larger organisms. In flies, however, there is no evidence that Ptc acts as a dependence receptor. Cells that cease to receive an Hh signal, for example, in *smoothened* (*Smo*) mutant clones (*11*), or that express high levels of Ptc (*5*, *12*) in areas outside the organizing region of the wing imaginal disc (anterior-posterior compartment border), survive and proliferate. In the organizing region, cells that do not receive an Hh signal do not die, but a complete block in Hh signaling in the wing primordium prevents the activation of other morphogenetic signals such as Decapentaplegic (Dpp) (*13*), leading to inhibition of wing development (*14*). In the *Drosophila* Ptc receptor, the consensus caspase recognition site is missing. This is not entirely unexpected because in both nematodes and flies, extrinsic death receptor activation of caspases seems to be absent (*15*). It is possible that Ptc-induced apoptosis could be a late evolutionary acquisition that was never present in insects, or that insects eliminated this function over the course of evolution.

Beyond normal development, the finding that Ptc1 may be a proapoptotic dependence receptor could have important implications for our understanding of human cancer. PTCH1 is a tumor suppressor protein that is mutated in patients with basal cell nevus syndrome (*16*, *17*) and in cells of various types of sporadic tumors, including those of the skin and brain [reviewed in (*18*)]. Mice carrying Ptc mutations also develop tumors of the cerebellum (medulloblastomas) (*19*). Mutations in PTCH1 may be one of the many ways in which the HH pathway is switched on, leading to activation of GLI transcription factors and the initiation of tumor formation [reviewed in (*18*)]. Indeed, expression of GLI1, a marker of HH pathway activation, is the hallmark of sporadic tumors such as basal cell carcinomas and medulloblastomas that arise from inappropriate HH pathway activity (*20*, *21*). Misexpression of GLI1 is sufficient to induce basal cell carcinoma–like tumors (*20*, *21*); and medulloblastomas and basal cell carcinomas require an active SHH-GLI pathway for maintained proliferation (*21*, *23*, *24*). In this context, the results of Thibert *et al.* suggest an additional twist. Is it possible that null mutations in PTCH1 leading to the absence of caspase-mediated cell death and pathway activation allow certain cells to survive and initiate tumorigenesis? Such a scenario could provide a possible reason for why PTCH1 loss-of-function mutations (versus those in other HH pathway components) are common in sporadic tumors: two effects for the price of one component. Nevertheless, given that the absence of Shh can induce PTCH1-mediated apoptosis, why does the activation of SHH pathway components downstream of PTCH1 [including SMOH (*25*, *26*)] in the apparent absence of SHH result in tumorigenesis? Can these components talk back to PTCH1 or prevent PTCH1-mediated apoptosis? Or is there a tonic level of SHH required to inhibit PTCH1-induced apoptosis and allow cancer growth?

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CLIMATE

Taking the Pulse of the Tropical Water Cycle

Georg Hoffmann

Oxygen isotope signals from high-altitude glaciers in the Andes (see the first figure) provide unique insights into past climate variability in the tropics (*1–3*). Some of these ice cores go back to the last glacial period and have proved that rapid climate variability such as during the Younger Dryas, a cold period at the end of the last glacial, affected the tropics at least as far south as 20°S.

In these tropical records, the isotopic shift from glacial to modern climate is about the same as in the better understood polar isotope records (5 to 6‰ in $\delta^{18}O$, where $\delta^{18}O$ is the ratio of ^{18}O to ^{16}O in the sample relative to a standard). The signals were therefore originally interpreted in terms of temperature, similar to those in Greenland or Antarctica (*2*).

In mid- and high latitudes, this interpretation is justified, because the isotopic composition of precipitation is largely controlled by temperature fluctuations on all time scales, from seasonal and interannual to glacial-interglacial. But in the tropics, things are more complicated. As well as temperature, factors such as amount of precipitation, intensity of water vapor recycling, and circulation changes affect $\delta^{18}O$. Several recent publications have taken a fresh look at how oxygen isotope records from the tropics should be interpreted.

Over the 20th century, ice cores can be dated relatively precisely, and direct observations are available. Vuille and co-workers (*4, 5*) analyzed the oxygen isotope variability in the tropical Americas from 1979 to 1998 with two different atmospheric general circulation models (GCMs) fitted with oxygen isotope tracers. They concluded that the isotopes are strongly influenced by precipitation anomalies caused by El Niño–Southern Oscillation (ENSO) on seasonal and interannual time scales.

During El Niño, rainfall amounts tend to be higher than normal west of the Andes and lower than normal on the Altiplano and in the Amazon basin (see the first figure). Although atmospheric temperatures are higher throughout the Central Pacific and the tropical Americas during El Niño, the oxygen isotopes are dominated by these precipitation changes. As a result, precipitation is isotopically depleted (low $\delta^{18}O$) over the tropical Pacific and enriched (high $\delta^{18}O$) on the Altiplano and in the Amazon basin.

Tropical South America varies between a warm/dry mode (El Niño) and a cold/wet mode (La Niña). Therefore precipitation and temperature act in concert to produce the Andean oxygen isotope signal (which is enriched during El Niño). This mechanism controls the oxygen isotopes in all available Andean ice core records (*1, 2, 6*). Throughout the 20th century, the records are closely correlated, even though the glaciers are situated in different climatic zones. The dominant variability in all records is decadal, unlike the typical ENSO variability of 2 to 5 years seen in most other tropical records. This difference may be a result of dating problems, smoothing of the snow after precipitation, or the variable influence of ENSO on precipitation in South America.

To aid comparison with other tropical records (*7–9*), an Andean Isotope Index

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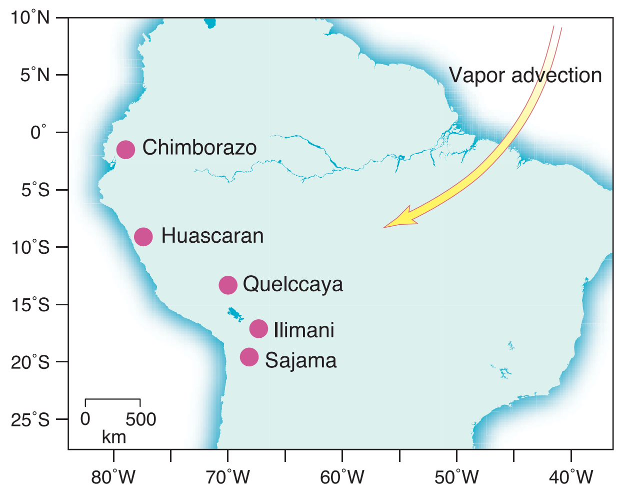


Tropical South America. Isotope records from four Andean sites have been used to construct the Andean Isotope Index (AII). The sites are Huascaran, Peru (*3*), Quelccaya, Peru (*1*), Illimani, Bolivia (*6*), and Sajama, Bolivia (*6*). An unpublished record from Chimborazo, Ecuador, shows similar decadal variations as the AII in the 20th century. The strong correlation between these records is a result of their common moisture origin in the tropical Atlantic and recycling in the Amazon basin.

(AII) has been constructed from the arithmetic mean of the four published Andean isotope records (*6*). In the second figure, this index is compared to three other tropical records. Similar to AII, the records are dominated by variability on a decadal time scale.

Precipitation observations in the 20th century were analyzed on a global scale and the found variability was associated to known climate modes (*7*). The leading spatial pattern of global precipitation is marked by negative precipitation anomalies over the Amazon basin when ENSO is in its high phase, and positive precipitation anomalies over the basin when ENSO is in its low phase. The pattern explains about 10% of the variability in the Tropics. These precipitation anomalies are the consequence of a displacement of the uprising and convectively active branch of the Hadley-Walker cell over tropical South America triggered by SST anomalies (*10*). Comparison of the temporal evolution of this precipitation pattern and SST records (see the second figure) with the AII provides convincing evidence for the influence of central Pacific temperatures on the oxygen isotopes via atmospheric teleconnections and precipitation anomalies.

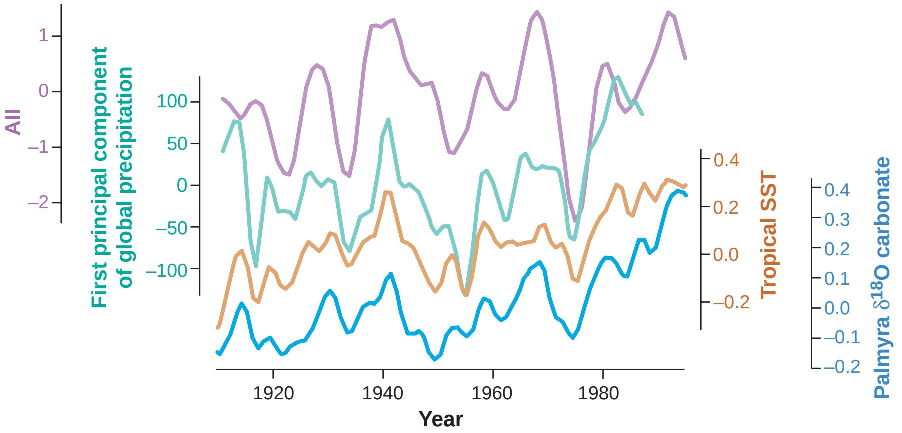
This comparison shows that past decadal variability in the tropics in both atmosphere and ocean can now be examined with a combination of terrestrial records (such as the AII) and marine records (such as coral records). However, extending the reconstruction of the AII, which could potentially go back to at least the 18th century, will require improved absolute dating of the ice core records (*11*).

What do these findings imply for the interpretation of the glacial-interglacial isotopic shift of about 5 to 6‰ seen in the tropical ice core records? Applying the relation between Pacific SSTs and the Sajama ice core record from 1961 to 1997 to the glacial-interglacial isotope shift, Bradley *et al*. (*12*) estimated that at the time of the last glacial, temperatures in the tropical Pacific were 3.5°C lower than today. This value is close to estimates of ~3°C inferred from other techniques (*13*). However, if this decadal calibration on such a long time scale is justified, it would mean that Pacific SSTs influence the oxygen isotopes through precipitation changes over tropical South America. Such a connection should lead to much wetter than modern conditions in the entire region (*14*). At least for the Amazon basin, this is in conflict with other indicators (*15*).

Although the decadal patterns of all records in the second figure are quite similar, the trends differ substantially on longer time scales. The oxygen isotopes over the Andes are sensitive to rainout intensity and convection height. They remain roughly steady during the 20th century, whereas the other records show a rising trend since the 1970s. The isotopes may thus be more sensitive to changes in tropical SST gradients than to tropical warming or cooling.

GCMs fitted with oxygen isotope tracers and forced with 20th century SSTs can successfully simulate the decadal variability in the AII (*6*). Use of these modeling tools will allow further investigation of the apparent decoupling of the oxygen isotopes from climate parameters such as SSTs and regional precipitation at different time scales. In particular, the effects of changes in the mean state of the tropical Pacific on the oxygen isotope signal should be studied both for a future greenhouse and for the last glacial.

It is now clear that the Andean ice core records track the pulse of the tropical hydrological cycle. But although we understand a little better what makes this cycle tick, we are still some way from a full diagnosis of its condition.



Tracking the tropical water cycle? Global, in particular, tropical, precipitation patterns change as a result of ENSO-associated SST changes. The Andean Isotope Index (AII) reacts to the varying rainout intensity over tropical South America. Here, the AII is compared with three observational series that track these different aspects of tropical climate: the temporal evolution of the leading mode of global precipitation (that is, the first principal component) (*10*); tropical Indo-Pacific SSTs (*11*); and carbonate $\delta^{18}O$ from a central Pacific coral, reflecting mainly sea surface temperature fluctuations (*12*). All records were low-pass filtered with a cutoff frequency of 5 years.

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