

depletion of Grk2 and β -arrestin 2 in cultured mammalian cells and zebrafish embryos blocks Hh signaling (11–13). Smo activation leads to the Grk2-mediated association of β -arrestin 2 with Smo, which then triggers the internalization (endocytosis) of Smo (12).

Kovacs *et al.* investigate the next important question: How does recruitment of β -arrestin 2 to Smo activate signaling? Using RNA interference in cultured mouse fibroblasts, the authors show that depletion of β -arrestin 1 or 2 prevents the movement of Smo to cilia as well as subsequent target gene transcription. The authors propose that Smo trafficking to cilia is mediated by Shh-enhanced association of the Smo– β -arrestin complex with the type II kinesin motor Kif3A. The finding that β -arrestin is required for both endocytosis and ciliary targeting of Smo seems contradictory; however, vesicles that carry Smo to the cilia may originate from the plasma membrane as recycling endosomes rather than directly from an intracellular source (the Golgi).

Kif3A, a component of the kinesin II motor complex, transports protein cargos within cilia. Materials are conveyed along microtubules at the core of the cilium by an elaborate intraflagellar transport system (1). This system is composed of a Kif3A-driven motor complex that moves toward the tip of the cilium and a second complex driven by the motor protein dynein that moves back toward the base. The link between cilia and Hh signaling emerged from the observation that mouse embryos lacking intraflagellar transport components, including Kif3A, have damaged Hh signaling (5).

Mice carrying mutations in the genes encoding Kif3A and other intraflagellar transport proteins suffer from developmental abnormalities caused by a lack of both Gli activator function (such as neural tube defects) and Gli repressor function (such as limb defects) (6). Does the discovery of a Smo– β -arrestin–Kif3A complex shed light on these complex phenotypes? The role of Kif3A in activating Gli proteins is consistent with its role in promoting Smo movement to cilia. However, Kif3A has a second role in Hh signaling that is probably independent of Smo. In the absence of Shh, Kif3A promotes conversion of Gli3 into a truncated repressor form, Gli3R (6). Thus, Kif3A represses target genes by promoting Gli3R formation in the absence of Shh, but promotes Gli activator formation by transporting Smo into cilia in the presence of Shh (see the figure). The switch between these two states may be triggered by the formation of the Smo– β -arrestin–Kif3A complex. This is reminiscent of the dual role played by the motor protein Costal2 in Hh sig-

naling in the fly *Drosophila melanogaster* (7).

Several seven-transmembrane receptors, such as those for somatostatin and serotonin, are located in primary cilia, so an important question is whether these receptors also rely on a β -arrestin–Kif3A complex for their localization. In mammalian photoreceptor cells, Kif3A transports arrestin and the seven-transmembrane receptor opsin through a specialized variant of primary cilia (14). Because many seven-transmembrane receptors associate with β -arrestin, but only a small number localize in cilia, additional factors must control ciliary localization. The Bardet-Biedl syndrome protein complex controls trafficking of seven-transmembrane receptors to cilia (15, 16). Unraveling how these and other mechanisms together regulate movement of transmembrane proteins to cilia will continue to shed light on Hh and other signaling pathways in primary cilia, illuminating new aspects of cell biology and potentially new paths to disease therapies.

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ATMOSPHERIC SCIENCE

Himalaya—Carbon Sink or Source?

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Chemical analysis of hot springs in the Himalaya suggest that the carbon released from mountain forming regions may warm Earth.

In 1845, the French mining engineer Joseph Ebelmen described how atmospheric CO₂ reacts with rock minerals to form dissolved salts and bicarbonate. He envisioned the possibility of a global carbon cycle, in which the CO₂ injected into the atmosphere by volcanoes is first transformed into soluble bicarbonate and then participates in the precipitation of carbonates in the ocean.

Today, the global carbon cycle and its influence on the long-term (million to billion years) evolution of climate are still a matter of research. The theory of plate tectonics gave a better framework for the concept of sediment recycling (1). The role of silicate weathering as a climate regulator has been strengthened by modeling of the carbon cycle (2, 3), a better understanding of the interrelationships with other biogeochemical cycles, and the accumulated data from the geological archive. In addition to this, previously unconsidered CO₂ inputs to

the atmosphere by the Himalayan range have been recently discovered (4, 5).

The key idea of today's carbon cycle models is that Earth sequesters CO₂ degassed from Earth's interior in limestone, thus preventing it from being released into the atmosphere and causing warming. The only valid sequestration mechanism at geological time scales is the weathering of Ca-Mg silicates and subsequent precipitation of carbonate in the ocean. Photosynthesis, weathering of carbonate rocks, and the burial of organic carbon into sediments are all sequestering processes that are balanced by return fluxes (respiration, precipitation of carbonates in the ocean, and oxidation of inland organic matter). But these processes occur on a time scale shorter than millions of years. The most recent estimate of pre-anthropogenic CO₂ consumption flux by silicate weathering reaction is 0.07 PgC/year (6) (see the figure).

Numerous uncertainties in this geological carbon cycle still remain, the principal of those being the amount of carbon entering the atmosphere now and in the past. The degassing flux was estimated based on the flux emitted by volcanoes in different geodynamic contexts and

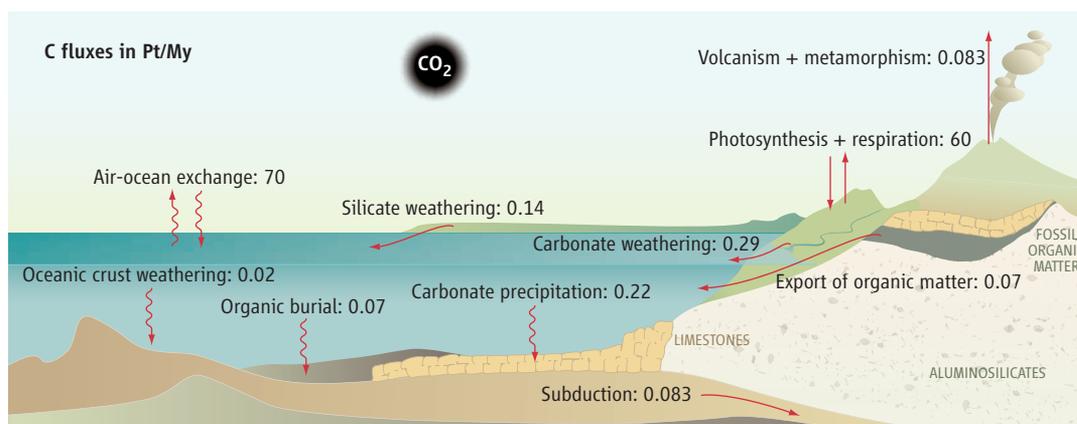
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include carbon from the mantle (magmatic) and carbon degassed from rocks in subduction zones (metamorphic) (7). This flux does not take into account CO_2 derived from orogenic zones (regions of mountain building), where, because of continental collision, organic-rich sediment and limestone may be buried at depths at which CO_2 is formed by metamorphic reactions.

Release of metamorphic CO_2 in collision zones has already been suggested (8). Evans *et al.* (4) have recently attempted to estimate the flux of metamorphic CO_2 based on the chemistry of Himalayan hot springs. They exploit the fact that carbon isotopes are fractionated when dissolved carbon species are transformed into gaseous CO_2 . A fluid containing dissolved carbon will preferentially lose the light isotope of carbon (^{12}C). The isotopic composition of the remaining carbon in the fluid can then be used to estimate the intensity of degassing.

The carbon isotopic composition measured in hot springs located near the main central deformation zone of the Himalayan range indicates that the flux of degassed CO_2 is considerable (up to 97% of the total initially dissolved carbon) (4). The authors concluded that the flux of metamorphic CO_2 injected into the atmosphere is four times the uptake by silicate weathering reactions in the Narayani Basin, a 32,000-km² catchment in Nepal. Extrapolated to the whole Himalayan Arc, the authors propose that metamorphic processes in the Himalaya add 0.02 PgC/year, a quarter of the global flux of CO_2 consumed by silicate weathering. Given the uncertainties in the silicate weathering flux, this result does not necessarily introduce a major imbalance in the global carbon cycle but shows that mountain belts may not be net sinks for atmospheric CO_2 . The results corroborate the conclusion reached by another study based on the composition of carbon isotopes and also on the thermodynamic modeling of the dissolved elements in these hot springs (5). If these studies are correct, then mountain building would inject CO_2 into the atmosphere and would warm Earth.

These conclusions contradict the famous "Raymo" hypothesis (9) that mountains are regions of active physical erosion that sustain high chemical weathering rates because



The geological carbon cycle. The natural regulation of atmospheric CO_2 implies different carbon reservoirs playing roles on different time scales. Ocean and biomass reservoirs play a role at time scales lower than a couple of thousands years. At longer (geological) time scales, carbonate weathering is balanced by carbonate precipitation in the ocean, but the volcanic input of CO_2 to the atmosphere is only compensated by the weathering of Ca-Mg silicate minerals in soils ($\text{CaSiO}_3 + \text{CO}_2 = \text{CaCO}_3 + \text{SiO}_2$). For each mol of C precipitated into carbonate, a mol of C is released to the atmosphere, and the net sequestration of atmospheric carbon is 0.07 PgC/year. The organic sequestration in the form of fossil organic matter buried in sediments is thought to be compensated by the oxidation of ancient organic matter on land (not shown). New findings (4, 5) in the Himalaya lead to a new flux of CO_2 degassing in mountain ranges and make mountains a locus of CO_2 production instead of CO_2 consumption. Fluxes in PgC/year or PtC/My.

these conditions favor the contact of water and mineral surfaces, an idea that is confirmed by the analysis of river data (6). In that case, how could the observed temporal relationship between mountain building and global glaciation periods in the geological record (10) be explained?

There are, however, three assumptions to this scenario. First, Evans *et al.* extrapolate from a measurement of the short-term flux to the geological long-term flux for the whole mountain range. Due to changes over the thermal history, an orogenic zone could well be a source or a sink of CO_2 . Second is that the organic subcycle of carbon in the Himalaya does not differ from the whole organic subcycle of carbon and is not a major flux of CO_2 consumption. This has been recently challenged by Galy *et al.* (11), who showed that the Himalaya scavenges a factor of 10 more CO_2 by organic burial than by chemical weathering. The third assumption questions the time scale at which a mountain range becomes carbon neutral. The CO_2 degassed by the Himalaya will ultimately react with silicate minerals and lead to the formation of carbonate. If these carbonates are incorporated into subduction or collision zones, heated and degassed, they will then liberate the sequestered carbon. On the time scale of this geological loop [typically 20 to 50 million years (My)], the net effect of metamorphic CO_2 on the global carbon cycle, at steady state, is null. If steady state is not achieved and a fraction of sedimentary carbon is re-injected into the mantle and degassed at mid-oceanic ridge or

hot spots, mountain ranges only become carbon neutral on greater time scales of billions of years.

Mountain ranges have several impacts on the global carbon cycle and hence global climate. Whether they are net sources or sinks of atmospheric CO_2 can only be resolved by considering the importance of different processes at their relevant time scales: the consumption of CO_2 by rock weathering (silicate and carbonate), the balance between organic matter burial and oxidation of sedimentary organic matter, and the fluxes of CO_2 degassing. Reconstructing the evolution of Earth's atmospheric CO_2 over geological time will depend on how these mechanisms and their respective time scales interact. Clearly, scanning mountain ground for CO_2 degassing is rich in promise.

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