

drives the assembly of DNA-PK and stimulates its catalytic activity *in vitro*, although does so much less efficiently than can DNA.

Taken together, these observations suggest a model in which KU recruits DNA-PKs to the small-subunit processome. In the case of kinase-defective DNA-PK, the mutant enzyme's inability to regulate its own activity gives the protein a new function, blocking the processing of precursor rRNA into mature 18S rRNA in the small-subunit processome. The resulting defect in global protein synthesis drives a p53-dependent loss of red-blood-cell precursors – a cell type that has an especially high physiological demand for protein synthesis. The parallels with NHEJ are intriguing: in that pathway, the complete deletion of DNA-PKs results in only a minor reduction in repair fidelity, and the joining of broken DNA ends is retained. By contrast, the kinase-inactive DNA-PKs mutant is wholly unable to carry out end joining.

The specific role of DNA-PK in precursor rRNA processing, and how it recognizes precursor rRNA *in vivo*, remains unclear. However, structural analysis of the yeast small-subunit processome⁶ has revealed that U3 acts as a molecular guide that docks the processome onto the precursor rRNA by forming four evolutionarily conserved duplexes (hinges) between the two components: two hinges in a highly branched region of the precursor rRNA, and two in a region that will become the mature 18S rRNA. These hinges are a prerequisite for three cleavage events, mediated by an RNA-cleaving nuclease enzyme, that release the 18S rRNA ready to make the small subunit.

Shao *et al.* show that DNA-PK and KU primarily interact with U3 at this hinge region. Thus, much as DNA-PKs recruits the DNA-cleaving enzyme Artemis during the NHEJ processing of DNA ends⁷, with U3, DNA-PKs might also help to recruit specific RNA-cleaving nucleases (such as UTP24) to the small-subunit processome to cleave the precursor rRNA for ribosome construction.

Structural studies suggest that the binding of DNA-PKs to KU and DNA could regulate the activation of DNA-PKs kinase activity allosterically, that is, by changing the conformation of the enzyme^{8–10}. In the future, it will be interesting to compare RNA- and DNA-dependent conformational changes in DNA-PKs. The physiological relevance of the broad array of RNA partners identified by Shao *et al.* in their irCLIP analysis also remains to be dissected.

Shao and colleagues' study has identified an interesting player in ribosome assembly that might efficiently couple DNA DSB repair with processing of precursor rRNA, which is highly transcribed from the naturally unstable ribosomal DNA template. Broadly, the findings encourage us to critically evaluate how dynamic redistribution of DNA-PK might allow the cell to couple DSB repair with the

regulation of protein synthesis. And, although further studies are required, we might have taken a step closer to deciphering the mysterious ribosomopathies.

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Palaeontology

Tiny fossil sheds light on miniaturization of birds

Roger B. J. Benson

A tiny skull trapped in 99-million-year-old amber suggests that some of the earliest birds evolved to become miniature. The fossil illustrates how ancient amber can act as a window into the distant past. **See p.245**

Dinosaurs were big, whereas birds – which evolved from dinosaurs – are small. This variation is of great importance, because body size affects lifespan, food requirements, sensory capabilities and many other fundamental aspects of biology. The smallest dinosaurs¹ weighed hundreds of grams, but the smallest living bird, the bee hummingbird (*Mellisuga helenae*)², weighs only 2 grams. How did this difference come about, and why? On page 245, Xing *et al.*³ describe the tiny, fossilized, bird-like skull of a previously unknown species, which they name *Oculudentavis khaungraae*.

The discovery suggests that miniature body sizes in birds evolved earlier than previously recognized, and might provide insights into the evolutionary process of miniaturization.

Fossilization of bones in sediments such as clay, silt and sand can crush and destroy the remains of small animals, and can flatten and decay soft parts such as skin, scales and feathers. By contrast, preservation of small animals in Burmese amber (which formed from the resin flows of coniferous trees about 99 million years ago) helps to protect their soft parts. A wide range of invertebrates⁴ and small



Figure 1 | Computed tomography scan of the skull of *Oculudentavis khaungraae*. Xing *et al.*³ have characterized this 99-million-year-old fossil bird.

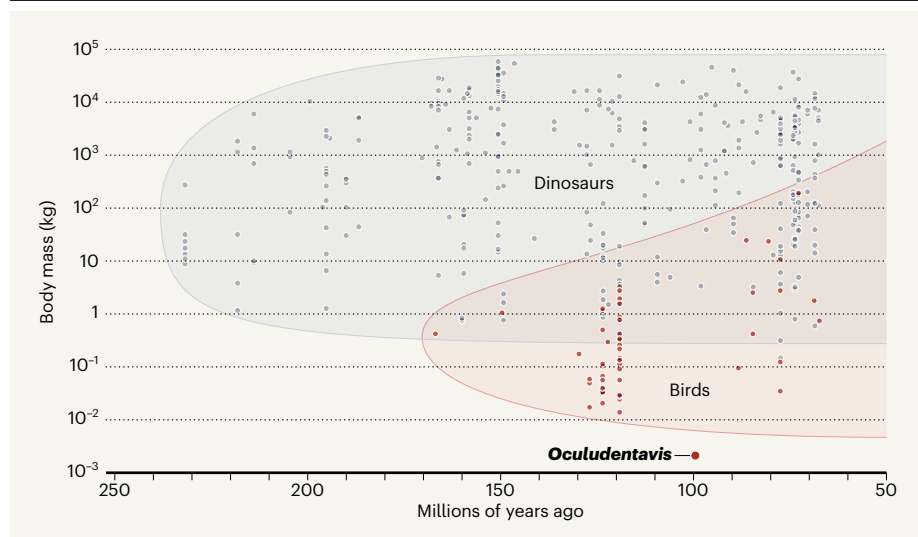


Figure 2 | Different size ranges of dinosaurs and birds. Dinosaurs varied from about 500 grams to many tonnes in weight. By contrast, the first birds were much smaller. The smallest fossil bird found so far from the Cretaceous period weighs in at about 12 grams (data taken from ref. 9). Xing *et al.*³ report that the tiny *Oculudentavis* weighed just 2 grams. This discovery provides new insight into the lower limits of vertebrate body size in the age of dinosaurs.

vertebrates, including lizards⁵ and birds⁶, have been found in Burmese amber. Specimens preserved in this material are rapidly emerging as an exceptional way to study tiny vertebrates from the age of dinosaurs^{5,6}.

It is in Burmese amber that the single known fossil skull of *Oculudentavis* has been preserved (see Fig. 1a of the paper³). *Oculudentavis* means eye tooth bird, a name that Xing *et al.* chose because of two unusual features of the skull, each of which provides evidence about the likely lifestyle of this 99-million-year-old species.

First, the skull is dominated by two enormous eye sockets containing scleral ossicles – rings of bone that form the eye skeletons of birds (Fig. 1). The opening at the centre of these ossicles is narrow, restricting access for light into the eye and providing strong evidence that *Oculudentavis* was active in well-lit, daytime environments.

Second, the jaws of *Oculudentavis* have many small teeth. This might seem odd, given the absence of teeth in today's birds, but teeth are in fact common among early fossil birds⁷. However, *Oculudentavis* has more teeth than other birds of the period, and these extend unusually far back in the jaws to a point just under the eye. On the basis of these facts, along with observations of the fossilized tongue, the authors suggest that *Oculudentavis* was a predator that mainly ate invertebrates. This diet differs considerably from the nectar-based diet of the smallest living birds, and suggests that extinct and living birds took different paths to miniaturization (although how diet might be involved in this process remains unknown).

Oculudentavis is just one fossil species. However, even single fossils can contribute

greatly to our understanding of the history of life on Earth. In this case, weighing perhaps 2 grams, *Oculudentavis* is about one-sixth of the size of the smallest known early fossil bird¹. This indicates that, only shortly after their origins late in the Jurassic period (which lasted from about 201 million to 145 million years ago), birds had already attained their minimum body sizes. By contrast, the smallest dinosaurs weighed hundreds of times more¹ (Fig. 2). Understanding when, how and why the lower limits of body size shifted in this way requires greater knowledge of the earliest fossil birds. But *Oculudentavis* is a stepping stone towards this.

The evolutionary relationships between

“Even single fossils can contribute greatly to our understanding of the history of life on Earth.”

Oculudentavis and other dinosaurs and birds are difficult to determine, but are central to clarifying the evolutionary implications of this discovery. Xing and colleagues' analysis suggests two possibilities. *Oculudentavis* could belong to the most common group of birds of the Cretaceous period (about 145 million to 66 million years ago), the enantiornithines. Alternatively, it could be much more closely related to dinosaurs, lying almost midway on the evolutionary tree between the Cretaceous birds and *Archaeopteryx*, the iconic winged dinosaur from the Jurassic.

This confusion is a result of the bizarre features seen in *Oculudentavis*. These include many characteristics that differ from those of

other birds, such as more-robust, fused bones, and proportionally enlarged sensory organs relative to the overall body size. The authors suggest that these features could have arisen from the constraints of evolutionary miniaturization or from ecological specialization. Both of these might have required *Oculudentavis* to have a strengthened skull and proportionally large eyes to maintain sensory capacity at such a tiny size. In addition, *Oculudentavis* has features that are not seen in dinosaurs or birds, but are present in lizards – these include the spoon shape of its scleral ossicles and the fact that its teeth are attached to the jaw bone by their sides, rather than being implanted in sockets. The challenge of determining how *Oculudentavis* is related to other early birds and bird-like dinosaurs would be greatly assisted by knowing more about its skeleton.

The past decade has generated much data on the dinosaur–bird transition, greatly advancing our understanding of this major evolutionary event^{7,8}. In the past few years, Burmese amber has yielded surprising insights, including previously unseen feather and skeletal structures in other extinct birds⁶. The study of small vertebrates preserved in amber, their ecosystems and their evolutionary relationships with one another is in a nascent phase. But *Oculudentavis* suggests that the potential for continued discovery remains large – especially for animals of diminutive sizes.

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