interference with chemotherapy.

Oncologist David Fisher, also at Dana-Farber, describes the work so far as an "enormous advance." He speculates that it might also be possible to design inhibitors to protect other normal tissues that are damaged by chemotherapeutic drugs. The lining of the gut—where damage causes nausea and vomiting—is one possibility, if a nonabsorbable version can be produced.

Davis says he doesn't know how long it might take to bring the current CDK2 inhibitor to market, as the drug is just beginning preclinical testing. But if it does eventually move into human trials, Fisher predicts, "the clinical community will pound on the door to test it." –JEAN MARX

EVOLUTION

Tooth Theory Revises History of Mammals

To paleontologists who study mammals, you are what you eat with. Teeth are often the only remains of tiny, extinct mammals, but they can reveal an animal's diet as well as its place on the family tree. The most important advance in mammalian dental evolution has long been regarded as the tribosphenic molar—a Cuisinart-like tooth that could both slice and grind. This was considered a key innovation, shared exclusively by placental mammals and marsupials, that helps explain their extraordinary success ever since the Cretaceous period.

Now three paleontologists propose that the tribosphenic molar evolved not once, but twice—a highly provocative idea. "It shakes a bedrock principle that we've held for a long time," says Andy Wyss of the University of California (UC), Santa Barbara. In the 4 January issue of *Nature*, the trio argues that this kind of molar independently appeared in the Southern Hemisphere in fossil relatives of the monotremes, an extremely ancient group of mammals that includes the platypus. Because the hypothesis is based on extremely limited evidence, many paleontologists are reacting cautiously. "I think many people would tend to take it with a grain of salt right now," says Michael Woodburne of UC Riverside. But Bill Clemens of UC Berkeley adds, "It's going to be very, very stimulating."

Mammal teeth have come a long way in the past 220 million years. The earliest relatives of placental and marsupial mammals had molars that sliced like pinking shears—good for chopping up insects but not for crushing tougher food. The tribosphenic molar, however, also incorporates a grinder: a cusp (called the protocone) on the upper tooth that fits like a pestle into the mortar-like basin (known as the talonid) of the lower tooth. This action allows tribosphenic mammals to crush seeds, pulp fruit, and grind up leaves.

For most of this century, all known Mesozoic fossils of placental and marsupial mammals had tribosphenic teeth. The fossils came from Asia, Europe, and North America and showed a clear step-by-step progression toward more and more tribosphenic features. Paleontologists concluded that mammals with this type of tooth most likely had arisen from a common ancestor that lived in the Northern Hemisphere during the Early Cretaceous. Meanwhile, they thought, the more primitive, nontribosphenic monotremes had evolved in the southern continents.

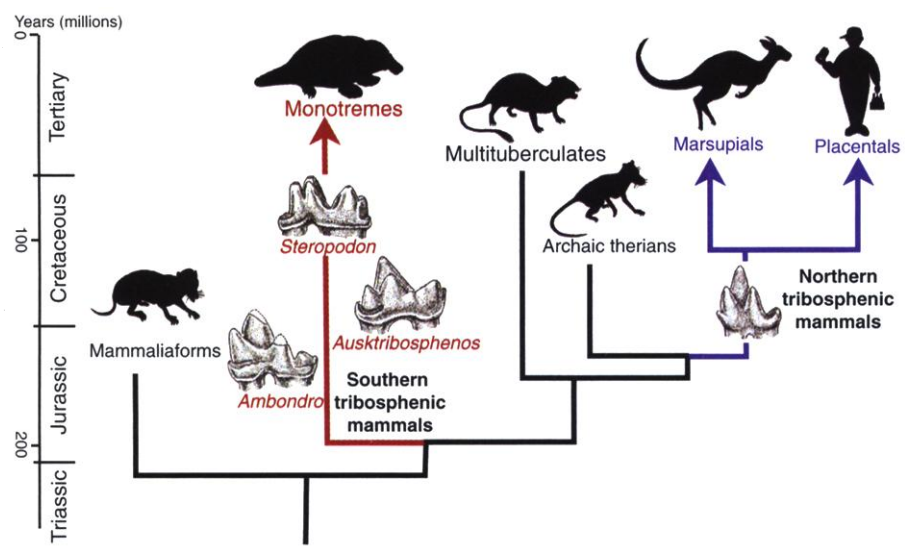
Cracks in the theory appeared in 1985, with a report of the jaw of a fossil mammal, called *Steropodon*, from Early Cretaceous rocks in Australia. The jaw clearly belonged to a monotreme, but it bore relatively advanced teeth that vaguely resembled tribosphenic molars. "This came as a tremendous surprise," says Richard Cifelli of the Oklahoma Museum of Natural History in Norman. Even bigger surprises were to come. In the late 1990s, unquestionably tribosphenic molars belonging to animals called *Ausktribosphenos* and *Ambondro* turned up in Australia and Madagascar, respectively. What's more, *Ambondro* was found in mid-Jurassic rock—evidence that the tribosphenic molar had originated not only in the "wrong" hemisphere, but at least tens of millions of years earlier than transitional molar forms in the north. By this time, Cifelli says, "the contradiction had become absolutely impossible to ignore."

Trying to resolve the puzzle, Cifelli teamed up with Zhexi Luo of the Carnegie Museum of Natural History in Pittsburgh, Pennsylvania, and Zofia Kielan-Jaworowska of the Polish Academy of Sciences. The trio picked 21 living and fossil mammals, examining the widest suite of features yet. They concentrated on 55 characteristics preserved in the teeth and jaws of the three new fossils from the Southern Hemisphere.

From similar features, the paleontologists divided the fossils into two distinct tribosphenic clans: the southern australosphenidans, which include *Ausktribosphenos*, *Ambondro*, *Steropodon*, and living monotremes; and the northern boreosphenidans, which include placental mammals and marsupials. The tribosphenic molar originated independently in both, they propose. By making that assumption, they say, paleontologists can continue to classify monotremes and other primitive mammals as distant cousins of marsupials and placentals, without having to assume that fully tribosphenic Jurassic mammals in the south somehow gave rise to later, less tribosphenic mammals in the north.

Not everyone is convinced. "I think they're sticking their necks out pretty far," Wyss says, noting that the remains of the southern fossils include only teeth and jaws—no upper teeth, skulls, or other bones. "There's a tremendous amount of missing information here." And the existing data haven't thoroughly convinced other experts, either. "Some of the characters that Luo and company have been using to link *Steropodon* with *Ambondro* and *Ausktribosphenos* may be suspect," Woodburne says.

But, if true, the hypothesis also robs paleontologists of a long-standing touchstone. "The tribosphenic molar has been something that we have hung our hats on forever because it is so distinctive," Cifelli says. Now, he adds, it may be time to admit that "we can have no more sacred cows"—or at least no more holy molars. –ERIK STOKSTAD



Coinci-dental? "Unique" mammalian molars actually may have evolved twice.

ILLUSTRATION: ADAPTED FROM Z. LUO *ET AL.*