# Melanoma Shrinks From Human Monoclonals

The first attempt to deploy human monoclonal antibodies in the fight against cancer has resulted in dramatic disappearance of tumors in patients with recurrent, malignant melanoma. Researchers say the experimental therapy — involving antibodies produced by cultured human cells — proved more effective and had fewer side effects than any current treatment for this tenacious form of skin cancer.

Surgery can cure 90 percent of early-stage melanomas. But when the black growths recur on the skin or the malignancy spreads to a new site, death generally follows within eight to 12 months.

Researchers studying this and other cancers have long sought to use monoclonal antibodies — biological molecules that bind only to particular target cells — to attack tumors directly or to shuttle toxins selectively to cancer cells. But most scientists make these antibodies in mouse cells, and the mouse "signature" that remains often triggers an immune reaction in human recipients. This can block the monoclonals' action, and sometimes causes a life-threatening form of immune shock.

Human monoclonal antibodies offer an obvious solution. But researchers who have coaxed human cells to produce such antibodies have obtained only small quantities and at great expense.

Donald L. Morton and Reiko F. Irie of the University of California, Los Angeles, figured that even small quantities of the antibodies might prove useful if applied directly to tumors. They focused on antibodies against gangliosides — molecular markers found on cancer cells but not on normal cells. Typically, a person with melanoma has only one of three kinds of gangliosides on his or her tumor cells.

The researchers isolated and cultured three kinds of white cells from melanoma patients. Each of these cell lines makes antibodies that bind to a specific ganglioside. When one of these antibodies binds to its matching ganglioside on a cancer cell, it triggers an immune response that kills the cell.

Morton and Irie injected tiny amounts of anti-ganglioside antibodies directly into the cancerous growths of 25 patients with recurrent melanoma. Some of these patients received a randomly assigned antibody. Of those, about 40 percent showed complete loss of skin tumors within days or weeks. For the other patients, the researchers first biopsied and analyzed the tumors to determine which marker the cancer cells bore. All of those patients' tumors disappeared after injection with the appropriate matched antibody, Morton said this week at the annual meeting of the American Society of Clinical Oncology in Washington, D.C.

Carol Westbrook, a University of Chicago oncologist, calls the results "quite impressive" and "very promising." Still, she notes, patients with recurrent melanoma face a high risk of death from metastases to the brain or other vital organs not accessible by direct injection. Indeed, most patients treated with the experimental antibodies have since died from melanoma metastases, although some have survived, including one who has lived three years beyond treatment.

"The desirable thing would be to have enough of the antibody so we could give it systemically and have it go all around the body," Morton says. "Hopefully in a year or so we'll be able to make these things in large quantities at a reasonable cost."

The researchers say they have seen no ill effects from their therapeutic molecules. Oddly, Morton adds, tests indicate that some patients produced significant quantities of their *own* anti-ganglioside antibodies in response to the injections. "We're activating specific immunity with this treatment," he says. "We don't know how, but we are." In Morton's view, that observation hints that scientists may someday induce the body to make its own supply of these antibodies to fight metastatic melanomas hidden in other organs.

*— R. Weiss*

## Deep rocks offer a glimpse into mantle

In a South African diamond mine, geologists have discovered rocks that originated in the heart of Earth's upper mantle, some 300 to 400 kilometers below the planet's surface. Scientists have hotly debated the makeup of this region, but until now they have lacked direct evidence to constrain their theories.

"These are, to date at least, the deepest known samples to come out of the Earth," says Stephen E. Haggerty of the University of Massachusetts in Amherst.

He and Violaine Sautter of the University of South Paris in Orsay collected the rocks from an extinct volcanic pipe called the Jagersfontein kimberlite, about 230 km southeast of Kimberley, South Africa. Kimberlites represent ancient conduits through which diamonds and other pieces of upper mantle are driven toward Earth's surface.

In a mine at the Jagersfontein, Haggerty and Sautter discovered two highly unusual rock fragments, containing numerous specks of the mineral clinopyroxene scattered within garnet. The specks are oriented along specific planes, indicating the mineral was once dissolved in the garnet under extreme pressure but has since come out of solution, they report in the May 25 SCIENCE. Laboratory experiments indicate that clinopyroxene dissolves in garnet only at pressures higher than about 130 kilobars, which corresponds to a depth of 300 to 400 km below the surface. The researchers say the evidence for the clinopyroxene-garnet solution suggests the rocks came from at least that depth — near the bottom of the asthenosphere, the partially molten section of the upper mantle.

The asthenosphere supports the more buoyant and rigid lithospheric plates that drift across Earth's surface. Never before have scientists found kimberlite rocks bearing telltale marks of asthenospheric pressures, although some finds may have originated at such depths.

The newly discovered rocks support a controversial theory concerning the Earth's structure. Seismic evidence collected from earthquake waves traveling through the mantle indicate that a transition zone beneath the asthenosphere, between depths of 400 and 670 km, separates the upper mantle from the lower mantle. Most scientists believe both the upper mantle and the transition zone share the same composition, consisting largely of olivine-rich rocks.

But Don L. Anderson at the California Institute of Technology in Pasadena contends the transition zone holds both olivine and a high concentration of eclogite — a rock made of garnet and clinopyroxene. This arrangement would tend to seal off the lower mantle from the upper mantle, preventing mixing between the two. A corollary of this theory holds that subducting pieces of oceanic crust do not sink into the lower mantle but instead stop in the eclogite-rich transition zone.

Haggerty says the Jagersfontein samples support Anderson's theory that the transition zone contains abundant eclogite, lending credence to the idea of a stratified mantle.

Geologist Joseph R. Smyth of the University of Colorado at Boulder calls the Jagersfontein rocks "exciting and very intriguing," but maintains they will not end the debate on the structure of the mantle.

*— R. Monastersky*