constituent. Or, as Alving poses the question: If we have antibodies to cholesterol, "why don't we disintegrate?" One possible answer, he suggests, is that cholesterol is rarely free in the body and is thus "masked" by other associated molecules; it may have to aggregate in unnaturally high concentrations before it can be recognized by antibodies. That, he says, might explain the observation that liposomes with less than 50% cholesterol rarely generate antibodies in mice.

Also unclear is the mechanism by which immunization with these liposomes clears excess dietary cholesterol from the blood and reduces plaque formation. Alving hypothesizes that the liposomes function in two ways. The antibodies they induce may tag the low-density lipoproteins (LDLs), the so-called bad cholesterol carrier, for clearance by scavenging macrophages. And the liposomes themselves may mimic the appearance of the LDLs, prompting cells to increase their number of LDL receptors and thus remove them from serum. In contrast, Kruth thinks the antibodies may have a different target: cholesterol-rich liposome-like particles he's found in atherosclerotic plaques.

At this stage, however, speculation in all areas far outstrips available data. In addition to follow-up animal studies, one future goal for Alving's team and EntreMed is the development of a simple, inexpensive test to gauge the levels of an individual's anti-cholesterol antibodies. Such an assay would be needed to help establish in a large population how levels of these antibodies correspond to total cholesterol levels, atherosclerosis progression, and overall health. If Alving's speculations prove correct, an individual's anti-cholesterol antibody level may be as important as blood pressure in determining the risk of heart attack or stroke. Alving himself finds comfort in the fact that he has a high level of these antibodies. "I certainly hope that it will be beneficial to me in the long run and protect me against heart disease. Data from the trials is giving me a lot of peace of mind," he told *Science*. It will be some time, however, before anyone knows if that solace is warranted or premature.

–**John Travis**

Boston-based freelancer P.J. Skerrett contributed reporting to this article.

PALEONTOLOGY

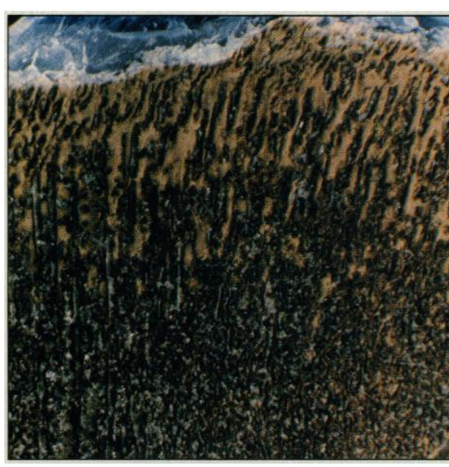
A Closer Look at the Dinosaur-Bird Link

Arrangements for family reunions, even for partly extinct families, rarely go completely smoothly. Over the past several years, dinosaur paleontologists have built a case that birds—not reptiles—are dinosaurs' closest living relatives by comparing the shapes of arms, shoulders, and claws. While this evidence is strong for one of the two main dinosaur groups, researchers have had difficulty fitting the second group into this family picture. Now comes evidence bringing that group into the avian fold, but the link is microscopic: the shapes of ancient cells.

Those cells belonged to a juvenile *Maiasaurus*, a duck-billed bipedal dinosaur—and a member of the disenfranchised group, known as the Ornithischia—that lived in Montana some 72 million years ago. On p. 2020 of this issue, paleontologist Claudia Barreto of the University of Wisconsin's School of Veterinary Medicine in Madison and her colleagues report that cells within the dinosaur's growth plates—discs of cartilage near the ends of bones that allow bones to grow—bear a striking resemblance to the cells of chicken growth plates. And they look very different from those of the growth plates of contemporary reptiles. "This work is very careful, very cautious, and very convincing," says paleontologist Kevin Padian of the University of California, Berkeley. "It means people can no longer say that dinosaurs are like reptiles because here they're doing things that we know only birds do."

Growth plates are made up of cells called chondrocytes. At the plates' boundary with the actual bone, chondrocytes die off, leaving behind their calcified extracellular matrix to serve as scaffolding for the osteoblasts (bone-forming cells) and blood vessels as they push into new territory. Using a light microscope, Barreto's team compared the *Maiasaurus* growth plates to those from a dog, a monitor lizard, and a chicken. They found that the plate-bone boundary of the dinosaur was very irregular, undulating up and down just as it does in contemporary birds. In contrast, the boundary zone in mammals and reptiles forms a straight line.

The team next found that the remnants of dinosaur chondrocytes themselves resemble those of birds. In mammals and reptiles, the cells are tall and have four distinct sides. In birds, the cells are shorter and ovoid in shape. That's the shape Barreto's group saw in the dinosaur plates. The researchers then used a scanning electron microscope (SEM) to peer into the extracellular matrix. In the *Maiasaurus* "the SEM showed calcified walls all around," Barreto says, as well as calcified lumps known as calcospherites. Again, this is identical to the pattern in birds and very different from what's seen in mammals and reptiles, who only have calcification and calcospherites on the longitudinal walls. "These growth plates point to a common ancestor for birds and dinosaurs. It's too complex to have evolved twice," Barreto concludes.


BARRETO, ET AL.

Growing likeness. Cells in this growth plate from a juvenile dinosaur bone resemble those from plates in birds.

Paleontologists who are more partial to reptilian relativity for dinosaurs, such as Larry Martin of the University of Kansas, argue that such a statement is too broad, and all Barreto has shown is a link between birds and the ornithischian branch of the dinosaurs. To include the other branch, the Saurischia, she will have to find this avian pattern in them as well. Barreto hasn't examined a juvenile saurischian yet ("That's the next step," she says), but she argues that many other features tie birds to saurischians. This, together with the growth plate evidence in ornithiscians, suggests to her that all the dinosaurs are related to birds.

And that general pattern not only links the ancient animals to modern avians, Barreto says, it also indicates the two dinosaur branches had one common ancestor. It had been argued that the two branches emerged separately from a diverse group of primitive reptiles called thecodonts. But here even paleontologists who favor the common ancestor theory think Barreto hasn't done the right comparisons to support that claim. "You need to look at crocodiles," says Jacques Gauthier of the California Academy of Sciences.

Crocs, next to birds, are presumed to be dinosaurs' nearest living relatives, deriving from that same general pool of ancient reptiles. If the birdlike growth plates are missing in crocs, Gauthier says, it implies the pattern arose in a dinosaur ancestor after the croc lineage went its own way. But if crocs do have these plates, the feature must have been older and more generalized, and says nothing about a common ancestor for the two dinosaur groups. So Barreto is off on another big game hunt, this time for crocodiles, but once again she's looking for something very small.

–**Joshua Fischman**