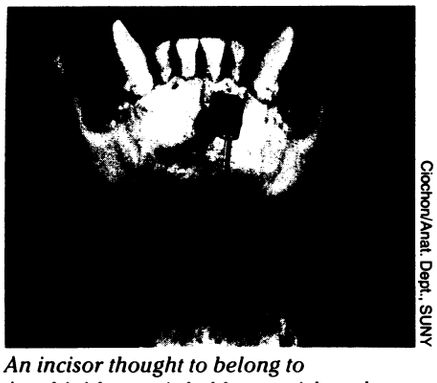

Ciochon/Anat. Dept., SUNY

An incisor thought to belong to Amphipithecus *is held on a stick to show its similarities with a gibbon ape jaw.*

thropoids: adapids or another prosimian group called the omomyids, which are related to modern tarsiers. Scientists' responses to Ciochon's group's findings appear to depend largely on where they stand on this other issue.

Philip Gingerich, director of the Museum of Paleontology at the University of Michigan in Ann Arbor and a strong proponent of adapid origins, is greatly encouraged by the new paper. "I basically agree with the interpretation of the authors," he says.

Eric Delson, a paleoanthropologist at Lehman College in New York City and a member of the omomyid-origin camp, doesn't think there is enough fossil evidence to determine that *Amphipithecus* is an anthropoid, although he admits the possibility. "But [even] if it is, I don't think it shows that adapids are related to anthropoids," he says.

If Ciochon's interpretation of *Amphipithecus*'s place on the primate tree is correct, then the Asian origin of anthropoids complicates the geographic picture of evolution. Ciochon has proposed one scenario in which anthropoids evolved from lower primates in Asia around 40 million years ago and spread, over thousands of generations, into Africa by crossing a narrow, swamplike sea. Meanwhile, he suggests, some early anthropoid forms spread to South America to become the ancestors of New World monkeys, for which there are 27-million-year-old fossils. Ciochon suggests that the anthropoids got to South America by crossing a series of volcanic islands in the Atlantic Ocean when it was much narrower than it is today.

Delson counters that the higher primates didn't necessarily evolve in Asia but that they, or their ancestors, could have been in a band north from Burma around the Bering Strait and down the west coast of North America. In Delson's scenario, the primates in South America originated in North America and are not descendants of African primates.

However hotly debated, says Gingerich, the recent findings "give us a rare view of the stage of evolution of primates 40 million years ago." — *S. Weisburd*

Research progress toward gene therapy

Rapid advances in laboratory research during the last few months have made the rare immune system disorder called adenosine deaminase deficiency likely to be the target of the first U.S. experiments in human gene therapy. In as little as two months a group of researchers from several institutions, led by W. French Anderson of the National Institutes of Health (NIH) in Bethesda, Md., may be ready to propose an experiment in which a normal human gene for adenosine deaminase (ADA) is transferred into bone marrow cells, which will then be returned to a patient. Currently, persons with ADA deficiency die early in childhood unless they receive a bone marrow transplant from a suitable donor.

The most striking laboratory data so far demonstrate the "correction" of defective immune system cells taken from a youngster with ADA deficiency, R. Michael Blaese of NIH reported this week in Gmienden, Austria, at the Workshop on Primary Immunodeficiency Diseases. In the disease, the lack of ADA enzyme allows the buildup of 2′ deoxyadenosine triphosphate, a chemical that is particularly detrimental to immune system cells, especially T cells. Blaese and Don Kohn have demonstrated that after the transfer of a normal ADA gene, T and B cells of the ADA patient act like normal immune system cells.

Although excited by the data, Anderson said in an interview, "We're not ready to treat this patient tomorrow. There are still a lot of things that need to be done." The researchers plan to make a formal proposal for a human gene-therapy experiment, he says, after they get results on monkey experiments, expected in the next two months.

Currently about a half dozen U.S. patients are candidates for such a gene-transfer experiment. These are children for whom there is no suitable bone marrow donor. This situation contrasts with that for Lesch-Nyhan disease, another enzyme deficiency that had been considered a likely focus of early genetic engineering attempts. Progress there has been slowed by the recent failure of a bone marrow transplant from a normal donor to ameliorate the disease.

Another important advance toward gene therapy was reported by Anderson earlier this month in Los Angeles at a meeting on tissue-specific expression of cloned genes. He and NIH colleagues Philip Kantoff and Martin Eglitis transferred a gene into mouse bone marrow cells. When the cells were transplanted into mice whose own bone marrow had been destroyed, they repopulated the marrow and after four months continue to produce cells containing the foreign gene. Most important, the gene transplanted into the animal's B and T cells produces its characteristic protein. Anderson says this experiment and similar ones performed in Germany are the first to show expression in an animal of a gene transplanted into bone marrow cells and no longer associated with the carrier virus.

The carrier virus, or vector, used is one of a series being developed by Eli Gilboa and his colleagues at Princeton (N.J.) University. They have been analyzing the Maloney murine leukemia virus and, in construction of vectors, are using their new information about viral function. For example, they have found unanticipated control regions within the genes for viral proteins.

"The guts of the virus are replaced with the gene of interest," Gilboa explains. In the experiments on mice, the gene of interest is linked to a control region from a mouse gene, and in the experiments on the human cells, it is linked to a control region from a virus, called SV40, that infects primates.

The resultant redesigned viruses appear to be the most efficient of any employed thus far for transferring foreign genes. When bone marrow cells are mixed with the virus-infected "producer cells," more than 80 percent of the bone marrow cells receive the foreign gene.

Gilboa continues to develop more effective carriers. In their most recent work, he and co-workers deleted from the virus a "promoter" region used in the expression of its own genes. Gilboa says, "This gene-transfer system will interfere minimally with the proper expression of the transferred gene."

The scientists are convinced that leukemia virus will not be transferred with the desired gene: The bone marrow cells are never exposed to functional viruses, and the cells that are returned to the body contain no viral genes. Gilboa adds that the deletion of the viral promoter will offer further protection.

Hopes for the application of gene therapy in the near future are pinned to an experiment now in progress: the transfer of a human ADA gene into monkey bone marrow cells, which were then returned to the monkey. This experiment, performed by Richard O'Reilly of Memorial Sloan-Kettering Cancer Center in New York City, with Anderson and colleagues, is expected to give a strong indication of whether the gene transfer will work in human patients. Will the ADA gene be expressed in "stem cells," the bone marrow cells that continue throughout life to give rise to T cells, B cells and other blood cells that have a limited life span and do not reproduce? Anderson says, "That's the critical data we're waiting for." —*J.A. Miller*