highly reflecting, specular nature of the rupture surface. Yet these reflections are unexpected: The geometry of the trenches will lead to compression of the slab before it undergoes tension when flattening at depth. This resulting deformation of the slab—in particular, a thinning before rupturing—is not an ideal condition to create a smoothly reflecting surface. If the reflection interpretation is correct, it would argue against thinning of the plate before rupturing. The tectonic situation is similar to that beneath Kamchatka, so the process seen here may reflect what happened there several million years ago.

The idea of slab tears is attractive because it can explain other related phenomena. A horizontal tear releases the slab from drag forces that hinder its movement. Below the crust, tearing leads to an influx of hot material from the asthenosphere (the region of low viscosity that underlies the lithosphere), which can explain both magmatic events and vertical motions observed at Earth's surface. Especially during continental collisions, when the lighter continental plate is buoyant but the denser oceanic lithosphere tends to sink, opposing forces of gravity provide the tension needed to create a tear (*12*).

The observed fragility of slabs has serious implications for the way the convective process is organized in Earth's deep interior. Seismologists have recognized for some time that only a fraction of descending slabs penetrate the boundary between the upper and lower mantle. The slab is cooler than the surrounding mantle, and because the phase transition requires higher pressure at lower temperature, the slab's conversion into perovskite is delayed; thus, the slab is temporarily buoyant. This buoyancy, combined with a much greater viscosity of the lower mantle (*13*), hampers slab penetration into the lower mantle. Slab fragmentation makes it even more difficult to pile up enough slab mass to overcome the resistance posed by the phase transition and by high viscosity. Detached fragments will need to equilibrate in temperature before changing to the denser phase, further delaying (or perhaps inhibiting) their sinking. The slowing of these processes limits mass flux between the upper and lower mantle and hinders the cooling of Earth's interior.

Further insights into these processes will likely require an increase in the resolving power of global tomography so that small blobs can be observed individually in the lower mantle (if they exist, they are currently blurred into larger structures). The seismic superarrays are a step in this direction but will never cover the oceans. For this, tentative efforts to observe seismic waves using floating sensors are promising (*14*). New tomographic techniques that overcome the resolution limitations of ray theory also need to be fully exploited.

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PHYSIOLOGY

What Determines Coral Health?

Genomic and cellular studies are revealing the physiological mechanisms of symbiosis and calcification, which are central to coral health.

Virginia M. Weis[1] and Denis Allemand[2]

Corals are to coral reefs as trees are to forests: They form both the trophic and structural foundation of the ecosystem. The trophic anchor arises from the intimate mutualism between corals and their intracellular symbionts—photosynthetic dinoflagellates that fix large quantities of carbon dioxide, making coral reefs among the most productive ecosystems on Earth. The structural anchor comes from the deposition of massive calcium carbonate skeletons that form the reef architecture and serve as habitat for a breathtaking diversity of organisms. Central to the severe global decline of coral reefs (*1*) is the dysfunction and collapse of both symbiosis and calcification in corals due to environmental stressors imposed by climate change. Insights into the physiological mechanisms that underlie healthy as well as stressed corals (*2*) are thus critical for predicting whether—and if so, how—corals will cope with rapid environmental change.

Genomic studies have shown that the genomes of early evolved animals such as corals are unexpectedly complex and remarkably similar to those of vertebrates (*3*). It now seems that complexity is the ancestral condition and that more recently evolved invertebrates, such as worms and flies, have over evolutionary time developed derived simplicity. The complexity in corals is evident in cellular pathways central to both symbiosis (*4*, *5*) and biomineralization (*6*). This information is providing a new foundation for developing testable hypotheses on coral physiology.

How do healthy corals maintain a stable partnership with their symbionts (see the figure, panels A and B), and how does this stability collapse under environmental stress? Similar questions have been posed for years in other better-studied host-pathogen and host-parasite interactions (*7*). Investigations of corals can be modeled on these studies. For example, which interpartner signaling events occur during initial contact between the partners? Does the host mount an innate immune response that is in turn modulated by the invading symbiont? And how does interpartner signaling and regulation change during the dysfunction and collapse of a symbiosis?

Recent studies in corals and anemones have started to address these questions. Initial interpartner lectin-glycan signaling events—so well described in other host-microbe interactions (*8*)—are present in corals during the onset of symbiosis, and a wide array of lectins have now been described in anemones (*9*). It remains to be shown to what extent these events confer interpartner specificity and whether there are other signaling mechanisms. Once inside the host cells, symbionts alter host

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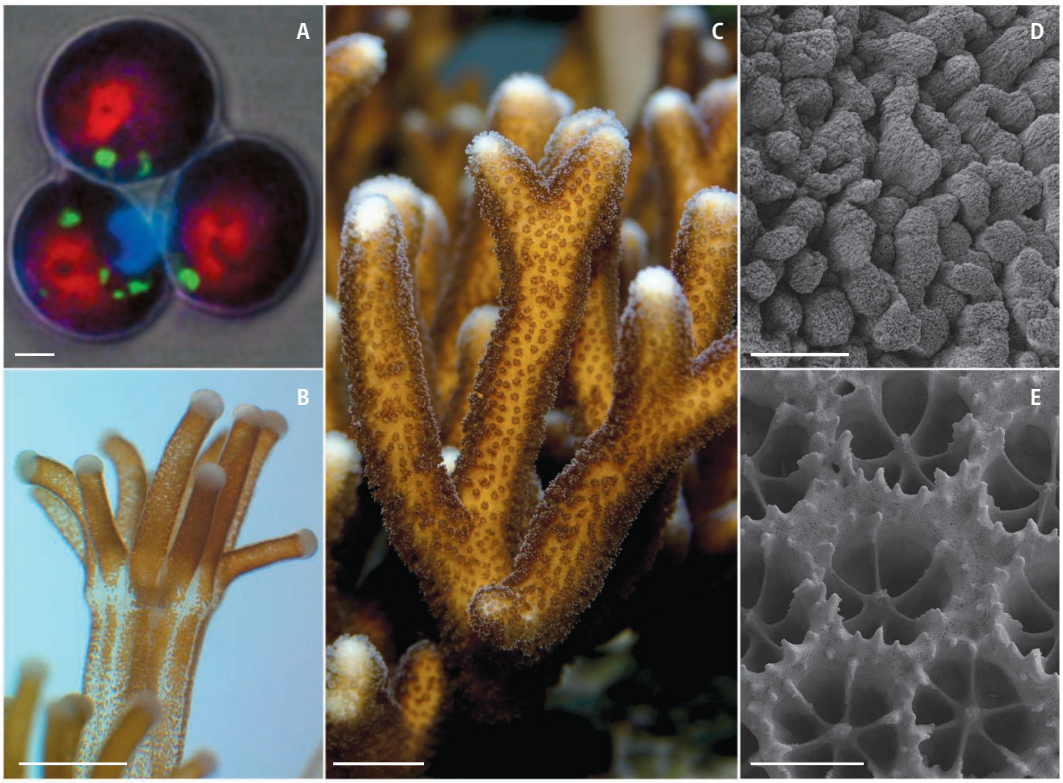

Calcification and symbiosis in the coral *Stylophora pistillata*. (**A**) Confocal micrograph (scale bar 2 μm) of an isolated coral cell with three resident symbionts in red, host mitochondria in green, and cell nucleus in blue. (**B**) Light micrograph (scale bar 0.5 mm) of a single polyp showing brown, spherical symbionts resident within the host. (**C**) A whole coral colony (scale bar 1 cm). Scanning electron micrographs of the skeleton at high [(**D**) scale bar 10 μm] and low [(**E**) scale bar 1 mm] magnifications.

cellular behavior in order to persist—for example, by interrupting host membrane trafficking such that host lysosomes fail to fuse with the vacuoles housing the symbionts (*10*). The same strategy is used by various intracellular parasites of vertebrates to persist within macrophages (*11*). Future cell studies should investigate the dynamics of symbiont invasion of host tissues and the coordination of cell division; genomic and metabolomic studies could provide insight into the types of nutrients moving between partners and the mechanisms of transport and regulation.

Changes to the stability of coral-dinoflagellate symbioses are central to coral bleaching, a phenomenon that results in the loss of symbionts from host tissues (*12*). Bleaching events attributed to global warming are threatening reefs worldwide (*1*). Elevated temperatures, often in concert with high light levels, cause severe oxidative stress in the symbiont that overwhelms its oxygen-handling mechanisms and damages proteins, lipids, and nucleic acids in both partners (*13*).

Bleaching may be a host innate immune response to a compromised symbiont (*14*). Concentrations of the immune effector nitric oxide (*15*) and two pro-apoptotic molecules, p53 and caspase (*16, 17*), are high in heat-stressed animals, suggesting that hosts become intolerant of symbionts and initiate processes to eliminate them. It is not yet clear which cellular events result in the loss of symbionts, but recent studies point to host cell apoptosis and autophagy (*17, 18*), two highly conserved immune mechanisms that are commonly used to eliminate detrimental microbial invaders in vertebrates.

Like symbiosis, calcification is central to coral physiology and health. Corals form the reef structure by biomineralization (see the figure, panels C to E). Biominerals are composite materials consisting of both mineral (calcium carbonate in the case of corals) and organic fractions. Genomic and cellular studies are revealing some pieces of the coral calcification puzzle. Two ion transporters, Ca^{2+}-ATPase (adenosine triphosphatase) and a Ca^{2+} channel, have been identified, and physiological studies suggest the presence of corresponding anion carriers (*19*). The intraskeletal, macromolecular organic matrix is central to the calcification process (*20*). However, whereas about 520 proteins have been identified in the matrix of chicken eggshell (*21*), just one protein has been identified in coral skeleton (*22*), with genomic and proteomic studies suggesting the presence of many others (*20*, *23*).

Regulation of calcification and calcifying cells is controlled by several mechanisms. Calcifying coral tissue expresses carbonic anhydrases, enzymes that interconvert inorganic carbon species critical for calcification (*24*). A homolog to bone morphogenetic protein (BMP), a signaling protein important in the development of mineralizing cells in vertebrates, has been characterized in corals (*6*). Coral BMP localizes to calcifying tissue and binds human BMP-binding proteins, suggesting a common evolutionary origin and function of mineralizing tissue in vertebrates and corals. As in some other mineralizing organisms, calcification in symbiotic corals is enhanced in light, but the physiological basis for this is still debated. Symbiotic dinoflagellates could be providing calcifying host cells with organic precursors for organic matrix synthesis when they are photosynthesizing in the light (*20*).

Calcification by corals is threatened by ocean acidification, caused by the dissolution of atmospheric carbon dioxide into seawater. The resulting decreased pH moves the inorganic carbon balance in seawater away from carbonate, which is required for calcium carbonate deposition. The expected pH decrease by 0.2 units during the next century may decrease calcification rates by up to 50%, as well as promoting skeleton dissolution (*25*).

What causes the extreme sensitivity of corals to decreased pH? The general hypothesis is that a decrease in seawater carbonate concentration is to blame, but this is probably not the whole story, because noncalcifying organisms such as marine worms and fish eggs are also affected by the pH decrease. Another factor may be pH-mediated perturbations in the homeostatic balance within organisms (*26*).

The study of coral physiology has entered an active and exciting era, spurred on by new information from genomic and cellular studies. With the very survival of coral reefs in question, never has the information coming from coral physiology been more important. A deeper understanding of the fundamental physiological mechanisms of symbiosis and calcification will contribute to our ability to predict how and whether corals will be able to adapt to and survive climate change.

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CELL BIOLOGY

Sorting Out Diabetes

Altered trafficking of storage vesicles that harbor a glucose transport protein in muscle and fat tissue may contribute to diabetes.

Charisse M. Orme and Jonathan S. Bogan

Early during the development of type 2 diabetes, insulin's ability to stimulate the cellular uptake of glucose from the blood is compromised (*1*). Muscle is the main tissue responsible for this absorption, and insulin enhances glucose movement into muscle cells through the GLUT4 transporter at the cell surface (*2*, *3*). This hallmark action of insulin is conserved in vertebrates, and the molecular machinery by which it occurs is thought to be similar among mammals. On page 1192 of this issue, Vassilopoulos *et al.* (*4*) identify a key protein that mediates insulin action in humans, but not in mice, a distinction with potential implications for understanding glucose metabolism and diabetes pathophysiology.

During fasting, when the concentration of circulating insulin is low, GLUT4 is sequestered from the plasma membrane, restricting glucose entry into the cell. After meals, an increase in insulin concentration triggers the insertion of GLUT4 transporters at the cell surface to facilitate glucose uptake and storage. Like other proteins that cycle to and from the cell surface, GLUT4 is internalized at the plasma membrane (via endocytosis) into endosomal vesicles. Yet unlike most "recycling" proteins, endosomal GLUT4 is targeted to a specific population of small, preformed vesicles that are poised for mobilization to the cell surface in response to insulin (*5*, *6*). These storage vesicles are present selectively in muscle and adipose tissue. Although much progress has been made toward understanding the intracellular insulin signaling pathways that control GLUT4 translocation, the specific membrane trafficking mechanisms involved remain poorly understood.

Vassilopoulos *et al.* focused on the role of CHC22, a constituent (heavy chain) of the clathrin protein complex, in the transport of GLUT4. Clathrin is a major component of a protein coat that surrounds vesicles involved in transporting proteins among the plasma membrane, trans-Golgi network, and endosomal system (*7*). Clathrin deforms membranes, facilitating vesicle formation. In humans, CHC22 is expressed selectively in muscle, but in mice, it is a pseudogene, and therefore not expressed at all. Vassilopoulos *et al.* show that unlike its ubiquitously expressed cousin, CHC17, which functions in endocytosis, CHC22 participates in a

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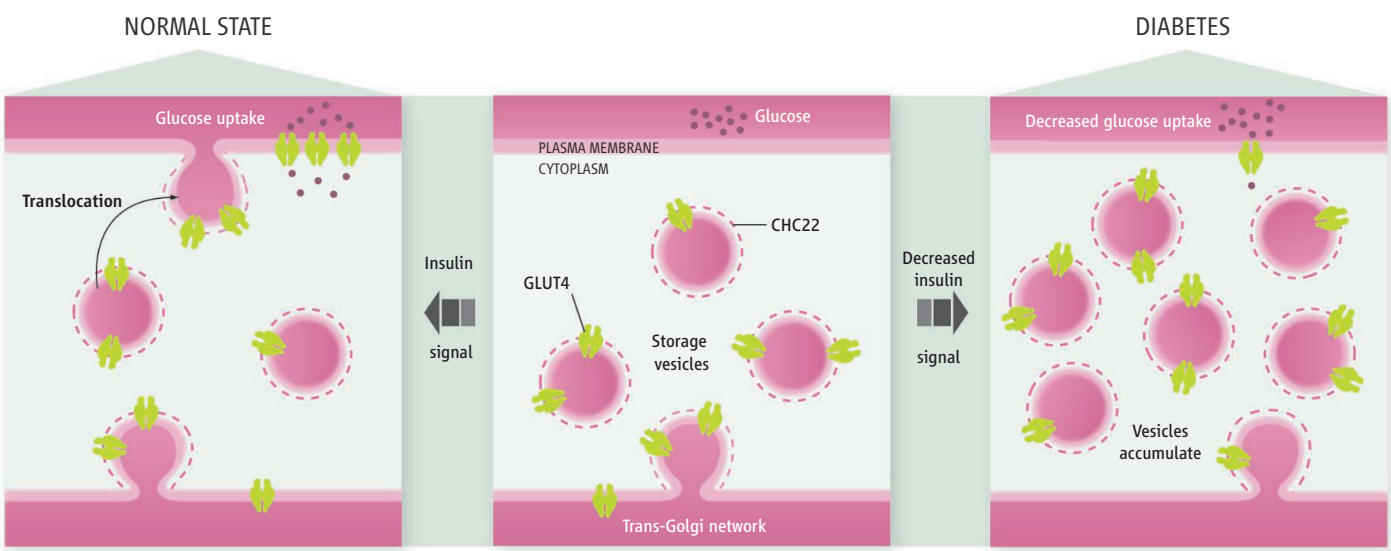

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Transporter sorting. The clathrin protein CHC22 mediates the formation of storage vesicles containing GLUT4 in human muscle cells. In diabetic humans, the storage vesicles accumulate and are not well mobilized to the cell surface by insulin. The vesicles arise from the trans-Golgi network (or possibly from recycling endosomes).

ERRATUM

Post date 10 July 2009

Perspectives: "What determines coral health?" by V. M. Weis and D. Allemand (29 May, p. 1153). The affiliation of Denis Allemand was incomplete. It should have read: "Centre Scientifique de Monaco, Avenue Saint-Martin, MC 98000 Monaco, Principality of Monaco, and Faculty of Science, University of Nice-Sophia Antipolis, F 06108 Nice Cedex 2, France. E-mail: allemand@centrescientifique.mc." The figure credit for panels D and E was incorrect. It should have read: "Panels D and E taken at Centre Commun de Microscopie Electronique, University of Nice-Sophia Antipolis."