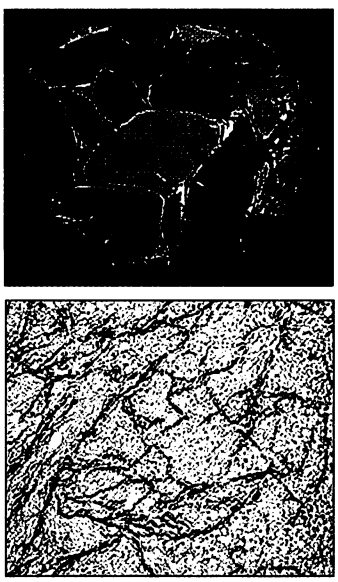
the conclusion that very aggressive eye melanomas have unusual blood channels after discovering distinctive looping patterns in slices of the tumors stained with a method called PAS that highlights extracellular matrix. Folberg also noted red blood cells apparently moving through channels formed by the matrix. When he then compared angiograms—pictures of the tumor blood vessels taken after a fluorescent dye had been injected into the patients' bloodstreams—with the PAS staining patterns of slices taken after those same tumors were removed, he saw similar looping patterns in both for the most aggressive tumors. That suggested, Folberg says, that the PAS-stained structures were conducting blood and represented a previously unknown type of blood channel that showed no signs of endothelial cells.

Blood vessel researcher Donald McDonald of the University of California, San Francisco, who co-authored the *American Journal of Pathology* commentary with Lance Munn and Rakesh Jain, both of Harvard, says he doesn't question the conclusion that tumors showing the looping patterns are particularly aggressive and deadly. That is "well documented," he says, but "I just don't buy" the team's assertion that the looping structures are blood-carrying channels.

McDonald, Munn, and Jain point out that the blood vessels of a tumor are a snarl of tubes, like a plate of hollow spaghetti. An angiogram of that plate would indeed show the noodles looping around in three dimensions. But if you were to slice the spaghetti crosswise as you would a tissue, says Jain, "you would see mostly cross sections of spaghetti," little circles or ellipses—not the looping strands. So, he and his colleagues conclude, the loopy structures that show up in the PAS-stained cross sections can't be the blood vessels seen in the angiogram. The red blood cells Folberg saw in the putative channels most likely leaked from ordinary tumor vessels, say the authors of the commentary.

Folberg counters that McDonald and Jain are mistakenly "assuming these things are conventional blood vessels," which, he says, they are not. The PAS-stained structures are sheets of extracellular matrix wrapped around masses of tumor cells, he says. To illustrate how they could form blood-conducting channels, Hendrix team member Andrew Maniotis resorted to a low-tech demonstration: He used spheres and cylinders of clay to represent masses of tumor cells and surrounded them with aluminum foil to represent the extracellular matrix.

When he pressed the clay blobs together tightly, as the cell masses would be within a tumor, in most spots, the aluminum foil covering adjacent blobs was in such close contact that no liquid could flow between them. But in some places, because of the curvature of the clay, there were openings that formed ribbonlike channels where liquid could flow. These, the team proposes, represent the blood channels that show up in the angiogram—loopy in shape because they follow the contours of the blobs. In addition, when Maniotis sliced through the clay mass and looked at the pattern made by the aluminum foil, he saw a pattern of back-to-back loops, similar to the PAS-stained pattern. The team recently took another form of the model, made from sausage skins bathed in contrast dye and stuffed with wax, and did a computerized tomography (CT) scan to trace the three-dimensional pattern of the dye in the channels. The CT scan images "look very similar to the angiograms," says Hendrix.



Claymation. The aluminum foil wrapped around clay in this model of tumor tissue (*top*) resembles the loopy patterns seen in a stained section of a real tumor (*bottom*).

Even if the skeptics accept that the clay and sausage-casing models show that such channels can exist in tumors, they say that Hendrix's group will need to do more to show that blood actually flows in the channels. And even if the channels do conduct blood, some question whether the blood flow would have much impact on tumor growth. Blood vessel researcher Adrian Harris of the University of Oxford in the United Kingdom notes that his team, as well as many others, has found that the same type of melanoma studied by the Hendrix group is full of conventional blood vessels. In that case, says tumor biologist Robert Kerbel of the University of Toronto, Ontario, any blood flowing in those channels "could be a very minor percentage of the total [tumor blood flow]."

Nelson Fausto, editor of the pathology journal, says he deliberately did not show the McDonald commentary to the Hendrix group for their comment because he wanted to let McDonald, Munn, and Jain have their say. But Hendrix will have an opportunity to present her team's models for scrutiny in a debate with McDonald scheduled for the Keystone angiogenesis meeting. Ultimately, however, the Hendrix team's hypothesis is more likely to stand or fall on the results of experiments in animals to nail down the contribution, if any, of the mysterious channels to tumor blood flow. **–MARCIA BARINAGA**

CREDITS: (TOP TO BOTTOM) MANIOTIS *ET AL. AM. J. PATHOL.* 155(3), 739 (1999); A. MANIOTIS, DEPARTMENT OF ANATOMY AND CELL BIOLOGY/THE UNIVERSITY OF IOWA

U.S. PRIZES

17 Get Science, Technology Medals

Researchers who plumbed the depths of the Antarctic ozone hole, helped show that modern cells are assembled from once-independent life-forms, and created reading machines for the blind were among those awarded National Medals of Science and Technology this week by President Bill Clinton. They will be honored at a 14 March ceremony.

A dozen investigators won the coveted National Medal of Science, which Congress created in 1959, while four investigators and one company gained the prestigious National Medal of Technology, created in 1980. Cellular biologist Lynn Margulis of the University of Massachusetts, Amherst, one of two women honored, helped win acceptance for the once-controversial idea that plant and animal cells are the product of partnerships between ancient, bacterialike organisms. Atmospheric researcher Susan Solomon of the National Oceanic and Atmospheric Administration, an unusually young medalist at 44, was honored for her studies of the South Polar ozone hole. Raymond Kurzweil, founder of Kurzweil Technologies, was recognized for his pioneering work on voice recognition, which has produced many modern aids for the visually impaired.

The other science winners, by field, are: Biology—David Baltimore, California Institute of Technology; and Jared Diamond, University of California, Los Angeles. Chemistry—Stuart A. Rice, The University of Chicago (UC); and John Ross, Stanford University. Economics—Robert M. Solow, Massachusetts Institute of Technology (MIT). Engineering—Kenneth N. Stevens, MIT. Mathematics—Felix E. Browder, Rutgers University; and Ronald R. Coifman, Yale University. Physical Sciences—James W. Cronin and Leo P. Kadanoff, UC.

Other National Medal of Technology winners are: computing innovator Glen Culler, Culler Scientific Systems; biotech industry pioneer Robert Swanson (deceased); ARPAnet founding father Robert Taylor (retired); and Symbol Technologies Inc., for development of laser bar code scanning and wireless local area network technologies. **–DAVID MALAKOFF**