the production of immunogenic DCs may simultaneously activate genes controlled by GSK3β or its targets. Such a mechanism could reflect feedback control mechanisms that attenuate T cell activation by DCs. Alternatively, the GSK3β or the β-catenin pathway could control aspects of DC function required for both immunogenic and tolerogenic T cell activation.

References

1. S. Manicassamy *et al.*, *Science* **329**, 849 (2010).
2. T. K. Starr, S. C. Jameson, K. A. Hogquist, *Annu. Rev. Immunol.* **21**, 139 (2003).
3. R. M. Steinman, D. Hawiger, M. C. Nussenzweig, *Annu. Rev. Immunol.* **21**, 685 (2003).
4. H. C. Probst, J. Lagnel, G. Kollias, M. van den Broek, *Immunity* **18**, 713 (2003).
5. E. S. Trombetta, I. Mellman, *Annu. Rev. Immunol.* **23**, 975 (2005).
6. S. Henri *et al.*, *J. Immunol.* **167**, 741 (2001).
7. P. Stoitzner, C. H. Tripp, P. Douillard, S. Saeland, N. Romani, *J. Invest. Dermatol.* **125**, 116 (2005).
8. K. R. Siddiqui, S. Laffont, F. Powrie, *Immunity* **32**, 557 (2010).
9. A. Jiang *et al.*, *Immunity* **27**, 610 (2007).
10. Y. Ding, S. Shen, A. C. Lino, M. A. Curotto de Lafaille, J. J. Lafaille, *Nat. Med.* **14**, 162 (2008).
11. W. J. Nelson, R. Nusse, *Science* **303**, 1483 (2004).
12. M. Martin, K. Rehani, R. S. Jope, S. M. Michalek, *Nat. Immunol.* **6**, 777 (2005).
13. H. R. Turnquist *et al.*, *Blood* **115**, 4758 (2010).

10.1126/science.1194185

GEOPHYSICS

Sedimentary Basins Feeling the Heat from Below

A major change may be taking place in underlying theories to explain sea level change over time scales of 2 to 20 million years.

R. Dietmar Müller

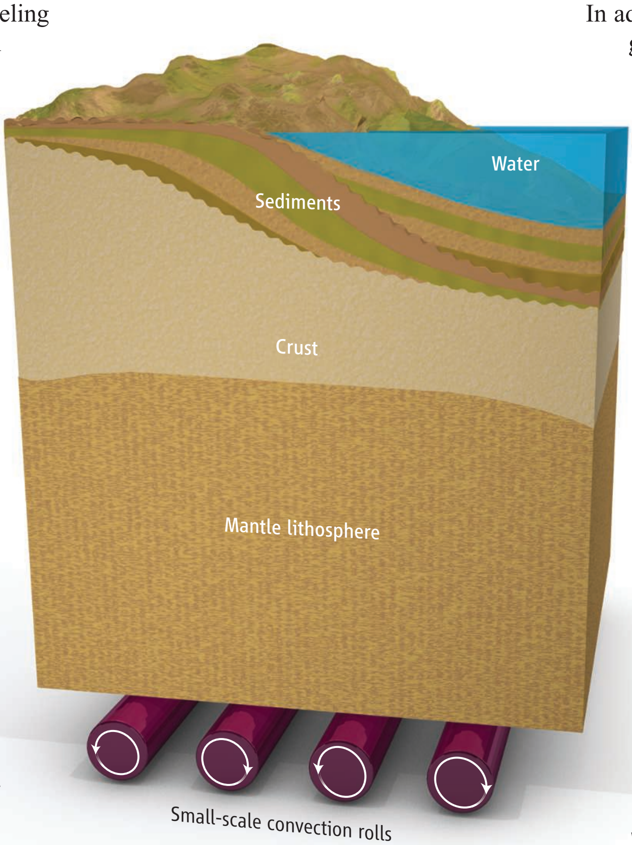
Sea-level changes through Earth's history have profoundly affected the surface environment, resulting in alternating advances and retreats of the sea, called transgressions and regressions. An understanding of the mechanisms behind these major shifts in coastlines, and the associated patterns of sediment deposition and erosion over different time scales, is central to unraveling Earth's tectonic and climate history. On page 827 of this issue, Petersen *et al.* (*1*) report results from geodynamic modeling that give a potentially radical shift in concept, namely that oscillations in sedimentary sequences over time periods from 2 to 20 million years may be driven by regional patterns of small-scale convection in the mantle.

The changes we may expect over the next few generations in sea-level rise due to melting ice-sheets are tiny compared with the vast sea-level fluctuations that have occurred over geological time, as documented by marine sedimentary sequences covering large parts of the continents. In a pioneering effort in the 1970s, Vail and colleagues (*2*) collated industry seismic and well data to propose a global sea-level curve, which was later refined by Haq *et al.* (*3*). These curves provide a global reference frame to understand advances and retreats of the sea globally over geological time scales.

It is accepted that long-term sea-level change over tens and hundreds of millions of years is primarily caused by fluctuations of the volume of the ocean basins, driven by the time dependence of mid-ocean ridge creation and destruction (*4*). The higher frequency changes in sea level, over tens to hundreds of thousands of years, are due to changes in ice volume, and thus the volume of water in the ocean basins, at least during times when continental ice sheets existed on Earth (*5*).

However, published global sea-level curves are plagued by the problem that sea-level oscillations at so-called intermediate time periods, from 2 to 20 million years, have defied explanation. Transgressions and regressions at these time periods are ubiquitous in the geological record, both during ice ages and during ice-free periods. Therefore, these oscillations cannot be ascribed entirely to ice volume changes, and tectonic cycles in the ocean basins are too slow to produce them. In addition, the global correlation of stratigraphic sequences involved has been questioned, mainly because much of the data on which global sea-level charts are based are not publicly available, and the dating precision of sedimentary sequences is not sufficient to demonstrate global correlation (*6*).

Petersen *et al.* argue that intermediate-period sea-level change expressed in sedimentary basin sequences may not be global but may be due to regional effects caused by small-scale upwellings and downwellings below the base of the lithosphere. Using a model sedimentary basin and a geodynamic simulation, they show that this mechanism can generate sedimentary sequences akin



Simmering sediment. Sublithospheric small-scale convection underneath sedimentary basins may be responsible for cycles of regional tectonic subsidence/uplift and oscillating coastlines over time periods of 2 to 20 million years. In turn, these transgressions and regressions of the sea give rise to alternating successions of shallow and deeper water sediments in sedimentary basins.

CREDIT: ADAPTED BY P. HUEY/SCIENCE

School of Geosciences, University of Sydney, Sydney, 2006 Australia. E-mail: dietmar.muller@usyd.edu.au

to those observed (see the figure). The idea that small-scale convection should occur beneath sedimentary basins is not far-fetched. The mechanism was originally proposed by Richter (*7*) and later invoked to explain the flattening of old ocean floor (*8*), volcanism along passive margins (*9*), and volcanic activity along some hotspot chains (*10*).

The model of Petersen *et al*. implies that globally correlative sea-level fluctuations, with global causal mechanisms, occur only at very long time scales (more than 10 to 20 million years) and at geologically short time scales (less than 1 to 2 million years). The fluctuations at intermediate periods may be regional in origin. Other tectonic mechanisms proposed previously, such as intraplate stress changes (*11*), resulting in flexure of the lithosphere, can produce individual events of regional sea-level change but are less likely to produce oscillations. Unraveling global from regional causes of sea-level change over intermediate time periods has wide-ranging implications for understanding how mantle convection and plate tectonic processes ultimately affect the evolution of Earth's surface. Understanding these processes is also essential for exploration of deep Earth resources in sedimentary basins.

What is required now is to find a way of using geological observations to determine the extent of the contribution of small-scale convection to intermediate-period sea-level change. The detailed history of small-scale convection underneath sedimentary basins will likely remain unknown. The solution therefore lies in proving or disproving the global correlation of intermediate period sea-level fluctuations, as expressed by the geometry and age of boundaries between sedimentary sequences. The issue is beginning to be addressed by the Integrated Ocean Drilling Program (IODP), with two transects drilled in 2009 off the coasts of New Jersey (*12*) and the South Island of New Zealand (*13*). These transects will provide data for estimating regional sea level based on two-dimensional (2D) sequence stratigraphic backstripping (*14*) in geographically disparate regions. A compilation of key observations in a public, shared community database, including seismic data, well data, stratigraphic and structural field observations, and absolute ages of sequence boundaries would also go a long way in helping resolve the origin of intermediate-period sea-level changes. This effort, which may be regarded as the stratigraphic equivalent of initiatives such as EarthScope (www.earthscope.org) or OneGeology (www.onegeology.org), will require collaboration between industry, government organizations, and academia to devise a data infrastructure that is simple enough to be adopted and extensively used by the community, yet allows for extensive automatic data mining similar to the efforts in other fields, such as genomics or astrophysics. Only this way will it be possible to demonstrate or refute the global correlation of intermediate period sequences and obtain better understanding of vertical motions of Earth's surface over geological time.

The potential 3D effect of small-scale convection on basin evolution raises intriguing questions, considering that the model of Petersen *et al*. is 2D. How common is small-scale convection underneath sedimentary basins? What are the geodynamic niche environments that initiate and sustain the process? In three dimensions, small-scale sublithospheric convection is thought to be arranged into convective rolls (*10*), resulting in differential subsidence and uplift. This effect should be detectable in large sedimentary basins, and a combination of 3D geodynamic models and 3D stratigraphic data should be able to unravel the orientation and scale of such rolls, which are presumably oriented orthogonal to the direction of absolute plate motion. The message from this thought-provoking paper is that a collaboration between stratigraphers, basin analysts, and geodynamicists may hold the key for unraveling the sea-level history of planet Earth.

References

1. K. D. Petersen *et al*., *Science* **329**, 827 (2010).
2. P. R. Vail, R. M. Mitchum, S. Thompson III, in *Seismic Stratigraphy and Global Changes in Sea Level,* C. Payton, Ed. (Am. Assoc. Petro. Geol. Memoir, 1978), vol. 26, pp. 83–97.
3. B. U. Haq, J. Hardenbol, P. R. Vail, *Science* **235**, 1156 (1987).
4. R. D. Müller, M. Sdrolias, C. Gaina, B. Steinberger, C. Heine, *Science* **319**, 1357 (2008).
5. K. G. Miller *et al*., *Science* **310**, 1293 (2005).
6. A. D. Miall, *Geology* **20**, 787 (1992).
7. F. M. Richter, *J. Geophys. Res.* **78**, 8735 (1973).
8. B. Parsons, D. McKenzie, *J. Geophys. Res.* **83**, (B9), 4485 (1978).
9. R. R. Boutilier, C. E. Keen, *J. Geophys. Res.* **104**, (B4), 7389 (1999).
10. M. D. Ballmer, J. van Huenen, G. Ito, P. J. Tackley, T. A. Bianco, *Geophys. Res. Lett.* **34**, L23310 (2007).
11. S. Cloetingh, *Geology* **14**, 617 (1986).
12. Expedition 313 Scientists, *IODP Prel. Rept.* 313; http://publications.iodp.org/preliminary_report/313/index.html (2010).
13. Expedition 317 Scientists, *IODP Prel. Rept.* 317; http://publications.iodp.org/preliminary_report/317/317pr_2.htm (2010).
14. M. A. Kominz, S. F. Pekar, *Geol. Soc. Am. Bull.* **113**, 291 (2001).

10.1126/science.1194560

AIDS/HIV

A Boost for HIV Vaccine Design

Dennis R. Burton[1,2] and Robin A. Weiss[3]

Antibodies that potently neutralize almost all HIV isolates could aid the rational design of a vaccine.

A major roadblock to the development of an effective vaccine against the human immunodeficiency virus (HIV-1) is the lack of an immunogen that elicits broadly protective antibodies (*1*). Passive transfer studies in animal models have associated protection with neutralizing antibodies and, encouragingly, serum studies show that a subset of HIV-infected individuals produces potent broadly neutralizing antibodies (*2*). Understanding the viral targets of such antibodies and how they achieve potent and broad neutralization has become a key endeavor in HIV vaccine research. On page 856 of this issue, Wu *et al*. (*3*) describe the isolation of particularly potent monoclonal broadly neutralizing antibodies using a novel selection strategy, and on page 811, Zhou *et al*. (*4*) solve the crystal structure of the most effective of these antibodies in complex with its target gp120, a viral envelope glycoprotein. These studies further invigorate the currently active field of discovering broadly neutralizing antibodies against HIV (*2*, *5*–*7*) and provide valuable molecular information for rational vaccine design.

The isolation of monoclonal broadly neutralizing antibodies from HIV-infected donors has so far proven immensely difficult. Following their initial characterization in the 1990s, only a few were available by early 2009. Part of the difficulty is that in HIV infection, a vast number of antibodies are produced to the viral glycoproteins (gp120 and gp41) that do not bind to the native trimeric spike formed by these pro-

[1]Department of Immunology and Microbial Science and IAVI Neutralizing Antibody Center, The Scripps Research Institute, La Jolla, CA 92037, USA. [2]Ragon Institute of Massachusetts General Hospital, Massachusetts Institute of Technology, and Harvard, Boston, MA 02114, USA. [3]Division of Infection and Immunity, University College London, London W1T 4JF, UK. E-mail: burton@scripps.edu; r.weiss@ucl.ac.uk