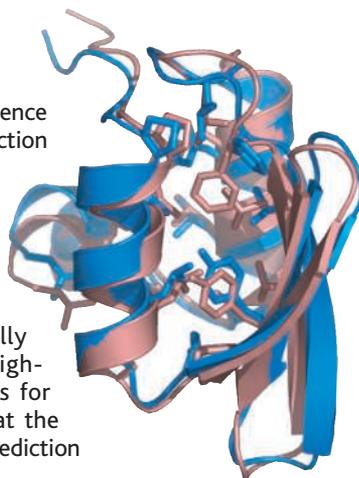
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Evolving Sequence and Expression

An analysis of the evolution of both gene sequences and expression patterns in humans and chimpanzees by **Khaitovich *et al.*** (p. 1850, published online 1 September 2005; see the 2 September Editorial by **Jolly**, the Perspectives by **Hauser** and by **McConkey and Varki**, and the news story by **Culotta**) show that in the brain, heart, liver, kidneys, and testes, the general patterns of evolution conform to a neutral theory. Similar patterns of selection were seen for protein sequence and gene expression. Genes that are expressed in more tissues have diverged less between species than genes expressed in fewer tissues, which suggests neutral evolution with negative selections, but genes on the X chromosome that are expressed in testes showed evidence of positive selection. Surprisingly, genes expressed in the brain have changed more on the human lineage than on the chimpanzee lineage, not only in terms of gene expression but also in terms of amino acid sequences.

Protein Sequence Structure Prediction

It has long been known that the amino acid sequence of a protein defines its structure; however, the prediction of structure from sequence remains a challenge. Now **Bradley *et al.*** (p. 1868) have achieved high-resolution structure prediction (<1.5 angstrom) for 5 sequences in a test set of 16 small protein domains (<85 residues). These results were obtained using a combination of improved conformational sampling methods, a physically realistic all-atom free-energy function, and high-performance computing. The free-energy basins for native structures are very narrow, suggesting that the primary bottleneck to consistent high-resolution prediction is conformational sampling.



Temporal Controls in Inflammatory Responses

Understanding control of cellular regulation requires not only a description of the signaling events and mediators involved, but also an understanding of the temporal properties of how signals are generated and sensed. **Covert *et al.*** (p. 1854) and **Werner *et al.*** (p. 1857) now provide insight into temporal control of signals that control the activity of a key mediator of inflammatory responses, the transcription factor NF- κ B. Signals from the receptor for the inflammatory cytokine tumor necrosis factor or from the Toll-like receptor 4 (TLR4), which recognizes bacterial lipopolysaccharide, result in either oscillating or stable patterns of NF- κ B activity, respectively, which in turn lead to distinct patterns of gene expression. Computational models and biochemical analysis reveal the regulatory events that produce the distinct temporal patterns of NF- κ B activity. The stable signal produced by activation of TLR4 appears to result from activation of two signaling pathways—a rapid one, and a slower one that requires protein synthesis and autocrine signaling.

SARS Spike, Up Close and Personal

The SARS coronavirus causes severe acute respiratory syndrome (SARS), which has a fatality rate of about 10%. Attachment to human cells is through a spike protein on the viral surface that binds to a cell-surface zinc peptidase, angiotensin-converting enzyme (ACE2). Now **Li *et al.*** (p. 1864; see the Perspective by **Holmes**) have determined the structure of the SARS coronavirus spike protein receptor-binding domain bound to the peptidase domain of human ACE2 at 2.9 angstrom resolution. The details of the interface suggest how a few residue changes led to efficient cross-species infection and human-to-human transmission in the 2002–2003 SARS outbreak. The structure could guide design of receptor-binding domain variants in the development of an effective SARS vaccine.