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Notch1, together with Manic Fringe, into Chinese hamster ovary cells, and analysed the resulting spectrum of *O*-linked sugars (these rare glycosylation patterns had already been seen in a particular class of EGF motif found in Notch[10]). The authors found that Manic Fringe adds *N*-acetylglucosamine to fucose through an unusual linkage. They confirmed their results by *in vitro* assays using different Notch1 constructs, and showed that the effects of Fringe on Notch signalling depend on *O*-linked — but not *N*-linked (asparagine-linked) — glycosylation pathways.

Brückner *et al.*[2] took a different approach. They prepared cellular fractions containing recombinant Fringe, and showed that they specifically catalyse the addition of *N*-acetylglucosamine onto fucose, and not the transfer of other donor sugars onto other acceptor sugars. They also conclude that Fringe extends *O*-linked fucose chains on Notch. Supporting evidence comes from Munro and Freeman[4], who show that Fringe — like many known glycosyltransferases — can be crosslinked to the nucleoside diphosphate UDP. And Fringe's active-site motif, DxD (where D denotes asparagine and x denotes any amino acid), is essential for Fringe's function in biochemical assays[1,2] and transgenic flies[1,4].

Where does glycosylation of Notch by Fringe take place? Early studies indicated that Fringe might be secreted from the cell, although this idea was always difficult to reconcile with genetic data showing that Fringe acts on Notch in the same cell. But it seems that Fringe — like other glycosyltransferases — actually functions in the Golgi apparatus[2–4], an organelle in the cellular protein-secretory pathway. Fringe localizes to the Golgi in mammalian fibroblast cells[3] and *Drosophila* cells[2,4]. Forced secretion of Fringe out of the cell reduces its ability to function *in vivo*[4], whereas its forced retention in the Golgi has few or no consequences[2]. Hicks *et al.*[3] show that Fringe must be expressed together with mammalian Notch1 in the same cell to have an effect on Notch signalling. It has no effect when expressed by the ligand-presenting cell or in a soluble secreted form. Brückner *et al.*[2] note similar effects of *Drosophila* Fringe. So, at least for full-length Notch, effective *O*-linked glycosylation might need to occur during its folding or maturation in the Golgi. This interaction between Notch and Fringe is presumed to be transient, contrasting with evidence that the two proteins associate in a stable complex[11].

Some details remain to be hammered out. For example, does Fringe affect the binding of ligands to Notch, or some other aspect of the ligand–receptor interaction? Brückner *et al.*[2] report that Fringe dramatically improves the binding of Delta to Notch, but were unable to detect the binding of Serrate, irrespective of the presence of Fringe. Moloney *et al.*[1] and Hicks *et al.*[3] show, however, that Fringe has no measurable effect on ligand binding to Notch, and suggest that glycosylation may instead influence ligand-induced conformational changes in Notch. This discrepancy might reflect the fact that Brückner *et al.* worked mainly with Delta, while Moloney *et al.* and Hicks *et al.* concentrated mainly on Serrate/Jagged. Alternatively, it might result from differences in methodology.

This body of work has finally settled the question of whether or not Fringe has glycosyltransferase activity, and offers a stunning example of how an important signalling pathway can be modulated by differential receptor glycosylation. Although Fringe is clearly not essential for Notch signalling, the glycosylation of signalling components is likely to be of widespread relevance. Both *Drosophila* and mammals possess proteins with limited similarity to Fringe and with distinct glycosyltransferase activities or substrate preferences. The human disease multiple exostosis is caused by mutations in glycosyltransferases[12], and deficiencies in fucose metabolism are known to underlie leukocyte-adhesion deficiency type II[13]. Perhaps we will also find mutations or variants of the human Fringe genes that result in human diseases. Such an event would surely lead to increased appreciation of the importance of protein–carbohydrate interactions in signal transduction and human biology. ■

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Global change

Silica control of carbon dioxide

Paul Tréguer and Philippe Pondaven

There is a popular view that the availability of iron, a trace nutrient, is a prime determinant of phytoplankton productivity in the oceans. But there are plenty of other influences on this primary productivity. Writing in *Paleoceanography*[1], Kevin Harrison looks at the role of silica and argues that variations in silica's oceanic cycle would have altered the species composition of phytoplankton. The implications are considerable: such alterations are likely to have had a large effect on levels of CO_2 in the atmosphere.

Dissolved CO_2 in the surface ocean is taken up by phytoplankton through photosynthesis, a process that requires nutrients such as nitrate, phosphate and silicate (dissolved silica), and trace metals that are available in surface waters only in limited amounts. Through respiration and microbial activity, CO_2 is then released back to the atmosphere. In principle, CO_2 uptake from and release to the atmosphere are balanced. But when more of the photosynthetic production is exported from the surface ocean to the depths, in the form of the remains of phytoplankton and other organic matter, more carbon is retained in the ocean and less returned to the atmosphere. This flux of carbon to the deep ocean is called the biological carbon pump.

It has already been hypothesized[2] that, in the equatorial Pacific, this pump is triggered by the availability of silicate. Harrison now takes the idea a lot further. He shows how variations in silicate inputs to the surface ocean can control levels of atmospheric CO_2 on a global scale. In particular, he considers that silicate controls can explain the rise in atmospheric CO_2 that occurred at the end of the Last Glacial Maximum, about 18,000 years ago, during the transition from glacial to interglacial conditions.

During the Last Glacial Maximum, atmospheric concentrations of CO_2 were 40% lower than they are now. Cores from polar ice sheets and from deep-sea sediments have revealed that more dust was delivered from the land to the ocean during glacial times. Dust contains iron, an essential trace metal for various marine microscopic algae. Hence the case for the 'iron hypothesis'[3], which holds that variations in atmospheric CO_2 are related to iron inputs to the ocean surface. In principle, the more iron delivered to the ocean, the greater is the photosynthetic activity and export of carbon from surface to deep waters. In turn, this implies that more CO_2 is extracted from the atmosphere than is returned to it, the balance being locked up in carbon sequestered in the ocean depths.

The iron hypothesis has been useful in

	Modern ocean	Last Glacial Maximum
Wind-borne silica	0.5	3.7
Primary production		
Carbon	3,827	3,827 (0%)
Silica	268	396 (+48%)
Export flux		
Carbon	241	320 (+33%)
Silica	134	198 (+48%)
Contribution to biomass (%)		
Diatoms	54	79
Non-siliceous phytoplankton	46	21

Figure 1 **The oceanic effects of higher silica inputs during the Last Glacial Maximum as compared with modern (interglacial) times. Units are teramol yr^{-1} (10^{12} mol yr^{-1}). The model from which these results come is based on that of Tyrrell[7], with inclusion of the ocean silica cycle[6]; river–ocean nutrient fluxes are assumed to be the same for both cases. In accordance with Harrison's new work[1], wind-borne silica input was set at 7.4 times higher in the Last Glacial Maximum. The argument is that conditions favouring siliceous diatoms (meaning fewer CO_2-generating non-siliceous species), and the increased export of carbon from surface waters to the deep ocean, can explain the lower levels of atmospheric CO_2 during the Last Glacial Maximum.**

explaining the low primary productivity of the nutrient-rich modern equatorial Pacific and Southern Ocean, caused (so the argument runs) by iron limitation. But its validity in periods in the past is questionable. For instance, after the decrease in dust delivered to the ocean at the end of the Last Glacial Maximum it took about 8,000 years for levels of atmospheric CO_2 to increase to those typical of interglacial periods. Because the residence time of iron in the ocean is only a few tens of years[4], iron alone cannot account for the variations in atmospheric CO_2 during this glacial–interglacial transition[5]. Consideration of conditions in the terrestrial biosphere during the transition, or of the physics of the ocean, cannot help much in explaining these variations[1]. So answers must be sought in changes in ocean biogeochemistry.

Harrison[1] concentrates on silicate, which has a residence time of about 15,000 years[6] — enough time to allow for the slow rise in atmospheric CO_2 after the decrease in dust delivery at the end of the Last Glacial Maximum. Harrison challenges the iron hypothesis. He points out that material transported by wind from land to sea also contains silica, which dissolves at least partly in the surface ocean. Silicate is needed by diatoms to build up their siliceous cell walls, and increasing silicate availability in the ocean favours the growth of diatoms over non-siliceous species of phytoplankton. A significant part of these non-siliceous species consists of coccoliths, which have shells of calcite (calcium carbonate). Counterintuitively, the production of calcite (by reaction between dissolved calcium and hydrogen carbonate) results in the production of dissolved CO_2, which can escape from the surface ocean to the atmosphere.

So dominance of diatoms over coccoliths means decreased calcite production in sea water and lowering of the flux of CO_2 from the surface ocean to the atmosphere. The result is a net decrease in atmospheric CO_2. To account for 40% less atmospheric CO_2 in the Last Glacial Maximum than in the ensuing interglacial, Harrison needs a dust-borne silica flux to the ocean that is higher by a factor of about seven. That figure is supported by the evidence from marine sediments.

During the Last Glacial Maximum, how did the biological carbon pump respond to the higher inputs of dust? To answer this question, we carried out a complementary calculation to Harrison's[1]. We used a simple biogeochemical two-box model, derived from that of Tyrrell[7], incorporating the ocean silica cycle and different key species of phytoplankton. Assuming, like Tyrrell[7], that phosphorus is the ultimate limiting nutrient, we found that increasing silicate dust inputs by a factor of about seven does not change the total primary production. But in the model, production becomes dominated by diatoms rather than non-siliceous species (Fig. 1). The generation of biogenic silica rises by about 50% over that of the best estimate for the modern ocean[8], and the export flux of organic carbon, mainly from siliceous organisms, rises by 33%. All in all, then, reduced CO_2 output from non-siliceous organisms and higher carbon sequestration in the ocean depths can account for the lower levels of atmospheric CO_2 during the Last Glacial Maximum. Likewise, changes in silicate control can explain the glacial–interglacial rise in CO_2.

There are other considerations, however, which have not been taken into account here. During the Last Glacial Maximum, not only was the wind-borne flux of silica dust different to that under interglacial conditions, but so too was the delivery of nutrients from rivers into the ocean. River inputs of silicate to the modern ocean are an order of magnitude higher than those from wind-borne dust[6]. So any reduction in river inputs would greatly affect calculations based on Harrison's scheme. However, Froelich *et al.*[9] have shown that the flux of silicate from rivers to oceans was even higher during the Last Glacial Maximum than it is now; that would further favour the dominance of diatoms over other phytoplankton species.

We have a long way to go before we have a secure appreciation of the links between nutrients, phytoplankton productivity and CO_2 in the atmosphere. But, at the least, Harrison's 'silica hypothesis' is a fresh illustration of how central marine biogeochemistry is in understanding the long-term variation of atmospheric CO_2 and of Earth's climate. ■

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Earth science

The extraterrestrial wedding ring

Richard J. Walker

A topic of hearty debate amongst geochemists is the origin of the so-called highly siderophile ('iron loving') elements in the Earth's mantle. This is a group of elements that includes two of our most highly prized commodities, gold and platinum. Put simply, there isn't much of them in the mantle, but there is a lot more than might be expected. In the paper on page 396 of this issue[1], Holzheid *et al.* lend weight to a theory that invokes an extraterrestrial explanation for this puzzle.

Apart from gold and platinum, the siderophile elements include iridium, osmium, palladium, rhenium, rhodium and ruthenium. They are characterized by their extreme affinity for metal (iron) magmas, and have a 10,000 times greater preference to partition into these magmas than the silicate magmas from which the mantle is largely formed. Consequently, during primary differentiation of the rocky planets into cores and mantles, these elements were almost totally concentrated in the metallic cores. In the Earth, for instance, about 99.99% of the planet's budget of highly siderophile elements resides in the core (which is not, alas, accessible for mining).

What Holzheid and colleagues have done is provide new experimental data suggesting that the highly siderophile elements were added to the Earth from meteorites after the