Fossil jaw tells tale of whale evolution

Paleontologists have unveiled the fossilized lower jaw of an ancient whale from India that, they claim, pushes the origin of these marine mammals back before 53.5 million years ago, earlier than previously thought. This primitive species provides new information on the profound evolutionary transformation that turned a group of four-legged land mammals into modern cetaceans—the whales, dolphins, and porpoises inhabiting the ocean today—say the researchers.

Other paleontologists, however, question the dating of the Indian fossil and whether it adds much to the story of whale origins.

Indian scientists found the controversial jaw bone more than 12 years ago in the Subathu rock formation of northern India, but they failed to finish an analysis of the animal. Sunil Bajpai of the University of Roorkee in India and Philip D. Gingerich of the University of Michigan in Ann Arbor collaborated on the current study. They described the animal, unofficially named Himalayacetus, at a meeting of the Society of Vertebrate Paleontology in Snowbird, Utah, last week.

The oldest accepted fossil whale, called *Pakicetus*, comes from rocks in the Indian subcontinent dated to 50 million years ago. Gingerich had previously calculated that there were scant odds of finding any other species prior to 52 or 53 million years ago.

Bajpai and Gingerich dated Himalayacetus using the shells of one species of tiny marine organisms called foraminifera, found in the same rock formation. The species of foraminifera suggests that the whale lived during the early Eocene epoch, whereas *Pakicetus* fossils have come from middle Eocene rocks.

Other researchers contend the dating rests on thin evidence. The foraminifera in the Subathu formation lived near the seafloor and provide less accurate age information than do surface foraminifera, says paleontologist Hans Thewissen of the Northeastern Ohio Universities College of Medicine in Rootstown. "The dating question is rather critical," he says.

Nonetheless, the find extends the geographic range of known whale fossils. Thewissen, Gingerich, and others have found whale remains in Pakistan, central India, and Kashmir but not in Himachal Pradesh, the home of Himalayacetus.

If Bajpai and Gingerich are correct about Himalayacetus, the Indian fossil would shift ideas about when whales invaded the oceans, says paleontologist Mark D. Uhen of the Cranbrook Institute of Science in Bloomfield Hills, Mich.

Paleontologists believe that *Pakicetus* and other early cetaceans were furry, four-legged creatures that lived mostly on land, venturing into the water to feed on fish. According to current thinking, the earliest whales hunted in rivers and were unable to feed in salt water. Indeed, *Pakicetus* is found in river sediments, and the mixture of oxygen isotopes in its bones suggests it swam in fresh water.

The Indian fossil, however, came from marine sediments containing oysters and other ocean species, indicating that Himalayacetus swam in salt water. The ratio of oxygen isotopes in its bones supports this interpretation.

"Before, we might have thought that [these early whales] were restricted to fresh water, but here is a record from a marine environment," says Gingerich.

Despite its marine predilection, Himalayacetus apparently lacked key adaptations to aquatic life. Later whales developed enlarged canals in their lower jaws that improved their hearing underwater. Himalayacetus, though, had the small jaw canals of a land mammal, reports Gingerich. It appears that the Indian whale had already gained adaptations for feeding in salt water even though it could not hear well in that environment, he says. —*R. Monastersky*

Epstein-Barr deaths tied to faulty protein

Most people don't even know when they've got Epstein-Barr virus. Usually, it strikes in early childhood, when the symptoms are a mild fever or nothing at all. A few people dodge the Epstein-Barr virus when young, contracting it in adolescence or later as mononucleosis, a manageable disease.

In about one in a million cases, however, Epstein-Barr virus sets off a chain reaction that causes immune cells to multiply recklessly, leading to fatal cases of mononucleosis, lymph cancer, or a shortage of disease-fighting antibodies. This syndrome—called X-linked lymphoproliferative disease, or Duncan disease—strikes boys almost exclusively and kills 70 percent of its victims before age 10. No one with Duncan disease has been known to reach age 40.

Two teams of scientists in Europe and the United States have now pinpointed a genetic mutation that causes this fatal sensitivity to Epstein-Barr virus.

Analyzing data from Britain, France, Germany, Italy, and the United States, researchers report in the October NATURE GENETICS that 9 of 16 unrelated patients with Duncan disease had mutations in the *SH2D1A* gene, which encodes a protein that plays an instrumental role in the immune system. Without a gene to provide the blueprint for a usable SH2D1A protein, Duncan disease appears inevitable, they find. No significant mutation appeared in 50 healthy men.

Another group of researchers from the United States, Austria, and Italy unveils the function of SH2D1A protein in the Oct. 1 NATURE. After studying defective signaling between immune cells in Duncan disease patients, they traced the problem back to the mutated *SH2D1A* gene. The researchers report that normal SH2D1A protein halts runaway proliferation of immune cells.

Viruses need to invade a living cell in order to replicate, and the host cell of choice for the Epstein–Barr virus is the immune system's own B lymphocyte, a white blood cell. The fever and fatigue that mononucleosis patients feel "is really the immune system bringing the B cells under control," says David N. Liebowitz, a virologist and oncologist at the University of Chicago. "The body recognizes they are infected and not normal and tries to kill them and prevent them from killing the host."

It is at this stage that Duncan disease goes beyond mononucleosis and poses a deadly paradox: The body puts up a massive immune response, but to no avail. Instead of killing rogue B cells, immune system T cells coexist peacefully with them, apparently because of the defective SH2D1A protein, says Juan Sayos, an immunologist at Beth Israel Deaconess Medical Center in Boston and a coauthor of the NATURE paper. Other immune cells also fail to kill off the infected cells.

T and B cells both have surface proteins called SLAM (for signaling lymphocyte–activation molecule) that hook up to each other like jigsaw puzzle pieces. This SLAM docking site enables the immune cells to communicate, wade into battle together, and reproduce indefinitely. Unfortunately, SLAM doesn't always know when to quit. Working SH2D1A protein on T cells normally modulates this immune process by limiting the SLAM protein's activity.

Tragically, people with a mutated *SH2D1A* lose this blocking capability, and their T and B cells keep signaling each other to multiply. "They proliferate out of control," says geneticist Alison J. Coffey of the Sanger Centre in Hinxton, England, a coauthor of the NATURE GENETICS paper. In the process, the T cells encourage reproduction of the virus-infected B cells, aggravating the disease, Sayos says.

The research may provide some basis for synthesizing the SH2D1A protein as a potential treatment for Duncan disease, although that possibility is still far off, Coffey says. Meanwhile, she and other researchers will look for this mutated gene in other diseases. —*N. Seppa*