from the scientific community on ways to encourage publishing null and negative findings.

Political infiltration

But some staff members at scientific agencies do not trust that the response to the president's orders will strengthen US science. "I expect it will be used to further politicize science by labelling research the administration doesn't like as 'not gold-standard'," says an NIH staff member, who requested anonymity out of fear of retaliation.

The DOE plan, for example, warns against relying on "highly unlikely and overly precautionary assumptions and scenarios" when using science in policy decisions. This language matches wording in Trump's first executive order, which criticized agencies for using a standard climate scenario that, according to the president's order, included "highly unlikely assumptions" about future emissions. In July, the DOE released a report touting the benefits of carbon dioxide and downplaying the risks of climate change, contrary to scientific consensus.

Trump's executive orders say that the goal is to "restore" science; in reality, the administration is actively undermining science, says Maryam Zaringhalam, a molecular biologist and senior director for policy at the Center for Open Science, based in Washington DC. She fears that political appointees will use the new policies' emphasis on issues such as reproducibility and transparency to raise questions about research they don't like, whether it's NIH research on mRNA vaccines or climate science at the US Environmental Protection Agency (EPA).

"It's gold standard for thee, but not for me," Zaringhalam says. "This is something that we are seeing play out over and over again."

Watch this space

The gold-standard-science policies are just a starting point. Scientists and policy specialists say that it could take time for agencies to appoint people to oversee these policies and flesh out procedures covering everything from grant-making to questions of scientific integrity and misconduct.

Some agencies have yet to release their new policies. At others, such as the FDA, political oversight is already under way. For example, political appointees at the FDA overrode career civil servants to restrict the use of COVID-19 vaccines.

For her part, Zaringhalam takes no comfort from the fact that many of the new policies sound reasonable on the surface, precisely because they do nothing to prevent the Trump administration from manipulating science that it doesn't like. Actions are more important than words, she says. "It's about watching what agencies actually do and seeing how that adheres to the gold-standard science principles."

LAWRENCE LAWRY/SPL

A huge analysis of DNA methylation in human tissue has revealed new anti-ageing targets.

HUGE EPIGENETIC ATLAS REVEALS HOW AGEING CHANGES OUR GENES

A map of DNA methylation changes in human organs could help researchers to discover more drug targets.

By Chris Simms

The visible effects of ageing on our body are in part linked to invisible changes in gene activity. The epigenetic process of DNA methylation — the addition or removal of tags called methyl groups — becomes less precise as we age. The result is changes to gene expression that are linked to reduced organ function and increased susceptibility to disease.

Now, a meta-analysis of epigenetic changes in 17 types of human tissue throughout the entire adult lifespan provides the most comprehensive picture to date of how ageing modifies our genes.

The study assessed DNA methylation patterns in human tissue samples and revealed that some tissues seem to age faster than others do. The retina and stomach, for example, accumulate more ageing-related DNA methylation changes than do the cervix or skin. The analysis also found universal epigenetic markers of ageing across different organs. This 'epigenetic atlas' might help researchers to study the link between DNA methylation and ageing and could aid in the identification of molecular targets for anti-ageing treatments.

"I think this is a great resource" to understand ageing, says Joao Pedro Magalhaes, a molecular biologist at the University of Birmingham, UK. "This meta-analysis of methylation data across organs is, to my knowledge, the largest such resource assembled to date. I am sure that it will be valuable to researchers."

The work is reported on the preprint server Research Square[1] and has not yet been peer reviewed.

Epigenetic atlas of ageing

Researchers can already analyse DNA methylation patterns in people's genomes to create ageing clocks — tools that measure biological age. However, there are unresolved fundamental questions about whether these signatures of ageing are shared across tissue types.

To elucidate how methylation relates to ageing, Nir Eynon at Monash University in Melbourne, Australia, and his colleagues conducted a meta-analysis of more than 15,000 samples taken from adults of different ages. They mapped out methylation changes across 900,000 potential sites in the DNA, then created an open-access atlas. "We had examples from people from 18 years old till 100 or so," says Eynon, so we can look at the epigenetic markers and how they change across the human lifespan.

Overall, the researchers found that the mean amount of methylation varies greatly between tissues, ranging from 39% in the cervix through to 48% in skin, 51% in muscle, 53% in the heart, 57% in the stomach and up to 63% in the retina.

Study co-author Macsue Jacques, also at Monash University, says that DNA methylation increases in almost all tissues as they age. The exceptions are skeletal muscle and lung, "which has more of a loss of methylation with age". Their analysis also found that different organs have distinct ageing patterns of DNA methylation. "Each tissue has a different shift that happens," Jacques says.

Ageing methylation targets

As well as examining differences between tissues, the researchers screened individual gene sites throughout each tissue genome. "We wanted to find a common ageing mechanism that goes across all the tissue types," says Jacques.

They found several genes that had methylation changes that were strong biological markers of ageing across several tissues. These included the developmental regulators *HDAC4* and *HOX*, which are related to senescence and age-related decline, and *MEST*, which has been associated with diabetes and obesity, two known accelerators of ageing[2].

The researchers identified high methylation of the protocadherin gamma (*PCDHG*) gene family as a driver of the ageing process in multiple organs. Other studies have shown that hypermethylation in the *PCDHG* gene family is linked to reduced white matter in the brain, a marker of accelerated cognitive decline[3].

Target body, not tissue, ageing

Jacques sees the atlas as a resource for accelerating discovery of the core molecular mechanisms of ageing throughout the body, as well as in individual tissues. She hopes that it could boost the search for anti-ageing therapies and raises the tantalizing idea of shifting from treating individual age-related diseases, such as cardiovascular disease or liver disease, to treating ageing as a whole.

Holger Bierhoff, an epigeneticist at the Leibniz Institute on Aging – Fritz Lipmann Institute in Jena, Germany, says that the big question with working on epigenetic clocks has always been 'what is causing ageing?'. "This work looks into the functional relevance of the methylation, rather than just using it as a timepiece for ageing."

Big as the study is, says Bierhoff, this is still a tiny fraction of the roughly 30 million epigenetic sites in the human genome, so it might not present the whole picture of age-related DNA methylation.

Eynon accepts that, but says that the data in their atlas could still help identify the mechanisms behind ageing and reveal how to slow it.

Previous work from a team involving Eynon has shown that exercise is associated with younger methylation patterns in human skeletal muscle, for example[4]. "There's almost no tissue in the body that is unaffected by exercise," he says, so this work might lead to a model of how exercise, and factors such sleep and diet, change pathways in many tissues throughout the body to keep us biologically younger.

1. Eynon, N. *et al.* Preprint at Research Square https://doi.org/10.21203/rs.3.rs-7184037/v1 (2025).
2. Reifsnyder, P. C. *et al. Aging Cell* **21**, e13666 (2022).
3. Schmithorst, V. *et al.* Preprint at medRxiv https://www.medrxiv.org/content/10.1101/2024.04.21.24306143v1 (2024).
4. Voisin, S. *et al. Aging Cell* **23**, e13859 (2024).

BACTERIAL COMMUNITY DISCOVERED MAMMOTH TEETH AND BONES

Sequencing techniques uncover the oldest-ever host-associated microbial DNA.

By Katie Kavanagh

An analysis of the bones and teeth of ancient mammoths (*Mammuthus*) has identified some of the microorganisms that lived in the animals' mouths and bodies more than one million years ago.

The study, published on 2 September (B. Guinet *et al. Cell* https://doi.org/g9z9b8; 2025), describes the oldest microbial DNA ever sequenced, and reveals that some species of pathogenic bacteria that have been linked to the deaths of African elephants (*Loxodonta africana*) once infected the mouths of their ancient cousins.

The findings offer "a good opportunity to get a global picture about what kind of bacteria or viruses we could find in this extinct species", says study co-author Benjamin Guinet, a palaeomicrobiologist at the Centre for Palaeogenetics in Stockholm, Sweden. Further research could provide insights into how microbes might have helped ancient animals to adapt to varied environments, and whether they might have been involved in the extinction of these species.

Pathogenic microbes

Previous research on ancient remains has focused mainly on the DNA of humans and human-associated microorganisms, and few

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DNA from pathogenic bacteria has been found in the teeth of prehistoric mammoths.