expression of apoE, accelerates Aβ clearance from the brain and, moreover, reverses abnormal behaviors in mouse models of Alzheimer's disease.

Expression of the *APOE* gene and the lipid transporter genes *ABCA1* and *ABCG1* (which facilitate the formation of apoE-associated lipoprotein particles) are increased by agonists of the nuclear receptors peroxisome proliferator–activated receptor gamma (PPARγ) and liver X receptor (LXR). These receptors form obligate heterodimers with the nuclear receptor retinoid X receptor (RXR) (*4*). LXR or PPARγ agonists can reduce the production of Aβ, as well as improve cognition, in mouse models of Alzheimer's disease. Cramer *et al*. tested whether the RXR agonist bexarotene, which activates both the PPAR-RXR and LXR-RXR receptors, would rapidly alter the amount of Aβ, and diminish behavioral abnormalities, in mice genetically engineered to express a mutant form of the *APP* gene. The authors observed rapid clearance of soluble Aβ from the brain, reduction in neuritic plaque burden, and reversal of behavioral deficits. The effects of bexarotene on Aβ metabolism required apoE expression, because they were not observed when the drug was administered to mice lacking the *APOE* gene. These observations strongly support the hypothesis that apoE plays a critical role in reducing Aβ amounts in the brain by enhancing Aβ clearance, and that strategies increasing apoE expression in patients might be truly disease modifying (see the figure).

Although Cramer *et al*. rigorously demonstrate that bexarotene clears Aβ by a mechanism dependent on apoE, the drug may enhance behavioral responses (in this mouse model of Alzheimer's disease) through an additional mechanism. Patients with Alzheimer's disease or type 2 diabetes show insulin resistance, and a small clinical trial demonstrated that the intranasal inhalation of insulin by Alzheimer's patients improved memory (*5*). PPARγ agonists and RXR agonists both have been developed as therapeutics for type 2 diabetes as "insulin sensitizers." The RXR agonist bexarotene, examined by Cramer *et al*., also reduces fasting glucose concentrations in mouse models of non–insulin-dependent diabetes (*6*). Thus, disturbance in the molecular pathway resulting in type 2 diabetes may also be critical in the mechanism of Alzheimer's disease

Although the study by Cramer *et al*. provides strong motivation for clinical trials, observations in mouse models of disease might not necessarily extrapolate to humans. The amino acid sequence of mouse apoE is not identical to any of the human apoE isoforms, and the transgenic mouse models in their study do not recapitulate the neurofibrillary tangle neuropathology of Alzheimer's disease. The rapid clearance of Aβ from the brains of mice may have unintended consequences in compromising blood-brain barrier integrity. Only carefully constructed clinical trials will determine whether this drug, or related drugs, benefits patients with Alzheimer's disease.

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GEOPHYSICS

At the Bottom of the Oceanic Plate

High-resolution seismic maps are providing a better picture of the processes involved in plate tectonics.

Hitoshi Kawakatsu

According to the theory of plate tectonics, huge plates below the Pacific Ocean are moving laterally at a speed of ~10 cm/year above a weak layer called the asthenosphere. Considering that the horizontal scale of a plate can be as large as 10,000 km (the thickness is ~100 km), how such a thin plate maintains its rigidity, while sometimes causing mega-earthquakes at the edge, is rather puzzling. Understanding what is happening at the bottom of the oceanic plate remains an open question even after some 40 years of success of plate tectonics. In the past few years, seismologists have reported sharp shallow seismic boundaries beneath oceanic basins that may define the bottom of the plate (*1*–*3*). On page 1480 of this issue, Schmerr (*4*) reports observations indicating the laterally varying nature of the bottom boundary of the oceanic plate.

The asthenosphere, named after a Greek word meaning "weak," is a viscous layer just below the lithosphere ("rock") that facilitates horizontal movement of the solid plate. The word existed before the birth of plate tectonics to explain the long-term ground deformation associated with removal of the ancient glacier. A continental lithosphere underlain by the weak viscous asthenosphere is uplifted after thousands of years from the deglaciation because of the slow deformation taking place in the asthenosphere. Compared to the continental plates, which are complicated in structure because of their long tectonic history, oceanic plates are young and their history should be much simpler.

Considering that the inside of the Earth is warmer, it is natural to assume that deep-mantle rocks are softer owing to the higher temperature. However, the high pressure at depth makes rocks harder, so there must be a minimum value of the softness. Theoretical estimates of how mantle rocks behave with depth indicate that this minimum occurs around 100 to 150 km beneath the ocean, the same depth range known for the seis-

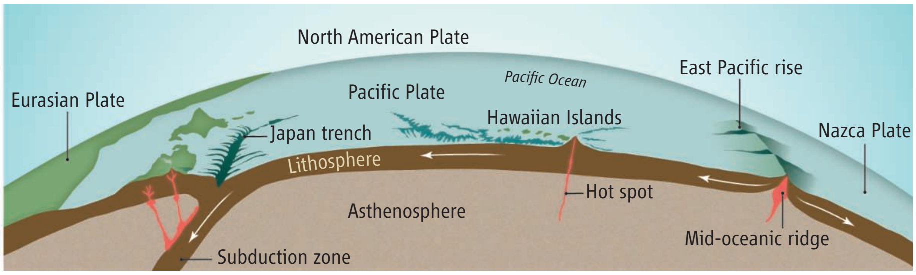

Plate tectonics in the ocean. The depth of the G discontinuity is around 50 to 100 km, and may vary with the age of the plate. The thickness of the transition region, the lithosphere-asthenosphere boundary, may be less than ~20 km.

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mic low-velocity zone (LVZ) (*5*). The question is whether this LVZ is weak or viscous enough to be consistent with the geodynamical property required for the asthenosphere (*6*). A further question is how the gradual change in temperature and pressure with depth can cause the observed large seismic-velocity reduction near the base of the lithosphere. This observed sudden drop in the seismic velocity around a depth of 50 to 100 km beneath the ocean is called the Gutenberg (or simply G) discontinuity, named after Beno Gutenberg who discovered the presence of the LVZ. The G separates the high-velocity oceanic lid from the LVZ; it is sometimes referred to as the lithosphere-asthenosphere boundary (LAB) because it invokes the idea that it is the boundary between strong lithosphere and weak asthenosphere (see the figure).

There are several ingredients that can make mantle rocks weaker: a small amount of melting (*7*) or water (*8*), and the size reduction of mineral grains. Among them, partial melting is the most effective for producing a sharp and large velocity drop at the G discontinuity, although the presence of water itself enhances melting. As the presence of a small amount of melt also lubricates the boundary (*9*), some argue that it even defines the LAB. In finding an intermittent G discontinuity beneath the Pacific, as distinct from the conventional view of a ubiquitous LVZ, Schmerr argues that a large amount of melt may exist in regions of the LAB where recent volcanism or melt production is known. As few G discontinuities have been observed where no volcanism exists, additional mechanisms are invoked—small-scale convections or mantle upwelling—that regionally enhance the discontinuity. However, as the reported properties of the G discontinuity show large scatter (*1*–*4*), further investigation is required. If we could map the G discontinuity beneath the entire ocean with accuracy, then we might be able to understand the enigmatic asthenosphere.

One of the key properties of the asthenosphere that is not well elucidated from both observational and theoretical standpoints is the strong seismic anisotropy known to exist in the LVZ (*10*, *11*). Seismic anisotropy is a polarization-direction dependence of seismic wave propagation that reflects the deformation history of mantle rocks. At present, we have neither a model of the asthenosphere that fully accounts for the observed properties of seismic anisotropy, nor do we have a well-constrained anisotropy structure of the LVZ. Thus, new seafloor observations and new analysis techniques combined with a large amount of seismic data from global land-based networks will be important to refine our understanding of the asthenosphere.

Plate tectonics started as a theory to explain the origins of the oceanic basin by investigating its shallowest part, leaving the deeper part of the lithosphere or lithosphere-asthenosphere system behind. Geophysical exploration of the ocean in the past several decades has focused on tectonically active areas, such as subduction zones, hot spots, and mid-oceanic ridges. Although these studies have elucidated the active part of the Earth's processes, the importance of normal, or tectonically inactive, oceanic areas, where the underlying structure may offer a textbook view of the deep mantle, might have been underestimated. Planned multidisciplinary ocean-bottom geophysical observations of the normal Pacific Ocean may finally shed light on the enigma of plate tectonics.

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ECOLOGY

Keystones in a Tangled Bank

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Ecological network studies highlight the importance of individual species to community conservation.

In the past decade, ecologists have increasingly applied complex network theory (*1*, *2*) to ecological interactions, both in entire food webs (*3*) and in networks representing ecological interactions, especially those between plants and their animal pollinators or seed dispersers (*4*). How important are individual species to the maintenance of such ecological networks? On page 1489 of this issue, Stouffer *et al.* (*5*) analyze terrestrial, freshwater, and marine food webs to infer the contributions of individual species to network stability. In a related field study on page 1486 of this issue, Aizen *et al.* (*6*) explore plant and pollinator webs on a landscape scale. Using a different field study design, Pocock *et al.* (*7*) recently focused on a local community in which several webs of different kinds of interactions and organisms form a composite network.

Stouffer *et al.* decomposed previously studied food webs into groups of three species linked by interactions (see the figure, panel A). Such species triads can form 13 different configurations or motifs that may be differentially represented in networks (*8*). Each species can belong to several motifs in a food web. The authors propose that most species tend to preferentially occupy certain motifs, giving them distinctive "motif profiles."

Previous simulation studies have shown that each trophic motif contributes to either an increase or a decrease in the probability of community persistence (*9*). Combining their findings with these previous observations, Stouffer *et al.* find that each species or entity can be assigned a probability of increasing or decreasing the persistence of a community to which it belongs. Families or higher taxonomic entities tend to occupy similar motifs across different communities, which suggests that they also have invariant effects on the future persistence of a community.

Aizen *et al.* analyzed flower visitation webs in 12 isolated hills of varying size in the Argentinian Pampas, 400 km south of Buenos Aires. They recorded 268 species of plants and insect flower visitors in standardized field surveys. The number of interactions decreased from larger to smaller hills, at a higher rate than expected from the well-established species-area relation (*10*). What could cause these interaction losses?

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