

to have successfully overcome these challenges.

The complement pathway has been implicated in synaptic pruning<sup>5</sup>, a developmental process in which the synaptic connections between neurons are continuously eliminated in the brain until early adulthood. Using a mouse model, Sekar *et al.* found that *C4* expression is upregulated during periods of synaptic pruning. By contrast, mice deficient in *C4* showed signs of decreased pruning. Thus, the authors postulate that increased *C4A* expression in individuals with schizophrenia results in increased synaptic pruning. Interestingly, studies of the brains of humans with schizophrenia have shown that affected individuals exhibit thinning and reduced synaptic structures in the cortical region of the brain compared with people without the disorder<sup>6–8</sup>. Hyperactive synaptic

pruning might explain these findings.

Unfortunately, because mice lack the two forms of *C4* found in humans, the question of why schizophrenia risk depends specifically on *C4A* expression levels remains open. Answering this question is now a priority, and can be expected to provide further mechanistic information.

Sekar and colleagues' study finally gives us the first real inroad into the molecular aetiology of schizophrenia, and perhaps a direction for the development of treatments. Although pruning undoubtedly represents a challenging therapeutic target, the authors' beautiful and comprehensive study gives much-needed inspiration for all those researchers who are trying to leverage genetics to advance our understanding of the biology of neuropsychiatric diseases. ■

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## CLIMATE SCIENCE

# A great Arctic ice shelf

Newly mapped features on the floor of the Arctic Ocean suggest that the Arctic basin was once covered by a one-kilometre-thick, flowing ice shelf derived from large ice sheets in eastern Siberia, Arctic Canada and the Barents Sea.

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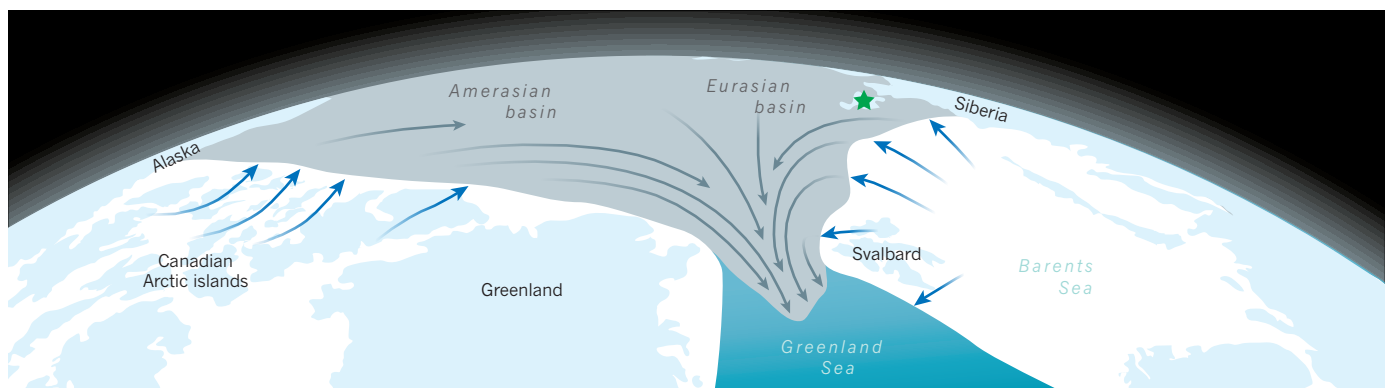
Ice cover across the Arctic Ocean has commonly been viewed as floating sea ice, formed as a relatively thin veneer from the freezing of seawater. Much effort has been directed towards understanding the behaviour of this form of ice cover and its recent precipitous decline<sup>1</sup>. But there has been a long-standing debate about a different kind of ice — ice of a thicker, more terrestrial origin, that might have existed across the Arctic basin in the distant past<sup>2</sup>. Writing in *Nature Communications*, Jakobsson *et al.*<sup>3</sup> bring this ancient ice shelf to life from a set of remarkable profiles

of elevated ridges that stand above the deep basins of the Arctic Ocean.

Early images<sup>4</sup> of portions of the Arctic sea floor revealed parallel grooves, scours and rumples — the telltale signs of ice having contact with and ploughing the sea floor. But the small number of features and their large geographic separation suggested to most scientists that floating and drifting icebergs were to blame<sup>5,6</sup>. Jakobsson and colleagues demonstrate that the ploughing pattern observed on widely separated ridges reflects a consistent and uniform direction of ice movement across the entire basin, as others have also reported<sup>7</sup>.

This key set of observations can be explained only by the presence of a single, widespread ice shelf (Fig. 1), one that flowed freely between large ridges, but became grounded and left its trail across the shallower regions of the Arctic basin. The ice shelf — estimated at some 4.1 million square kilometres on the basis of the numbers given in Jakobsson and colleagues' paper — was four times the area of all the ice shelves now found in Antarctica, including the immense Ross and Ronne–Filchner ice shelves. It must have been about 1 kilometre thick, allowing it to float over the great depths of the Amerasian and Eurasian basins, but touching down and ploughing across the shallower regions.

By tracing the glacial furrows towards their points of origin, Jakobsson and co-workers conclude that land-based ice sheets must have fed the ice shelf from three separate centres: the eastern Siberian lowlands; the Scandinavian regions of the Barents Sea; and high Arctic islands in north central Canada (Fig. 1). Furthermore, the authors found evidence — in the form of microfossils and of magnetic properties in sedimentary cores collected from some



**Figure 1 | Sketch of an ancient ice shelf across the Arctic Ocean.** Jakobsson *et al.*<sup>3</sup> report evidence of a one-kilometre-thick ice shelf (grey region) that covered the entire Arctic basin during the penultimate glaciation. Blue arrows indicate feeding ice streams from the Canadian Arctic islands, Siberia and Svalbard; grey arrows represent flow lines of the ice shelf. Modern locations of Greenland, Svalbard, Alaska and Siberia are shown in pale blue; green asterisk indicates the location of the New Siberian Islands. The rough locations of the Amerasian and Eurasian basins beneath the Arctic Ocean are also indicated. (Figure adapted from ref. 3.)

of the ridges — that this Great Arctic Ice Shelf (GAIS) existed not during the most recent glaciation (the Wisconsinan, about 22,000 to 18,000 years ago), but instead about 160,000 to 140,000 years ago, during the penultimate glaciation.

The antiquity of the GAIS helps to explain why some evidence is missing for the ice sheets that fed it. The regions from which the ice was derived are now shallow, broad shelves and coastal plains of Canada, Russia and north-western Europe. During the Wisconsinan and the subsequent sea-level rise, these regions were exposed to erosion and sedimentation, which may have masked the direct footprint of the ice sheets<sup>2</sup>. Even so, some regions that are clearly in the path of the ice sheets that covered eastern Russia have yielded no evidence of glaciation at all<sup>8</sup>. These areas include the remote New Siberian Islands, which may not have yet undergone complete geological examination<sup>9</sup>.

An ice shelf of the extent suggested by Jakobsson and colleagues' work is very different from the expansive sea ice that covers the Arctic Ocean today. Sea ice constantly opens and closes, providing gaps for light; this allows photosynthesis to occur and thus to fuel the vast Arctic marine ecosystem. Just as scientists contemplate the effect of more open water as Arctic sea ice is progressively reduced in response to climate change, an equally daunting task is to imagine how the ecosystem could function under the continual darkness and cover that the GAIS would have caused. A more limiting scenario for life could not be imagined, with the exception of the subglacial lakes that lie beneath the Antarctic ice sheet.

Equally important is the role that the GAIS must have had in regulating ocean chemistry while not greatly changing sea level. The implications of the changes in ocean chemistry for estimates of ancient sea levels can be appreciated by considering how climate scientists conventionally reconstruct sea-level oscillations. To reconstruct ancient glaciations largely lacking geological features that directly indicate shorelines, scientists have used the geochemical history of the ocean recorded in the shells of marine plankton called foraminifera. Glacial oceans are enriched in heavy-oxygen atoms (<sup>18</sup>O), and so the change in chemistry over time — measured as the ratio of light-oxygen atoms to heavy oxygen in foraminifera shells — is used to gauge sea-level changes caused by the comings and goings of large ice sheets<sup>10</sup>.

This method has been validated for the most recent glacial cycle, because direct measures of sea level are an exceedingly good match to estimates based on ice-sheet volume and changes in ocean chemistry<sup>11</sup>. But estimates for sea-level change during the penultimate glaciation have always been problematic, because the few direct shoreline records of sea level are higher than estimates based on the oxygen-isotope record corresponding to that period<sup>12</sup>. Jakobsson and co-workers' reconstructed

GAIS seems to explain this mismatch, and reminds climate scientists that they should check their assumptions as they continue to account for glacial ice and its effects on sea level during the numerous glacial episodes of the past 2.5 million years. ■

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## AGEING

## Out with the old

The selective elimination of cells that have adopted an irreversible, senescent state has now been shown to extend the lifespan of mice and to ameliorate some age-related disease processes. [SEE ARTICLE P.184](#)

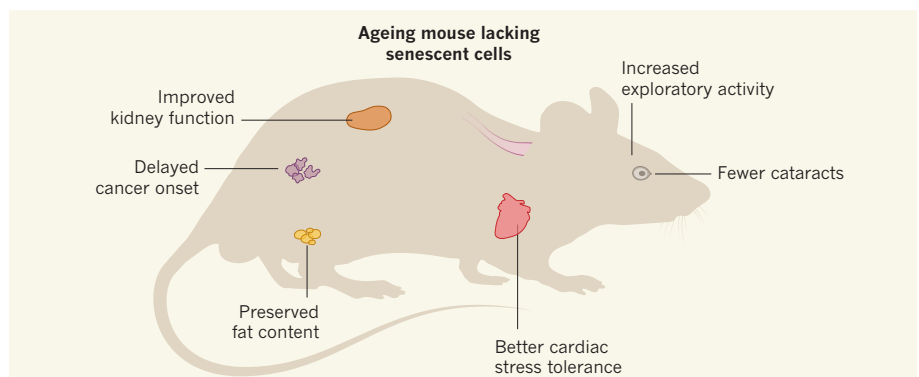
JESÚS GIL & DOMINIC J. WITHERS

The ability to fight the ageing process has been a long-held human desire. Although this quest often seems to be driven by vanity, ageing is the major risk factor for many of the diseases that plague modern society. More than 50 years ago, it was suggested that ageing is linked to a state of arrested cell growth known as senescence<sup>1</sup>, but this link has remained unproven, and the molecular basis for organismal ageing has been elusive. In this issue, Baker *et al.*<sup>2</sup> (page 184) demonstrate that the removal of senescent cells does indeed delay ageing and increase healthy lifespan (healthspan).

Senescence is a cellular state in which cells permanently stop dividing. It is mediated by two signalling pathways — the

*p53* pathway and the *p16<sup>Ink4a</sup>-Rb* pathway. Senescent cells secrete a complex cocktail of factors called the senescence-associated secretory phenotype (SASP), which includes matrix metalloproteinases (enzymes that break down the extracellular matrix) and pro-inflammatory signalling molecules. Such cells have been shown to accumulate during ageing, and their presence has been associated with a broad range of diseases, including diabetes, kidney disease and many cancers<sup>3</sup>.

The group that performed the current study previously showed that removing senescent cells from a mouse model of accelerated ageing delays the onset of several disease-related processes<sup>4</sup>. However, the relevance of these observations to the normal ageing process was unclear. Baker *et al.* have now directly tackled this uncertainty using a genetically engineered



**Figure 1 | Improving healthspan.** Senescent cells, which are in a state of irreversible growth arrest, accumulate in various organs during ageing and are associated with age-related diseases in many tissues. Baker *et al.*<sup>2</sup> selectively eliminated senescent cells in ageing mice. This increased healthy lifespan, reducing many age-related, disease-associated abnormalities.