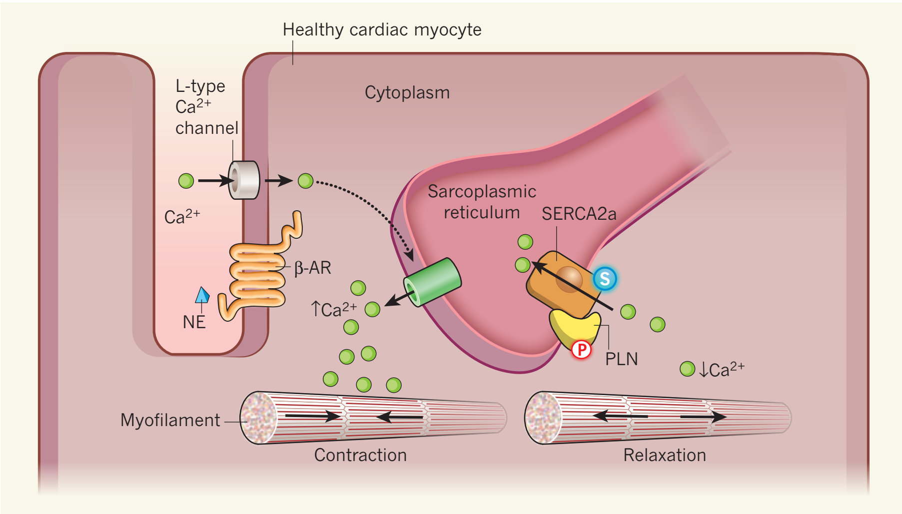

Figure 1 | The SERCA2a calcium pump and its modification by SUMO1. In a healthy cardiac myocyte, noradrenaline (NE) released from sympathetic nerves stimulates β-adrenergic receptors (β-AR) to enhance the activity of L-type calcium-ion (Ca^{2+}) channels on the cell membrane, leading to Ca^{2+} entry into the cell. This in turn triggers the release of a large amount of Ca^{2+} from the sarcoplasmic reticulum into the cytoplasm, and leads to myofilament contraction. Noradrenaline stimulation also causes phosphorylation (P) of phospholamban (PLN), releasing its inhibitory effect on the sarcoplasmic-reticulum Ca^{2+}–ATPase pump, SERCA2a. Activated SERCA2a binds Ca^{2+} ions from the cytoplasm and pumps them back into the sarcoplasmic reticulum, allowing the myofilaments to relax. Kho *et al.*[1] show that only SERCA2a modified by SUMO1 (S) can transport Ca^{2+} ions and maintain a healthy heart. In a failing heart (not shown), SUMO1 is depleted and SERCA2a remains in the un-SUMOylated form. It therefore cannot bind ATP and cannot effectively pump Ca^{2+} back into the sarcoplasmic-reticulum lumen, so relaxation of cardiac muscle is impaired.

that are known to be mutated in patients with familial dilated cardiomyopathy and those with conduction-system disease, suggesting that these disorders may also be attributable to defective SUMOylation[9].

However, SUMO1 deficiency also causes degradation of the transcription factor SRF by caspase enzymes[9], which are involved in programmed cell death. Therefore, restoring SUMO1 activity by introducing the SUMO1 transgene may block this and other cell-death pathways in the failing heart and lead to the observed recovery. Further investigation is needed to determine the cause of the reduced SUMO1 levels seen in heart failure: the protein does not undergo degradation and there is no evidence that gene transcription is inhibited.

In contrast to the stimulation of SERCA2a by SUMO1, some potassium-ion channels in the cell membrane are inhibited by SUMOylation[10,11]; they regain their ion-selective activity when SUMOylation is blocked or reversed. Furthermore, there is evidence that SUMOylation could be critical for transport processes into the nucleus[6,12]. It might therefore also facilitate Ca^{2+} transport across membranes, for example by imparting structural features of an 'on/off' switch to the ion channels.

Kho *et al.*[1] suggest that targeting SUMO1 could be an attractive approach to modifying specific pathogenic molecular pathways in heart failure. Although the results look promising, some caution is warranted. SUMO1 is ubiquitous in its expression and biochemical function, and many of the heart's regulatory proteins and transcription factors are known to be SUMOylated[9,13], which could interfere with target specificity. Dysregulation of SUMO conjugation can contribute to the progression of some human cancers[6]. Also, SUMO1 might bind to other proteins that modulate SERCA2a either directly or indirectly, leading to unwanted changes in Ca^{2+} handling[9,13]. Nonetheless, therapeutic targeting of SUMO1 to treat heart failure remains an attractive proposition and should lead to new areas of investigation[5]. ■

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CARBON CYCLE

A dent in carbon's gold standard

The global uptake of carbon by land plants may be greater than previously thought, according to observations based on the enigmatic Keeling curve of rising atmospheric carbon dioxide. SEE LETTER P.579

MATTHIAS CUNTZ

Estimates of how much carbon is taken up each year by the world's land plants are derived mainly from models of the carbon cycle. Worldwide measurements of terrestrial carbon exchange have yielded an estimate[1] of this global carbon uptake as 123 ± 8 petagrams carbon per year (Pg C yr^{-1}; 1 Pg is 10^{15} g). This is so close to earlier estimates derived from models and biomass production that 120 Pg C yr^{-1} can be taken as carbon's 'gold standard'. But Welp and colleagues[2] remind us, on page 579 of this issue, that we should not be complacent — land ecosystems might be taking in considerably more carbon than we thought.

Our atmosphere is a perfect blender. Changes in its levels of trace gases — such as carbon dioxide — reveal variations in the total influx and uptake of its constituents. So if you measure the carbon exchange of a forest ecosystem, for example, you get the net exchange of all the carbon taken up by the trees for photosynthesis and all the carbon released by the trees and soils through respiration. These gross-exchange fluxes — photosynthesis and respiration — are much larger than the net ecosystem exchange that is actually measured. On the global scale, the net flux is only a few per cent of the gross fluxes. Because small changes in photosynthesis and respiration can have big consequences for the net carbon uptake of terrestrial ecosystems, the interplay between photosynthesis and respiration must be well described in carbon-cycle models if they are to reliably project into the future. It is, however, almost impossible to measure individual components on scales larger than the size of a leaf, let alone on a regional or continental scale.

This is where Welp *et al.*[2] take advantage of the composition of oxygen isotopes in CO_2 — the chemical signature of which changes if one ^{16}O oxygen atom in CO_2 is replaced by a heavier ^{18}O atom. Carbon dioxide dissolves in water and exchanges its oxygen with water's oxygen to equilibrium, so CO_2 is tagged by the water it comes into contact with. Different waters have distinct isotopic compositions owing to evaporation processes in soils and leaves — the lighter molecules evaporate faster, and the heavier ones fall behind. As a result, the oxygen isotopic composition in CO_2 is very sensitive to photosynthesis and respiration: more photosynthesis means more ^{18}O, and hence higher oxygen-isotope ratios in the atmosphere.

Using an impressive 30-year record of the isotopic composition of atmospheric CO_2, Welp *et al.*[2] assess the mean atmospheric residence time for oxygen atoms in CO_2. Their 11 time series were started in the 1970s by the late Charles Keeling, alongside the famous record of total atmospheric CO_2 at Mauna Loa in Hawaii (Fig. 1). Welp *et al.* identified a strong correlation between the observed interannual variability of the oxygen isotopes and the El Niño–Southern Oscillation (ENSO). Such a correlation has previously been established for the isotopic composition of water[3] and, consequently, is now found in the oxygen isotopes of CO_2 as well. From the mean residence time of the oxygen atoms in CO_2, Welp *et al.* arrive at a best guess of global productivity of 150–175 Pg C yr^{-1} — some 25–45% more than the gold standard.

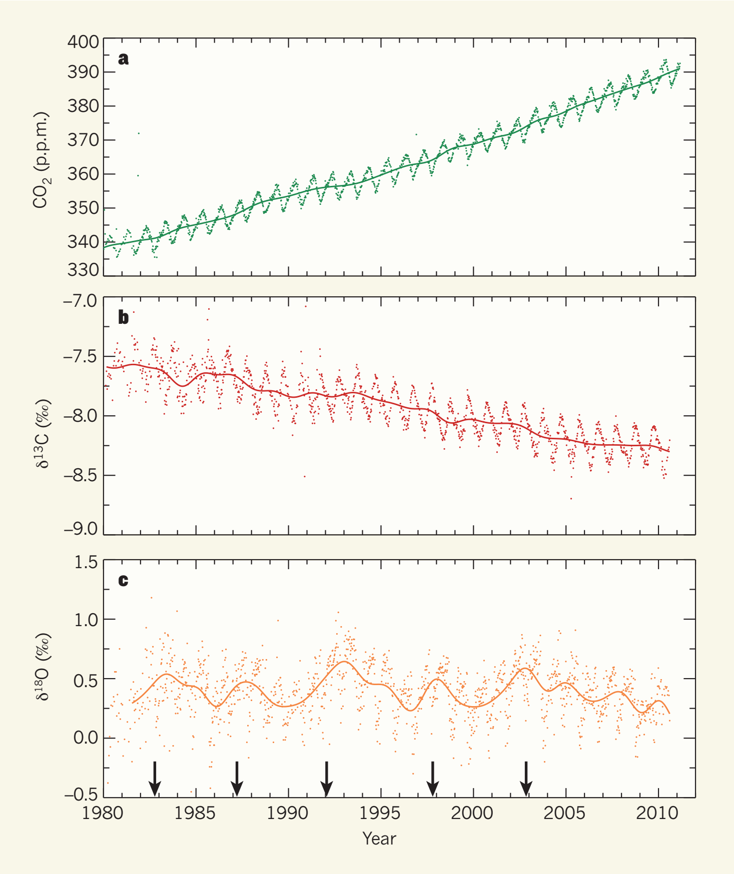

Figure 1 | Atmospheric CO_2 concentrations and isotope composition measured at Mauna Loa, Hawaii. a, Keeling curve of CO_2 concentrations since the 1980s (ref. 7). Dots are single measurements or daily averages; line indicates the long-term trend. **b**, Carbon-isotope composition of the CO_2 at Mauna Loa. Here, $\delta^{13}C$ is the deviation of the $^{13}C/^{12}C$ ratio from a standard value. Because the carbon cycle is the major influence on both CO_2 concentrations and $^{13}C/^{12}C$ ratios, the curves in **a** and **b** correlate well with each other (that is, the downward trend in **b** mirrors the upward trend in **a** and so do the seasonal variations). **c**, The oxygen-isotope composition of the CO_2 is influenced not only by the carbon cycle, but also by the water cycle, and so does not correlate simply with CO_2 concentration; $\delta^{18}O$ is the deviation of the $^{18}O/^{16}O$ ratio from a standard value. Welp and colleagues[2] find that the interannual variations in $\delta^{18}O$ correlate with the El Niño–Southern Oscillation (arrows indicate El Niño events). Their analysis of the oxygen-isotope data also provides a new estimate of global carbon uptake on land. p.p.m., parts per million. (Data are publicly available on the Scripps Institution of Oceanography website[8].)

This inference hinges on a set of assumptions and estimates. It depends, for example, on how many CO_2 molecules actually enter a plant before one molecule is fixed by photosynthesis. The authors think that plants eventually fix some 43% of all CO_2 molecules entering a leaf; however, if this were only 34%, the isotope-based estimate would fall to about 120 Pg C yr^{-1}, the current gold standard.

The global value of 43% is derived from carbon-cycle models and remains uncertain, because it depends on the details of the models' formulation. It also depends on the distribution of different plant types. For example, some savannah grasses and maize (corn) fix carbon more efficiently through the C_4 metabolic pathway, rather than by the usual C_3 route, thereby enabling them to fix about 60% of the CO_2 molecules that enter the plant. Hence, the global abundance and distribution of C_4 plants are important in estimates of global productivity, whether these are derived from modelling, actual measurements or isotope-composition data. One carbon-cycle model, for example, increased global productivity by more than 20% simply by substituting a new map of C_4-plant distribution[4].

So it looks as though we are stuck with model-based estimates that are hard to validate globally. But other isotopes might yet come to the rescue: the isotopic composition of the carbon atoms in CO_2 provides a measure of the percentage of carbon that is fixed[5]. This could constrain estimates such as that offered by Welp *et al.*, but it could also constrain C_4-plant distribution and therefore help non-isotopic estimates of global production as well. And the carbon-isotope estimate of the percentage of carbon that is fixed might be further refined with the help of carbonyl sulphide, a new tracer of leaves' ability to take up CO_2 (ref. 6).

Gold does not tarnish easily. With their approach, and by making their long-term records publicly available, Welp and colleagues[2] are preparing the ground to combine these pieces of information and polish up carbon's gold standard of the future. ■

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