implicated in human diseases, the study provides a suggestive framework for developing targeted therapies and understanding disease progression in a human-relevant biological context.

The second study[2] delves into the genome of the mouse lemur, uncovering thousands of previously unannotated genes and more than 85,000 splice junctions (sequences at which RNA segments are joined) that are absent in mice. This extensive mapping provides considerable enhancements to the existing *M. murinus* genome annotation[5], offering insights into the evolutionary trajectory of primates. Notably, the research highlights the streamlined organization of the lemur immune system, which will serve as a useful comparison when studying immune function and antibody diversity. This work underscores the potential of the mouse lemur to be a bridge between rodent models and human biology, facilitating a deeper understanding of genetic regulation and expression patterns that are more representative of humans than are conventional models.

A particularly innovative aspect of the research is the development of an experimental framework for reverse genetic analysis — an approach in which the function of a gene can be discerned by disrupting its sequence and looking for a change in observable characteristics (phenotype). The researchers identified naturally occurring nonsense mutations (those that completely disrupt the gene product) in three primate immune genes that are absent in mice: *CD58*, *GBP1* and *CLEC4E*. They could then analyse the transcriptional phenotypes resulting from these mutations. This approach takes advantage of the natural genetic diversity of mouse lemurs, allowing for detailed functional studies of primate-specific genes. Such analyses are a promising complement to conventional genetic-engineering methods, particularly for genes that have crucial roles in primate-specific traits and diseases.

This first-generation atlas focused on generating single-cell transcriptome data, but it will be interesting to acquire other types of data, such as information about epigenetic modifications to DNA and the accessibility of packaged DNA (chromatin), both of which have a role in regulating gene expression. These data could be used for further comparative analyses to explore the evolution of gene-regulatory networks. Furthermore, spatially mapping the identified cell types and assessing tissue arrangements and architectures would be a promising direction for future studies. In particular, it would be interesting to understand how the organization of cells according to metabolic function, which occurs in the gastrointestinal tract and liver, compares with that in primates that have different diets, lifestyles and exposures to microorganisms.

The authors indicate that no primate was harmed for the sake of generating the atlas and that the tissues were obtained opportunistically from natural deaths. However, this also limits the comprehensiveness of the atlas, and in particular this version does not include sampling of developmental time points, such as early embryonic stages. In the future, data sets from other male and female individuals at several life stages will help to further map cellular diversity in this species.

Should biomedical researchers adopt mouse lemurs over other primate models? It might be difficult to convince the field of the usefulness of the animals over the combination of current organismal models that also have *in vitro* counterparts, such as pluripotent stem cells (cells that give rise to any cell type) or organoid models. The same ethical oversight is applied to this species as to any other primate, yet the evolutionary distance is substantial. Other primates that are evolutionarily closer to humans, such as macaques and common marmosets (*Callithrix jacchus*), have more deeply established genetic, experimental and rearing protocols — so they might make a wiser investment for research.

The use of mouse lemurs as an experimentally tractable model primate therefore remains unclear, particularly in countries with strong regulations and cultural concerns regarding primate research. Nevertheless, these animals present opportunities to study primate behaviour and physiology[6] from a fresh perspective, and the work by the Tabula Microcebus Consortium could foster further development and commitment from researchers in these fields. The authors should be commended for providing a considerate and empathetic view of how to work with and learn from some of our closest living relatives. A biobank of validated pluripotent stem cells and tissue-resident adult stem cells would be a great asset for evolutionary developmental biologists and biomedical researchers for modelling lemur biology *in vitro*.

Overall, the creation of this mouse-lemur cell atlas marks a sizeable step forward in primate research. It not only provides a robust foundation for future studies on primate biology and disease but also establishes a blueprint for developing other emerging model organisms. The two studies underscore the importance of building collaborative cell atlases as a baseline for integrating new model organisms into biomedical research. The outlook is bright for the mighty mouse lemur as a model organism, hopefully providing inroads for discoveries in primate genetics and disease.

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Evolution

Humans occupied diverse habitats 70,000 years ago

William E. Banks

Ecological modelling reveals that the range of habitats *Homo sapiens* occupied in Africa increased before the species established a lasting presence in Eurasia. **See p.115**

Homo sapiens spread across the globe owing to our capacity to adapt culturally and technologically to a diverse array of environmental conditions (ecological niches). Successful migrations of *H. sapiens* out of Africa resulting in long-term populations elsewhere began shortly after 60,000 years ago, when groups moved out of the African continent in a sustained manner. Towards the end of the last ice age, a little more than 20,000 years ago[1], hunter-gatherers had reached as far as the American continents. What is it about our species that enabled humans to populate the globe? On page 115, Hallett *et al.*[2] address this question and describe the results of an interdisciplinary study that identifies changes in the ecological niches occupied by *H. sapiens* hunter-gatherer populations in Africa before

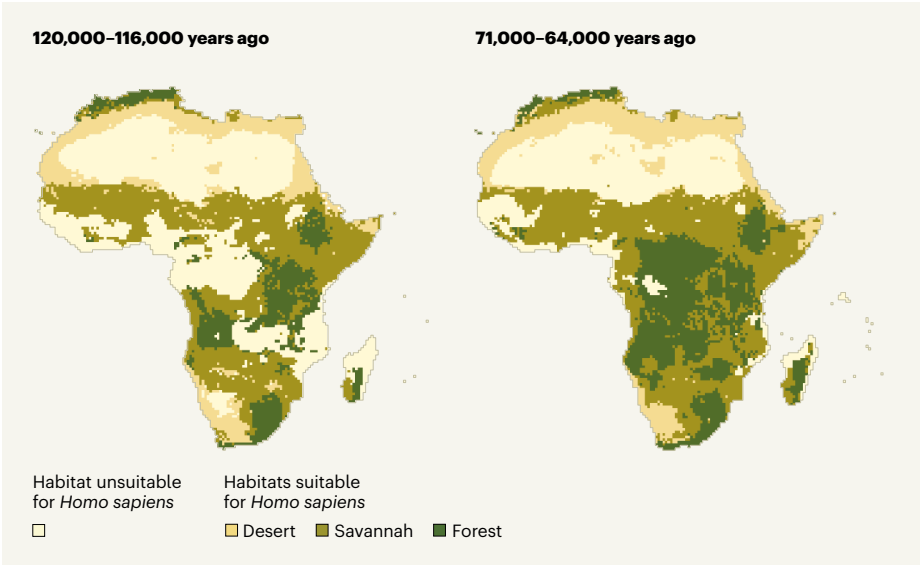

Figure 1 | Habitat-occupation patterns for *Homo sapiens* in Africa. Hallett *et al.*[2] used ecological modelling and examined archaeological data to determine changes in the habitat niches of humans over time in Africa. Humans began to occupy more-diverse habitats by 70,000 years ago, before they established a long-term presence in Eurasia starting around 60,000 years ago. (Adapted from Fig. 3 of ref. 2.)

their sustained expansion into regions outside the continent.

The authors examined a continent-wide database of African archaeological data and the dates associated with this evidence. Hallett and colleagues used these data and variables derived from palaeoclimatic simulations to estimate past ecological niches — a niche being the range of environmental conditions and associated resources that enable a population or species to live and reproduce.

The correlative methods that the authors used are valuable in providing an understanding of the range of environmental conditions and their corresponding geographical locations that were inhabited by past populations. These methods provided a way to examine niche dynamics across periods of pronounced climatic variability from roughly 120,000 to 15,000 years ago, a time frame that encompasses the past two glacial and interglacial cycles. This long-term evaluation makes Hallett and colleagues' study particularly interesting.

The authors report that the overall niche occupied by humans began expanding (Fig. 1) roughly 70,000 years ago, and that this expansion peaked around 50,000 years ago. This niche expansion is characterized by a rise in the occupation of both forest and desert environments and greater ranges of annual temperature for the latter. Hallett and colleagues conclude that this tendency by *H. sapiens* to occupy and extract resources from a wider range of habitats, encompassing a broader spectrum of climatic conditions, demonstrates the ecological flexibility that would have been necessary for success as *H. sapiens* moved into Eurasia and encountered new environments.

The authors also infer that an increased tendency to move between diverse habitats and regions would have increased the rate of encounters between different hunter-gatherer groups. This phenomenon, in turn, might have had a role in shaping the tapestry of cultural features that defines our species.

Hallett and colleagues' analysis is an excellent example of the powerful interdisciplinary research that is becoming increasingly common in archaeology and anthropology. It was only around 25 years ago[3] that ecologists began routinely to use correlative methods for modelling ecological niches. Since then, scientists have intensively developed and refined this approach to understand species' distributions and evolution[4].

Archaeologists also soon recognized the value of such methods for interpreting culture–environment relationships and cultural evolution[5]. Although this approach is still not routinely used, methods that incorporate the modelling of ecological niches are increasingly common in archaeological and anthropological investigations[6]. This provides insights into niche dynamics and human–environment relationships that were not available three decades ago.

The authors' study is an excellent piece of science. However, there are factors worth keeping in mind when conducting such work to ensure that scientists are best able to interpret results and, more importantly, compare findings and take full advantage of the data. It is crucial that researchers explicitly state what exactly they are attempting to estimate ecologically[7]. In other words, to what extent do we think that we are approaching an estimate of the fundamental niche — the set of environmental conditions that a species can occupy — as opposed to the actual occupied niche? Such precision is necessary so that archaeologists and anthropologists can compare results effectively.

Using robust methods, Hallett and colleagues make the case for a sustained expansion of the *H. sapiens* niche across Africa from 70,000 years ago. Yet this does not necessarily mean that all African populations, across different regions, expanded their respective ecological niches. It is necessary to examine individually these various cultural trajectories and their potential niche dynamics[8] to understand the full range of culture–environment relationships present across the continent during the time frame studied. It is also useful to examine technological changes to gain an in-depth understanding of the cultural behaviours behind ecological niche dynamics over time and to determine whether and how specific technologies or innovations correlate with the ability to inhabit specific past niches[9,10].

Homo sapiens were not the first members of our genus to leave Africa. Long before they embarked on this journey, earlier members of the genus *Homo* occupied a diverse range of environments outside the continent[11,12]. When these hominins left Africa around two million years ago, it is argued, they might have tracked the same habitats that they occupied in Africa[13]. Some research[14], however, indicates that new ranges of environmental conditions were probably occupied once hominins exited Africa. Other ancient members of our genus were permanently present across Europe, including at high latitudes, by at least 900,000 years ago[15,16].

It is reasonable to assume that the range of such occupied environments across Eurasia represented an overall expanded niche from that of their African ancestors. I would argue that we should not assume that *H. sapiens* were unique in their ability to expand their niche — specific cultural behaviours are not necessarily correlated with biological taxonomy or specific species within our genus[17].

Methods to model ecological niches are powerful tools for understanding the environmental contexts in which past cultural behaviours occurred. This is especially useful for trying to identify the mechanisms that shaped these diverse cultural trajectories throughout prehistory. This is truly an exciting time to be an archaeologist.

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Medical research

Mitochondria exit neurons and drive cancer spread

Anand K. Singh & Yuan Pan

Neurons often receive organelles called mitochondria from other cells. It emerges that neurons donate mitochondria that support cancer-cell spread. **See p.252**

Neurons can support cancer initiation, growth and migration and can drive therapy resistance through various mechanisms, such as immune-cell modulation[1]. Such discoveries underpin the emerging field of cancer neuroscience. Much research has been done to understand the interplay between cancer cells and neurons and how cancer cells can exploit neuronal signalling to support malignancy. On page 252, Hoover *et al.*[2] reveal a previously unknown role for tumour-associated neurons in aiding tumour spread.

One way in which neurons support cancer is by boosting tumour-cell metabolism[3], but how this occurs remains to be fully understood. Mitochondria, organelles that have a central role in producing the energy needed for processes such as metabolism, can be transferred between cells in three ways: by 'floating' freely from one cell to another; in vesicles; or through cellular structures called tunnelling nanotubes that connect cells[4].

Cancer cells can meet their high energy demands by obtaining mitochondria from certain kinds of neighbouring cell[5]. For example, in one type of brain tumour, cancer cells capture mitochondria from adjacent non-neuronal brain cells called astrocytes[5]. This enables the tumour to reprogram its metabolism and switch from generating energy through one type of metabolic process called glycolysis to using another, more efficient process known as oxidative respiration, which generates the energy-carrying molecule ATP through a pathway that requires mitochondria[5].

In the tumour microenvironment, normal cells called fibroblasts can form tunnelling nanotubes and transfer mitochondria to breast cancer cells and prostate cancer cells[6,7]. Transfer of mitochondria from endothelial cells to cells of a skin cancer called melanoma increases cancer-cell proliferation and reduces tumour-cell death[8]. Cancer cells can also manipulate immune cells called cytotoxic T cells to donate healthy mitochondria to them, and the tumour cells send damaged mitochondria to the cytotoxic T cells. This prevents these T cells from effectively performing their antitumour immune function[9].

To examine whether mitochondria move between neurons and cancer cells, the authors developed a mitochondrial-transfer mapping tool called MitoTRACER, which they used to examine mouse models of cancer. In this system, if engineered cells receive mitochondria, they stop making one type of fluorescent protein and start making a different type, thereby labelling recipient cells. Hoover and colleagues report that mitochondria are transferred from neurons to cancer cells (Fig. 1). This phenomenon occurred for various types of the disease, including breast cancer, melanoma and prostate cancer.

The mitochondrial transfer induced metabolic reprogramming of the recipient cancer cells, which increased their capacity for oxidative respiration. They gained metabolic advantages and resistance to stress.

Mitochondrial transfer also enhanced the 'stemness' of the recipient cancer cells – the stem-cell-like characteristics that help them to self-renew and generate progeny cells. The transfer also increased cancer spread to elsewhere in the body.

Cancer cells that acquired neuronal mitochondria had an increased ability to grow without needing to be in contact with other cells (anchorage-independent growth), as demonstrated by the cells forming sphere-like structures *in vitro*. This ability of cancer cells to grow independently of anchorage is associated with their stemness potential. Such a characteristic is associated with mitochondria and metabolic changes. By tracing cells in mice, the authors discovered that cancer cells that had acquired neuronal mitochondria at primary tumour sites were found at distant locations such as the brain and lungs more often than were cancer cells that did not acquire neuronal mitochondria.

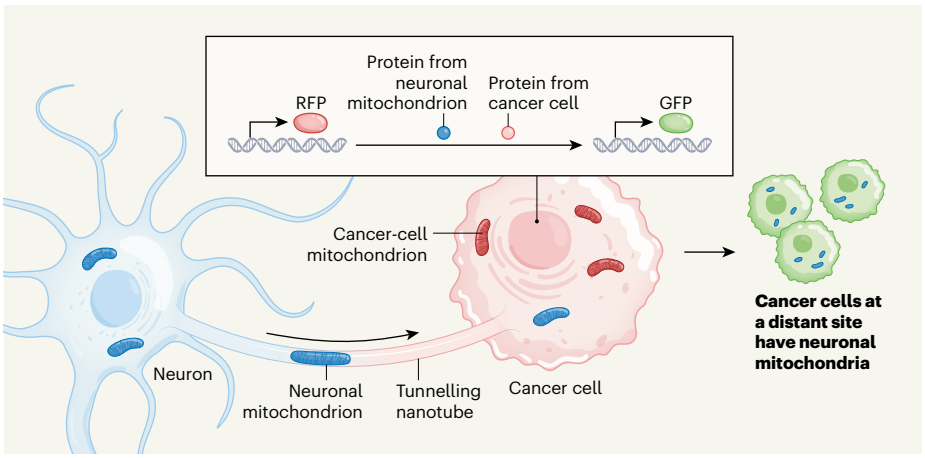

Figure 1 | The transfer of organelles from neurons to tumour cells helps cancer to spread. Hoover *et al.*[2] used *in vitro* experiments and *in vivo* mouse models to examine whether energy-producing organelles called mitochondria are transferred from neurons to cancer cells. The authors developed a fluorescent labelling system called MitoTRACER that enabled them to identify and label tumour cells if neuronal mitochondria entered them. Mouse tumour cells were engineered to express a fluorescent protein called RFP. If the cells received neuronal mitochondria, these engineered organelles provided a protein that entered the cancer-cell nucleus (helped by a protein already present in the cancer cell). These events caused the recipient cancer cells to switch from making RFP to making a different fluorescent protein, called GFP. Hoover and colleagues report that cancer cells took up neuronal mitochondria through tubular structures, called tunnelling nanotubes, that connect cells together. These recipient cancer cells spread to sites in the body distant from the initial site of tumour growth.