

in pre-mating rituals, just as certain birds use colourful tail fans, wings and head crests to attract mates. Communication was also suggested as the function of the colourfully

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patterned feathers on the tails, wings and heads of some dinosaurs<sup>6–8</sup>. Modern birds are renowned for the diversity and complexity of their colourful displays, and for the role of these aspects of sexual selection in bird evolution, and the same might be true for a wide array of extinct animals, including dinosaurs and pterosaurs.

A key conclusion from Cincotta and colleagues' work is that feathers, and all the complex abilities they offer both for insulation and signalling, originated once, at the origin of the clade Avemetatarsalia, which includes dinosaurs, birds and pterosaurs. It is possible that feathers evolved independently in several groups of dinosaurs as well as in pterosaurs, but the shared structural complexity of the pigments, and the inferred shared genomic heritage and shared pattern of developmental stages of these organisms, make a single point of origin more likely<sup>4,9</sup>.

If so, this point of origin was probably in the Early Triassic, some 250 million years ago (on the basis of the age of the earliest-known avemetatarsalian fossils<sup>10</sup>). A series of discoveries over the past 25 years, including the study by Cincotta and colleagues, has therefore now shifted the origin of feathers to 100 million years earlier than was originally thought on the basis of the discovery of the earliest-known bird fossil, that of *Archaeopteryx*<sup>11</sup>, which lived in Germany around 150 million years ago. Until now, much of the discussion about the origins of feathers has focused on their use in flight – an adaptation that arose in dinosaurs called theropods during the Middle to Late Jurassic epochs (about 165 million years ago)<sup>5</sup>. This new evidence will probably lead to a refocusing on the capacity for insulation that feathers provide as being, presumably, the main reason for their development, followed by their use for signalling.

The presence of feathers for insulation in the Avemetatarsalia suggests that the ancestors of pterosaurs and dinosaurs, and ultimately of birds, were warm-blooded to some degree, and lived faster lives than many of the other reptiles of their day – having the capacity for more-sustained activity throughout the day and the ability to run fast for longer. The time window of the origin of feathers, in the

Early Triassic, coincides with the recovery of life from the end-Permian mass extinction, during which more than 90% of species became extinct on land and in the oceans. The reptiles ancestral to mammals, called synapsids, were already walking high on their limbs, were warm-blooded to some extent and perhaps had hair. I have previously suggested<sup>12</sup> that this period could mark a crucial time of arms races between synapsids and avemetatarsalians, each competing with the other as herbivores and as carnivores, and establishing the roots of a new kind of physiology at the same time.

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### Polymer chemistry

## Tailor-made enzymes for plastic recycling

**Eggo U. Thoden van Velzen & Giusy Santomasi**

Waste streams of the plastic poly(ethylene terephthalate) that can be recycled into material suitable for food packaging are limited, creating a shortfall of feedstocks. An enzyme has been discovered that widens the feedstock options. **See p.662**

Plastics are exceptionally useful materials for packaging and all kinds of consumer items, but poorly managed plastic waste contributes to land and ocean pollution. This problem can, in principle, be prevented by recycling (Fig. 1). However, many plastic products were not designed for mechanical recycling, which involves melting and reprocessing, and therefore produces lower-quality material than the original plastic.

Items that are made predominantly from certain polymers, such as the widely used poly(ethylene terephthalate) (PET), can be converted back into the molecular building blocks (monomers) from which the polymers were made. The monomers can then be purified and repolymerized to make new plastics, a form of 'closed-loop' recycling. Standard chemical depolymerization processes are energy intensive and require large amounts of bases and acids, and are therefore not economically or ecologically viable. A potential solution is to use enzymes, but the lack of enzymes that have suitable activity for industrial-scale plastic depolymerization has hindered the development of this recycling strategy. On page 662, Lu *et al.*<sup>1</sup> report an engineered variant of an enzyme that brings closed-loop recycling nearer for commonly used PET-based products that were not

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designed for mechanical recycling.

A wide variety of packaging is made from PET, such as trays, tubs, cups and blister packs, and the demand for transparent, food-grade recycled PET (rPET), in particular, has risen greatly over the past two decades<sup>2</sup>. The highest-quality rPET is made from drinks bottles collected through deposit-refund systems, because these bottles are designed for recycling, and because the collection method precludes sorting mistakes. The number of countries using deposit-refund systems is growing steadily, boosting the amount of high-quality rPET that is produced. Even so, the market for PET drinks bottles is relatively small, and cannot supply sufficient material for the much larger PET-packaging market. Moreover, the shortage of collected and sorted PET bottles has driven up the cost of this feedstock enormously.

It is therefore essential for non-bottle PET to be collected and recycled into food-grade, transparent rPET. Various approaches have been adopted to achieve the required quality of material. Some recycling companies accept trays that have been specifically designed for recycling – that is, trays that do not contain components made from other polymers. Others have developed chemical recycling processes involving depolymerization,



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**Figure 1 | Plastic bottles collected for recycling in Surabaya, Indonesia.** Currently, only certain types of waste poly(ethylene terephthalate) (PET), such as drinks bottles, can be recycled to make food-grade recycled PET. Lu *et al.*<sup>1</sup> report an enzyme that could be used to recycle other waste streams of PET.

filtration and repolymerization of coloured PET bottles. But these feedstocks still have limited volumes.

By contrast, collected and sorted waste PET trays are available for free in increasing quantities in various European countries – in fact, a service fee is sometimes even paid to companies that recycle them. This PET waste comprises a mixture of trays and ‘clam-shell’ packaging used for food, as well as cups, tubs and blister packs. The most abundant PET trays are used to pack meat, fish and cheese under modified atmospheres that help to preserve the food, and consist of a PET film covered with a layer of a different plastic – polyethylene. The inner polyethylene layer allows the trays to be sealed quickly and reliably, which is crucial for maintaining food safety. This important layer, however, complicates mechanical recycling, because it mixes with the transparent PET to produce an opaque blend. This blend can be used to produce trays, but the lion’s share of the market is transparent food-grade rPET.

Attempts to recycle sorted PET trays using chemical processes have been unsuccessful. These processes typically involve boiling the plastic at 195 °C in ethylene glycol with alkaline catalysts, a method known as saponification.

However, residues from non-PET materials (such as polyethylene, printing inks, labels and so on) form gels in the boiling ethylene glycol that hinder filtration and further processing of the saponified PET.

Recycling based on the enzymatic breakdown of PET might help to solve these problems. Enzymes and microorganisms that depolymerize PET have previously been described, including a promising PET-degrading bacterium that uses a pair of enzymes to do the job<sup>3</sup> – but this worked only for amorphous (non-crystalline) PET films, and the depolymerization was incomplete. More-active enzymes have since been discovered, but none was able to break down common PET waste completely within acceptable processing times. The interest of commercial recycling companies has therefore been limited. Lu and colleagues’ enzyme might change all this.

The authors used a machine-learning system to predict mutations to PET-degrading enzymes (PETases) that might improve the thermal stability and activity of the enzymes. By engineering and testing the mutants, the team identified an enzyme that contains five mutations compared with

wild-type PETase, and which has superior PET-degrading activity relative to wild-type and engineered alternatives. Lu *et al.* name their enzyme functional, active, stable and tolerant PETase, or FAST-PETase for short.

FAST-PETase depolymerizes PET completely under relatively ‘mild’ conditions – that is, either at room temperature within a week, or at 50 °C within a day. Amorphous PET can be depolymerized directly, whereas PET that is more than 25% crystalline (such as that used to make bottles) requires a thermal pretreatment to make the plastic amorphous. The authors show that the enzyme can degrade samples from 51 untreated PET products that had previously been used by consumers, demonstrating its ability to cope with a variety of raw materials. Notably, because the enzymes operate at just 50 °C in aqueous solution, any residues from non-PET materials in the mixture will not melt and form gels, making the depolymerized PET solution easier to filter and process further than those produced from saponification.

The authors demonstrate that FAST-PETase can be used for closed-loop recycling, producing about 2.8 grams of colourless PET from 3 g of coloured PET. If a commercial process could be developed using FAST-PETase, a

substantial fraction of plastic packaging waste (in the region of 10–15% for the Netherlands, for example) could finally be recycled in a closed loop to make food-grade transparent rPET, ready for the production of new trays, tubs, cups and blister packs.

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## Neuroimaging

# Brain changes after COVID revealed by imaging

**Randy L. Gollub**

Imaging before and after infection by the SARS-CoV-2 virus reveals substantial changes in the brain after infection. The work sets an example for the high standards required in large longitudinal neuroimaging studies. **See p.697**

Myriad neuropsychiatric symptoms have been attributed to infection with the SARS-CoV-2 virus<sup>1,2</sup>, from lost sense of smell and taste to headaches, memory problems and more. Knowing precisely how the brain is changed by infection would help us to understand these debilitating symptoms. Large-scale brain-imaging studies can provide quantitative measures of subtle changes – but conducting these studies presents a formidable challenge. On page 697, Douaud *et al.*<sup>3</sup> describe 785 sets of brain scans that mark the first step in tackling this challenge head-on.

The UK Biobank is a large-scale biomedical database and research resource that gathers and shares genetic and health-related information for about half a million people ([www.ukbiobank.ac.uk](http://www.ukbiobank.ac.uk)). Of those, 100,000 participants have undergone, or will undergo, a magnetic resonance imaging (MRI) session<sup>4</sup>. In 2020, the biobank launched a COVID-19 repeat-imaging study (see [go.nature.com/3gyv6qe](https://go.nature.com/3gyv6qe)) in which participants who had completed their medical-imaging session before the start of the pandemic returned for an identical, second scan session.

The biobank has released the data from 785 sets of these ‘before and after’ scans, from people between the ages of 51 and 81; 401 of the participants had tested positive for COVID-19 between the two sessions, and 384 had not. The variant that infected each person was unknown, but the scans were conducted before the emergence of the Omicron variant. Douaud *et al.* explored these data, comparing scans pre- and post-pandemic to distinguish

the effects of infection from those caused by pre-existing conditions.

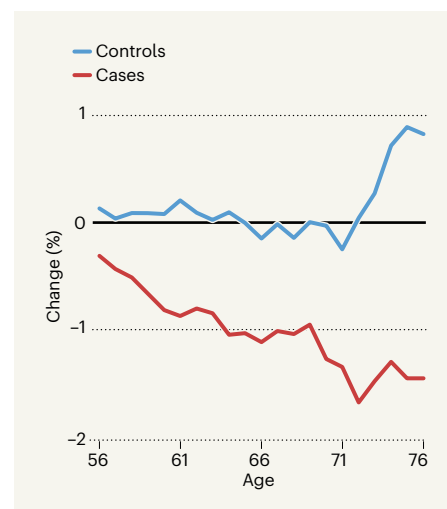
Viral effects on the brain are likely to be so subtle that they can only just be detected by current imaging methods. It was essential that the UK Biobank’s brain MRI scans were consistently gathered, well calibrated and of high quality<sup>4,5</sup>. All of the biobank’s imaging centres have identical MRI machines and methods for using them to collect the brain scans<sup>4</sup>. In addition, Douaud and colleagues used benchmark data from a separate group of biobank participants who had undergone longitudinal brain scans before the pandemic<sup>6</sup>. That the researchers adhered to such high standards is important because – unlike established medical tests, such as those that measure blood glucose levels – industry standards for capturing and analysing complex brain-imaging measurements are still evolving.

The UK Biobank neuroimaging session includes six types of MRI scan, each of which reveals distinct features of brain structure and function<sup>5</sup>. An automated processing pipeline extracts specific features called imaging-derived phenotypes (IDPs) from the scans<sup>5</sup>. Each IDP conveys different information – the volume or microstructural tissue properties of distinct brain structures, for instance, or the strength of neural connectivity between pairs of brain regions. More than 2,000 IDPs are generated for each person from each scan session. In addition, Douaud *et al.* developed a set of IDPs to test the hypothesis that areas of the brain involved in taste and smell would be altered, given that these senses are

often impaired in COVID-19. They used computational models from a previous biobank imaging study<sup>7</sup> to help disentangle any brain changes related to COVID-19 infection from ageing-related changes in brain structure and function that occurred between scans.

These heroic efforts revealed significant differences between the people who had tested positive for SARS-CoV-2 (the case group) and those who had not (the control group). For instance, those in the case group exhibited a decrease in thickness and tissue contrast in some areas of the brain cortex compared with those in the control group (Fig. 1); such changes are often associated with worsening brain health. The case group also displayed increases in markers of tissue damage in brain regions connected to the smell and taste systems. No differences were detectable between the groups’ primary olfactory pathways, but this is to be expected – these are notoriously challenging regions for MRI owing to imaging artefacts that occur at air–tissue interfaces. Whole-brain analyses confirmed these results and showed diffuse atrophy in other brain regions.

It is surprising that Douaud and colleagues identified these brain changes, given that most people in the case group experienced mild to moderate symptoms of COVID-19. Even when the authors excluded from their analysis the small number of people who



**Figure 1 | A decrease in thickness in one region of the brain’s cortex after COVID-19.** Douaud *et al.*<sup>3</sup> compared brain scans from 785 people who had undergone one imaging session before the pandemic and a second after its onset, to determine how infection with the SARS-CoV-2 virus altered the brain. They studied various facets of brain structure and function, including cortical thickness in various brain regions. This graph shows the average percentage change in thickness in one cortical region – the left orbitofrontal cortex – between the two scan sessions in people of various ages. Thickness decreased more in people who had tested positive for COVID-19 (cases) than in those who had not (controls). (Figure adapted from Fig. 1 of ref. 3.)