

fluids; silica gel may lubricate quartz rocks and fine powder may ease sliding in carbonate rocks. Hirose and Bystricky have found support for another hypothesis: fault weakening through dehydration of embedded phyllosilicate clays. They carried out high-velocity friction experiments on natural serpentinite (a phyllosilicate) under conditions mimicking an earthquake and measured the heat generated by friction and the resulting rock strength. An observed increase in humidity implied that water was lost from the serpentinite during sliding. Dehydration requires temperatures of about 500°C, which the authors argue might be attained where bumpy asperities rub together. — JB

Geophys. Res. Lett. **34**, L14311 (2007).

CLIMATE SCIENCE

Trop Chaud?

The summer of 2003 was the hottest on record in Europe over the past 500 years; the summer of 2006 was almost as hot, and the heat was even more widespread. Were these extremes part of a trend that can be expected to continue? Della-Marta *et al.* compiled 54 temperature records from western Europe (6 based in Scandinavia, 12 in the Iberian Peninsula, and 36 in the central region) to determine how the daily summer maximum temperatures there have changed since 1880. They found that the length of summer heat waves has doubled and that the frequency of hot days has nearly tripled over that interval. These changes are the result of a combination of a long-term trend toward higher temperatures and a significant increase in the intrinsic variability of western European daily summer maximum temperatures, particularly in the central region. — HJS

J. Geophys. Res. **112**, D15103 (2007).

IMMUNOLOGY

A Regulatory Trio

Immune responses rely on many regulatory strands that may act independently or cooperatively. Madhav *et al.* provide evidence for the intersection of three prominent regulatory mechanisms in mice that develop in response to tumors. Their study builds on the previous identification of an immune-suppressive dendritic cell (DC) subset present in lymph nodes that

drain from tumors. Although the potent tryptophan-degrading enzyme indoleamine 2,3-dioxygenase (IDO) produced by these cells already has its own direct immune-suppressive credentials, it emerged that this source of IDO could rouse local regulatory T cells. These cells also possess their own direct suppressive activity, but in this case provided additional feedback on IDO-expressing DCs to induce the expression of the cell-surface protein PD-L1, which curbed the proliferation of T cells in culture. Blocking PD-L1 with antibodies or growing tumors in IDO-deficient mice interfered with the inhibitory activity exerted by regulatory T cells. This study raises the question of whether equivalent suppressive pathways induced by IDO-producing DCs and linked through the activity of regulatory T cells might also develop in response to tumors in humans. — SJS

J. Clin. Invest. **117**, 10.1172/JCI31911 (2007).

BIOCHEMISTRY

Studying Ions in Depth

Detailed understanding of how particular proteins function in human cells can provide the foundation for pathophysiology-based therapies, but it rarely is feasible to study these proteins directly. Instead, bacterial substitutes are usually more tractable, and the application of homology modeling and site-specific mutagenesis of mammalian proteins can yield useful insights. Forrest *et al.* offer a rigorous example of this approach, starting with a previously published structure of a bacterial amino acid transporter, LeuT, which is representative of transporters that couple the movement of small molecules, such as leucine and serotonin, to the transmembrane Na⁺ gradient. From an analysis of a structure-based sequence alignment of LeuT

with the serotonin transporter (SERT), they find that the carboxylate of a buried glutamate in LeuT, in which leucine transport is Cl⁻-independent, occupies the same location as a chloride ion (coordinated by a serine) in SERT, which exhibits Cl⁻-stimulated serotonin transport. Changing the serine to a glutamate or aspartate had no effect on the basal transport activity of SERT but fully abrogated the stimulation by Cl⁻, and further mutagenesis of other Cl⁻-coordinating residues in other amino acid transporters confirmed the predicted effects on activity. Other modulators of leucine transport by LeuT include the tricyclic antidepressants, as shown by Singh *et al.* (see also Zhou *et al.*, *Science Express*, 9 August 2007) — GJC

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