involve the presence of engulfing cells, and occur by at least two distinct mechanisms[9].

One is a form of cell death called entosis, in which living cells that are destined to die invade a neighbouring cell and become engulfed[10]. Another mechanism is cellular cannibalism, in which living cells that will be ingested are targeted by a type of engulfment that resembles phagocytosis — the process typically used by immune-system cells such as macrophages to ingest and destroy dying cells[9]. Such cellular murders can support the survival of particular cells in a population that benefit from the metabolic banquet derived from ingesting and degrading whole cells[11,12].

The authors examined the mechanism of senescence-associated engulfment and found that, although entosis could occur in the type of tumour cell studied, the engulfment of senescent cells did not involve the proteins required for entosis[10]. The authors analysed the gene-expression profile of cancer cells treated with chemotherapy drugs (most of these cells were senescent), and found that genes characteristic of phagocytosis were expressed. This gene expression peaked within a timeframe that correlated with the cellular engulfment. Senescent cells were also observed to engulf dead cells added *in vitro*, providing further evidence for the authors' model that senescent cells engulf cells by phagocytosis.

Cell cannibalism in cancers has been reported previously[9,12]. However, Tonnessen-Murray *et al.* specifically identify an association between cannibalism and senescence, and show that this phenomenon might make a substantial contribution to the persistence of senescent cells in cancer tissues. The authors observed that cannibalism by senescent breast cancer cells occurs irrespective of whether or not the cell has functional p53, a notable tumour-suppressor protein that can control entry into senescence[13]. The authors tested chemotherapy-induced senescent cells of other types of cancer, including lung cancer and a bone cancer called osteosarcoma, and found that these cells also cannibalize neighbouring cells. Together, these findings suggest that cell cannibalism might be an activity that is broadly associated with the induction of senescence, rather than being linked to particular types of cancer or to the status of proteins such as p53. It will be important to investigate whether cannibalism is linked to senescence in other contexts, for example during tissue development when senescence can occur[14,15], or in aged tissues that accumulate senescent cells[3].

Entosis in cancer-cell populations can promote competition between individual cells in which 'winner' cells ingest and kill neighbouring 'loser' cells, removing them from the population[16]. Whether cells behave as winners or losers depends on certain cellular characteristics, for example differences in the tension of the internal cellular framework called the cytoskeleton[16]. It would be interesting to investigate whether senescent cells choose particular target cells to cannibalize in a competitive fashion. In cancers, complex mixtures of cells coexist in the tumour microenvironment, and this cellular composition changes over time or in response to anticancer therapy. The authors propose that cell cannibalism might affect cancer progression by supporting the SASP response. However, it is worth considering whether it might also contribute directly to cancer progression by removing particular cells from the tumour microenvironment. And if normal cells are found to be removed by senescent cells in aged tissues, this depletion might contribute directly to tissue degeneration.

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Palaeoclimate

Fresh evidence in the glacial-cycle debate

Eric W. Wolff

An analysis of air up to 2 million years old, trapped in Antarctic ice, shows that a major shift in the periodicity of glacial cycles was probably not caused by a long-term decline in atmospheric levels of carbon dioxide. **See p.663**

During the past 2.6 million years, Earth's climate has alternated between warm periods known as interglacials, when conditions were similar to those of today, and cold glacials, when ice sheets spread across North America and northern Europe. Before about 1 million years ago, the warm periods recurred every 40,000 years, but after that, the return period lengthened to an average of about 100,000 years. It has often been suggested that a decline in the atmospheric concentration of carbon dioxide was responsible for this fundamental change. On page 663, Yan *et al.*[1] report the first direct measurements of atmospheric CO_2 concentrations from more than 1 million years ago. Their data show that, although CO_2 levels during glacials stayed well above the lows that occurred during the deep glacials of the past 800,000 years, the maximum CO_2 concentrations during interglacials did not decline. The explanation for the change must therefore lie elsewhere.

Understanding what caused the shift in periodicity, known as the mid-Pleistocene transition (MPT), is one of the great challenges of palaeoclimate science. The 40,000-year periodicity that dominated until about 1 million years ago is easily explained, because the tilt of Earth's spin axis relative to its orbit around the Sun varies between 22.1° and 24.5° with the same period. In other words, before the MPT, low tilts led to cooler summers that promoted the growth and preservation of ice sheets.

But after the MPT, glacial cycles lasted for two to three tilt cycles. Because the pattern of variation in Earth's orbit and tilt remained unchanged, this implies that the energy needed to lose ice sheets[2] had increased. One prominent explanation[3] is that atmospheric levels of CO_2 were declining, and eventually crossed a threshold value below which the net cooling effect of the decline allowed ice sheets to persist and grow larger.

Ancient air trapped in Antarctic ice can be extracted from cores drilled from the ice sheet, allowing the CO_2 concentration to be measured directly, but the ice-core record extends to only 800,000 years ago[4]. Estimates of CO_2 concentrations from earlier periods have been made by measuring the ratio of boron isotopes in shells found in ancient marine sediments[5,6]. This proxy measurement depends on a chemical equilibrium controlled by ocean acidity, which, in turn, is closely related to the atmospheric CO_2 concentration.

But the estimates of CO_2 levels inferred from such measurements are necessarily imprecise and must be verified using more-precise, direct measurements. Scientists have therefore formulated plans[7] to find and retrieve deep ice cores that reach back to before the MPT (see go.nature.com/33mw4yk). One project has recently been funded by the European Union, and hopes to retrieve million-year-old ice in 2024.

Yan *et al.* tried another approach to finding similarly old ice, but nearer the surface of Antarctica. In regions known as blue-ice areas, the combination of ice flow against a mountain barrier and surface ice loss by wind scouring and sublimation (transformation of ice directly into water vapour) leads to upwelling of old ice towards the surface. The authors therefore studied two cores, 147 and 191 metres deep, that were drilled to bedrock in the blue-ice region near the Allan Hills in Antarctica (Fig. 1).

The researchers improved and applied a relatively new method[8] to date this old ice. The concentration of argon-40 in Earth's atmosphere is slowly increasing with time as it is produced from the radioactive decay of potassium-40. By measuring the ratios of argon isotopes in air extracted from cores, the age of ice can be determined. The authors also measured the ratios of deuterium (a heavy isotope of hydrogen) to hydrogen in the ice, which can be used as a proxy of temperature at the time the ice was deposited.

Yan and colleagues concluded that ice in the lowest 30 m of each core is up to 2.7 million years old. However, the uncertainty of 100,000 years in this dating precludes their samples from being matched to particular parts of Earth's tilt cycle. Moreover, the authors found abrupt age discontinuities with depth in the cores, which suggests that the layers of ice within them have been disturbed. The authors therefore treated the measured concentrations of deuterium and CO_2 as snapshots of climate and atmospheric composition that corresponded to an approximate age of the ice, rather than as an ordered time series. On the basis of the deuterium values, they make a plausible case that the observed range of measured CO_2 values represents most of the actual glacial–interglacial range.

Unfortunately, in the oldest ice samples, there was evidence that the CO_2 concentration had been artificially enhanced by gas produced from the breakdown of organic material at the base of the ice sheet. A few samples from about 2 million years ago were potentially not affected by this issue, but were insufficient in number to allow any conclusions to be drawn about the range of CO_2 levels at that time.

However, Yan *et al.* obtained samples from about 1 million and 1.5 million years ago that they consider to be undisturbed by the artificial addition of CO_2. In both periods, the maximum CO_2 concentrations are similar to those of interglacials from the past 500,000 years, peaking at 279 parts per million (p.p.m.). But the minimum value of 214 p.p.m. is much higher than the lows of around 180 p.p.m. that occurred during recent glacial maxima (the periods that corresponded to the maximum extent of ice).

The authors conclude that the relationship between CO_2 levels and Antarctic temperature was similar before and after the MPT. The fact that the pre-MPT ice does not contain very low ratios of deuterium to hydrogen that would be characteristic of extremely cold Antarctic temperatures, nor low CO_2 levels characteristic of recent glacial maxima, is probably just a consequence of the shorter period of the glacial cycles. Such low values are generally not found in the first 40,000 years of post-MPT glacial cycles either.

"These data force us to look elsewhere for the cause of the longer glacial cycles."

Although Yan and colleagues' data points cannot be placed within a tilt cycle, it seems likely that the CO_2 concentrations are not very different at the crucial points in cycles when the ice sheet is either lost (before the MPT) or continues growing (after the MPT). This forces us to look elsewhere for the cause of the longer cycles, perhaps refocusing efforts on understanding whether changes to the nature of the ice-sheet bed caused by glacial erosion[9] altered the characteristics of the ice sheets and their vulnerability to melting.

Yan and colleagues' data add much-needed precision to the previously reported estimates of CO_2 levels made using data from marine sediments[5,6]. However, their tantalizing snapshots of the pre-MPT world emphasize the need for a complete, undisturbed time series of greenhouse-gas concentrations that can be put into context with the climate cycles at that time. Let us hope that the planned new ice cores will provide that.

SEAN MACKAY

Figure 1 | Blue ice near the Allan Hills region of Antarctica. The environmental conditions in this area draw ancent ice to the surface. Yan *et al.*[1] have analysed air trapped in an ice core drilled from this region to obtain the first direct measurements of atmospheric carbon dioxide levels from more than 1 million years ago.

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