looks "like things are falling into place" for an impact-driven extinction at the end of the Cretaceous, he says.

Norman MacLeod of The Natural History Museum in London is less sanguine, noting that while the statistics are "consistent" with an impact, they are also consistent with a more drawn-out decline on the same order of time as the disappearance of the mammoths. "A lot of things—climatic cooling, a sea-level fall, and probably volcanic activity—were coming together at the end of the Cretaceous. The ammonites [could have] started crashing 5000 years before the meteorite arrived. That's still enough time" for other extinction mechanisms to work, he says.

And of course, the Bay of Biscay alone won't resolve the fate of all ammonites, much less Cretaceous life in general, around the globe. "It's an exemplary study," says David Jablonski of the University of Chicago, but what's needed is to "expand the geographic and taxonomic coverage."

Broader geographic samples are beginning to come in, and the gap between the last fossil and the impact debris layer is shrinking elsewhere too. For example, far to the south of Zumaya, the Cretaceous ammonites of Seymour Island off Antarctica have fueled the extinction controversy since the late 1980s, when William Zinsmeister of Purdue University and his colleagues concluded that the ammonites and other large marine animals there petered out over 50 meters of sediment—well before the impact. Using these fossils and other evidence from tiny, shelled marine plankton called forams, Zinsmeister, MacLeod, and others had argued that while a few extinctions in some parts of the tropics may have been catastrophic, animals at high latitudes suffered less or not at all at the time of the impact.

Now Zinsmeister is shifting his stance in the light of additional field collecting on Seymour Island. The new data, which he presented at last month's meeting of the Geological Society of America, imply that "the changeover is much more abrupt then we said earlier," he says. Still, Zinsmeister is not yet so impressed by Marshall's statistical method as to suggest that most species went out precisely at the impact. He and his crew searched the vicinity of the impact layer intensively last field season—and found no ammonites. So he suspects that many species went extinct under the environmental stresses of the late Cretaceous, and then "along came Big Bertha and that was it." The idea of the impact as merely the final stroke for a few stragglers, rather than a principal trigger, has many supporters. It may take a pile of statistical readings, from many different pages of the fossil record, to change the minds of paleontologists.

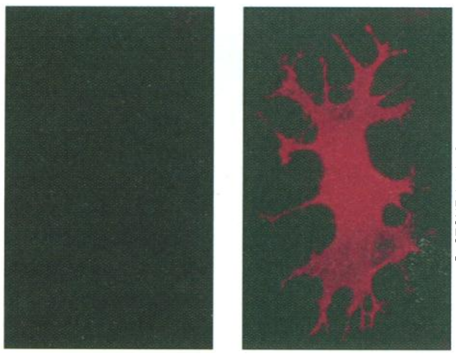
–Richard A. Kerr

DEVELOPMENTAL BIOLOGY

Hedgehog's Patterning Call Is Patched Through, Smoothly

In the parlor game Telephone, Alice whispers something to Bob, who transmits it to Carol, and so forth until a hilariously skewed message emerges at the far end of the chain. Cells in a developing embryo trade news that shapes their fates in much the same way, with extracellular growth factors, cell-surface receptors, and intracellular courier molecules acting as go-betweens. But in one important kind of phone call between cells, involving the powerful Hedgehog (Hh) family of pattern-forming proteins, a key party has long been hidden—the receptor on the cell surface. As a result, researchers couldn't tell where the message went after reaching the cell or why it is sometimes dangerously distorted, spurring cancerous cell proliferation.

Now the mystery party has been unmasked, revealing not one molecule but a dynamic duo. The receptor molecule for the vertebrate protein Sonic hedgehog (Shh)—which transmits a signal that can help embryonic hands tell thumb from little finger, for example—is a membrane-bound protein called Patched (Ptc), according to two reports in the 14 November issue of *Nature*. But Ptc itself doesn't transmit the signal to the cell interior; instead, these reports and other recent work suggest that its usual job may be to interrupt signaling by another molecule called Smoothened (Smo). Shh's arrival distracts Ptc from this job, allowing Smo's message to get through.


D. STONE, W. ANSTINE, A. ROSENTHAL

Smoothed out. The signaling molecule Sonic hedgehog binds to embryonic cells expressing the protein Patched (red stain, *right*), but not to cells expressing another receptor candidate, Smoothened *(left)*.

Molecular biologist Norbert Perrimon of Harvard Medical School says "there is no precedent" for this arrangement in the annals of cell biology, and notes that it helps explain data that last summer led some researchers to finger Smo itself as the Shh receptor. The work may also help researchers understand why mutations in the gene encoding Ptc predispose some people to a common skin cancer. Neurobiologist Doros Platika, chief executive officer of Ontogeny Inc. of Cambridge, Massachusetts, which has an exclusive license to develop medical therapies using Shh and Ptc, is already thinking about possible treatments for such cancers. "We're delighted with this news," he says.

Developmental biologists have long known that Hh shuttles signals from cell to cell in fruit fly embryos, directing them to carry out tasks such as setting up repeated body segments or organizing eyes, wings, and limbs. In vertebrates, Shh and its cousins play similar roles, lending pattern to bone, muscle, and neurons. But until recently, no one knew the identity of the Hedgehog proteins' receptor. Although the overlapping distribution of Hh, Ptc, and related proteins in fly embryos led geneticist Phil Ingham of the Imperial Cancer Research Fund in Oxford, England, to propose in 1991 that Ptc is the Hh receptor, his lab lacked the biochemical facilities to test whether the two molecules actually bind to each other. Then, this summer, experiments in Ingham's lab and in the labs of molecular biologists Markus Noll at the University of Zurich in Switzerland and Joan Hooper at the University of Colorado showed that Smo has a chemical structure typical of a receptor, and that mutant flies with defective Smo can't respond to Hh signals. That persuaded most researchers that Smo was a better candidate than Ptc.

But now it seems that Ingham's first guess was right. A group led by Arnon Rosenthal, a molecular neurobiologist at San Francisco's Genentech Inc., reports in *Nature* that mouse Shh doesn't bind biochemically to cells producing the mouse version of Smo, but does bind to cells making mouse Ptc. A second group, led by Harvard Medical School developmental geneticists Valeria Marigo and Cliff Tabin, boosted the case by injecting messenger RNA encoding Ptc into *Xenopus* frog eggs, which lack natural Ptc at this stage. Shh bound to the injected eggs but not to unaltered eggs, further showing that Ptc can scoop up Shh in living cells. The team also demonstrated that their experiments were mimicking true biological conditions by showing that the binding between Ptc and Shh could be blocked with an antibody known to interfere with Shh's signal in living tissue.

That's "very compelling" evidence that Ptc is the primary Hh receptor, says Roel Nusse, a developmental geneticist at Stanford University. But Columbia University developmental biologist Gary Struhl suggests that the story is even "more baroque." In the 1 November issue of *Cell*, Struhl and colleague Yu Chen try to reconcile the new findings with the earlier evidence suggesting a role for Smo. They argue that Ptc and Smo work together: Unbound Ptc, they propose, inhibits Smo from releasing a signal into the cell cytoplasm, but when a Hedgehog protein binds to Ptc, it triggers structural changes in Ptc and perhaps Smo that somehow free Smo's signal. Rosenthal and his colleagues propose similar models based on experiments indicating that Shh, Ptc, and Smo can bind together in a single complex. Says Rosenthal: "This finding links the sometimes conflicting evidence implicating both Patched and Smoothened as the Hedgehog receptor."

The new findings could also pave the way to treatment for basal-cell skin cancer, the most common form of cancer in humans. Researchers at Yale University and Stanford reported earlier this year that people carrying a mutation in the gene encoding Ptc suffer a high risk of this cancer (*Science*, 14 June, pp. 1583 and 1668). Now Rosenthal suspects Smo is the real culprit, reasoning that altered Ptc can't maintain its usual brake on Smo, allowing Smo to send a continuous signal that may activate cancerous cell division. "If we can find small molecules that inhibit Smoothened," says Rosenthal, "they could serve as therapeutic agents." And that would be something to phone home about.

–Wade Roush

ASTRONOMY

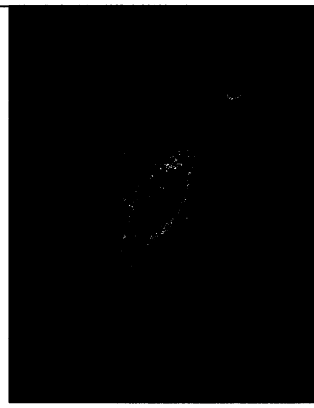
Quasar Pairs: A Redshift Puzzle?

When Galileo observed Jupiter through his homemade telescope in January 1610, he saw four stars in a straight line on either side of the planet. He rightly concluded that they were satellites of Jupiter—the odds against a coincidental alignment of the nearby planet with four distant stars are huge.

In a similar vein, Halton Arp of the Max Planck Institute for Astrophysics in Garching, Germany, has spent more than 25 years asserting that quasars, objects most astronomers believe are at the far edges of the universe, are actually the companions of relatively nearby galaxies. If he is right, the implications would be as revolutionary as those of Galileo's claim, which supported the idea that the Earth orbits the sun just as Jupiter's moons orbit the planet. The astronomical ruler, called redshift, that places the quasars and the galaxies at very different distances would be in jeopardy—and so would many of cosmologists' basic beliefs about the universe. Astronomers have largely rejected Arp's claims, but now he is presenting his most systematic study of quasar-galaxy pairings yet.

In a pair of papers soon to appear in *Astronomy and Astrophysics*, he and his colleague Hans-Dieter Radecke report that they examined 24 Seyfert galaxies, nearby galaxies that have brilliant, active nuclei, and found that 12 of them were accompanied by pairs of x-ray sources—almost certainly quasars with high redshifts—aligned on either side of the galaxy. The alignment implies, says Arp, that the galaxy itself ejected the quasars, in spite of the discrepancies in redshift. Arp believes he has struck a fatal blow at astronomers' favorite distance measure. "The astronomical establishment should be convinced by now," he says.

It isn't. "The theoretical implications [of this find] would be profound, if true," says theorist Jim Peebles of Princeton University. Andrew Wilson of the University of Maryland, who studies active galaxies, says "In some cases, the pairings are quite striking. [This is all] very hard to explain in terms of conventional cosmological theory." But Peebles, Wilson, and others say that 12 cases are not enough to spark a revolution, and that the high frequency of pairings could just be chance alignments that look impressive because the sample is small. "History teaches us that there can be apparent excesses that went away when a larger sample was observed," says Wilson.



JEAN LORRE/PHOTO RESEARCHERS

Distance dilemma. Are quasars around NGC 1097 connected to it?

Arp has been looking for convincing statistics for more than a quarter of a century, uncovering dozens of similar unnerving alignments and associations, especially among so-called active galaxies. His explanation is that quasars are created in and ejected by these galaxies, and have an "intrinsic" high redshift that has nothing to do with distance. Current physical theory cannot explain such an effect. As astronomers now understand redshift, it reflects the expansion of the universe. The more distant an object is, the faster it is being carried away by the expansion, which stretches its light to longer wavelengths—toward the red end of the spectrum.

Arp bases his latest assault on redshift on data from the German x-ray satellite Rosat. Examining the data, Radecke found far more x-ray sources than usual in the neighborhood of 24 Seyfert galaxies. When Arp looked at the Rosat maps of the sources, he found pairs of x-ray sources aligned across half the galactic nuclei. Although redshifts have not been measured for the majority of these sources, "99.9% of [such objects] have historically turned out to be high-redshift quasars," Arp says.

That was the case for the one pair of sources where redshifts have been measured—the two companions of a distorted, violent galaxy called NGC 4258. Wolfgang Pietsch of the Max Planck Institute for Extraterrestrial Physics in Garching, who discovered this particular quasar pair in the Rosat data, recalls that he "thought that it was rather unlikely that it could be a chance coincidence that the galaxy is showing up with these paired sources." However, he cautiously adds: "It's small number statistics, and therefore very unlikely things may happen."

Arp has heard that reaction before. "It has always been like this," he says. "There's a flurry of comment, worry, and anxiety, but after that, everybody slips back to the old way" of doing astronomy. Wilson acknowledges that some astronomers tend to ignore observational evidence that contradicts established theory. And Peebles agrees that "it would be very bad if we ignored evidence for new physics, since I'm sure there is new physics [out there] for us to discover. However, as a theorist, I'll be cautious as long as the observers disagree."

But there is a tried and tested way of proving Arp's point. Four centuries ago, Galileo proved himself right about Jupiter's moons by observing their motion around the planet, thus establishing a physical connection. In the case of the quasar pairs, similar observations "could be done by measuring diffuse emission connecting the paired sources to the galaxy," says Pietsch. Or, if the quasars were ejected by galaxies at high speeds and emit radio signals, their motion across the sky might be measurable with a radio interferometer. If someone succeeded in detecting such physical connections or proper motions in the companion objects, Arp's alignments might turn out to be the start of a revolution after all.

–Govert Schilling

Govert Schilling is an astronomy writer in Utrecht, the Netherlands.