over whether biodiversity matters at all. A study on page 852 may help bring the two camps together by showing that both arguments can hold true—depending upon whether one looks at microcosms or across an entire ecological community. "It's a nice paper," says David Tilman, an ecologist at the University of Minnesota, Twin Cities. "It resolves what's been a brewing controversy the last few years."

As far back as Darwin, biologists have suggested that exotic species should have a harder time taking root in a diverse ecosystem, because a whole web of species should more efficiently tie up such critical resources as nutrients, light, and water than would a single species, leaving fewer resources for the invaders. That notion has been supported by theoretical models as well as experiments with plots of grasses and a marine microcosm, among others (*Science*, 19 November 1999, p. 1577).

Flip-flop. Natural tussocks *(inset)* richer in species were more invaded, but the reverse pattern held in manipulated tussocks.

But in large-scale settings such as parks, many land managers and scientists have found that the reverse holds true: Invaders tend to be more successful in diverse ecosystems. Diversity might matter within small experimental plots, biologists have suggested, but in nature other factors that operate across a broad scale—such as good soil and lots of water and sun—seem to swamp the effects of biodiversity and enable both native and exotic plants to flourish.

To explore these two ideas, Jonathan Levine, an ecology graduate student at the University of California, Berkeley, studied a stretch of the South Fork Eel River in northern California that's dotted with tussocks of a sedge called *Carex nudata*. Anchored on rocks where they trap soils, these tussocks are miniecosystems containing other grasses, forbs, and mosses. These tiny islands, about two-thirds the size of a sheet of letter paper, are being invaded by three European plants: Canada thistle, common plantain, and creeping bent grass.

Levine started with a broad look across the ecological community, counting how many exotic plants had invaded the tussocks along a 7-kilometer stretch of river. The more diverse a tussock was, the more invaders it had, he found, as practical experience had suggested. Although that implied a limited role for diversity at the community level, Levine still suspected that diversity could be a major factor at the local scale. To decouple biodiversity from other factors, he manipulated the number of species on individual tussocks. He weeded 65 tussocks along a few dozen meters of river of everything except the sedge, then transplanted onto them anywhere from one to nine native species, creating tussocks with similar plant cover but differing levels of diversity. The next spring, he added seeds of the three invading plants to each tussock. This time, the opposite was true: The more native species there were, the fewer weeds took hold. In short, diversity does matter in fending off invasives, says Levine, but its effects are wiped out by other factors at larger scales.

Levine wanted to know what those factors might be. One clue was that in the natural ecosystem, the tussocks that had the greatest natural diversity and the highest number of invasive species tended to lie farther downstream. Levine wondered if, compared to upriver plants, downstream tussocks were simply deluged with more seeds of both native and exotic plants washing downriver. To find out, Levine added vast quantities of seeds—enough to wipe out any differences in seeds coming from upstream—from the three invaders to 190 tussocks that varied naturally in diversity along 7 kilometers of river. This time, the invaders were equally successful in colonizing diverse and less diverse communities. The upshot, says Levine, is that in this particular large-scale system, the most important factor influencing invasion abundance was the number of seeds—as opposed to either diversity or resource conditions. Levine says his findings support growing suspicions that the most effective way to stem invasions is not just to try to maintain diversity but to stop nonnative seeds or organisms from getting into an ecosystem in first place. "A lot of people are coming down to propagule pressure," or seed number, as the critical factor across large ecosystems, he says.

Not everyone buys that conclusion, however. Philip Grime of the University of Sheffield in the United Kingdom, for example, believes that if one looks across all studies on invading species, resource supply is just as important as seed number in giving invasives a leg up, and biodiversity doesn't play a role at any scale. So the argument over the role of diversity seems likely to continue.

—JOCELYN KAISER

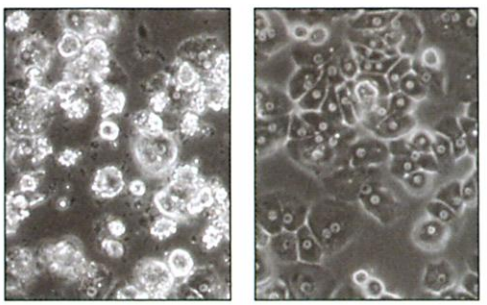
CANCER RESEARCH

Caution Raised About Possible New Drug

For the past 4 years, the protein known as TRAIL has dazzled cancer researchers with its discriminating ability. The molecule appears to kill off many types of cancer cells while leaving normal cells unscathed. And it does the job without any measurable toxicity in animals. Not surprisingly, drug developers have been eager to move the protein into human trials. But now TRAIL's march to the clinic may have hit a roadblock.

In work reported in this month's issue of *Nature Medicine*, a team led by cell biologist Stephen Strom at the University of Pittsburgh in Pennsylvania found that, previous studies notwithstanding, TRAIL kills normal human liver cells, both in culture and in tissue slices from normal individuals and patients with hepatitis or other liver diseases. "The data are clear and convincing," says molecular biologist Shigekazu Nagata of Osaka University Medical School in Japan, who wrote an accompanying commentary on the study. "TRAIL can kill human [liver cells], but it does not kill monkey or mouse liver cells."

If the results hold up, they could dash plans by the biotech firms Genentech in South San Francisco and Immunex in Seattle to jointly develop the potential anticancer drug, dubbed TRAIL/Apo2L. The study also points up a possible pitfall in the standard drug-discovery strategy. Researchers test po-



CREDITS: (TOP PHOTOS) JAY LEVINE; (BOTTOM) M. JO *ET AL.*, *NATURE MEDICINE* 45, 564 (2000)

Warning sign. Human liver cells at left die from apoptosis after TRAIL treatment. Untreated cells are at right.

tential drugs in a variety of cells, but they rarely use healthy human liver cells, says Strom, who is a liver expert, because the cells are very hard to obtain. Now, he says, "we have to be cognizant that we might miss some things. There is not really much in these preclinical studies [of TRAIL] that could have been done differently."

Strom did not set out to study TRAIL's role as a cancer drug. With graduate student Minji Jo and their colleagues, he was trying to find the molecular players that bring about liver cell death in diseases such as hepatitis and alcoholic cirrhosis. Previous work had shown that TRAIL kills cancer cells by triggering a form of cell suicide called apoptosis, and the team wanted to find out whether TRAIL-induced apoptosis might also be involved in the premature death of diseased liver cells.

Much to their surprise, the researchers found that TRAIL readily induces apoptosis in cultured liver cells from both sick individuals and healthy liver donors. Because the protein had never before been shown to trigger death in animal liver cells, "we thought [the result] was a fluke," perhaps an artifact of the team's culture conditions, recalls Strom.

Further work ruled out that possibility. For example, the team found that TRAIL also induces apoptosis in cells anchored in liver slices. And, in accord with previous findings, the researchers found no effect of TRAIL on cultured human epithelial cells derived from liver tissue or on rat, mouse, or monkey liver cells. "The animal cells are resistant in the culture dish, in whole livers, and in the live animal," Strom sums up. "This was not a culture artifact."

So why do human liver cells remain susceptible to TRAIL when other normal cells appear to fend the molecule off? Work a few years ago suggested that tumor cells succumb because they, unlike normal cells, fail to make a so-called decoy receptor that sops up TRAIL and prevents it from triggering the receptor that, in turn, programs cell suicide (*Science*, 8 August 1997, pp. 768, 815, and 818). But Strom and his colleagues found no differences between human liver cells and others in the production of either the decoy or regular TRAIL receptors. "This is very difficult to explain," says Nagata, whose own work focuses on apoptosis. "Perhaps, some factor is produced by mouse or monkey hepatocytes but not humans' that can inhibit TRAIL."

Researchers at Immunex and Genentech think there might be a simpler and, from their view, more favorable explanation for the Pittsburgh team's findings. Often, especially in the standard bench-top purification method used by Strom's group, TRAIL proteins clump together, forming "multimers" that are more toxic to cells than more natural preparations, says Douglas Williams, executive vice president and chief technology officer at Immunex. "The studies being reported are interesting," he adds, "but they have not been performed with the material we have been producing here at Immunex and Genentech."

To see whether that accounts for the discrepancy between the current observations and those made previously, Strom and the Immunex-Genentech workers will exchange their TRAIL preparations, and each group will redo the tests with the other's material. Until the results are in, TRAIL's fate will hang in the balance. "There is no magic drug for cancer at the moment," Nagata says.

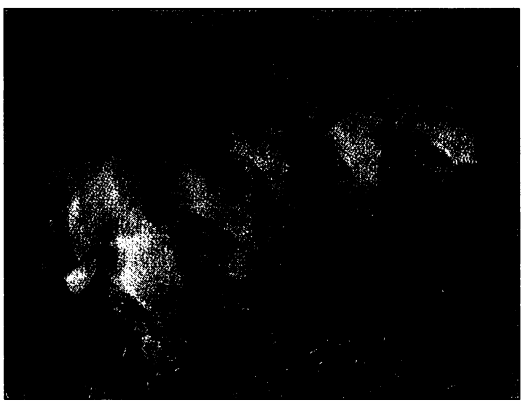
–TRISHA GURA

Trisha Gura is a science writer in Cleveland, Ohio.

ADVANCED TECHNOLOGY PROGRAM

Grants Evoke Squeals Of Delight and Anger

It's easy to understand why the "Three Little Pigs" is David Ayares's favorite children's story. On 14 March Ayares's company, PPL Therapeutics Inc. of Midlothian, Scotland, surprised the scientific community by announcing that it had successfully cloned a pig from an adult cell, taking a small but vital step toward its goal of mass-producing organs to be transplanted into humans.

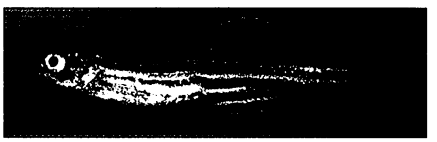


Corporate pork? ATP-funded research by PPL Therapeutics led to these cloned pigs.

Last week Ayares told a version of the story to an audience at the U.S. National Academy of Sciences, recounting how a $2 million grant last fall from a beleaguered federal research program had rescued his U.S.-based project. The grant came just in the nick of time, he said, as the company was ready to pull the plug because success seemed too far away. But unbeknownst to Ayares, at the very moment he was relating his story, a Big Bad Wolf on Capitol Hill

ScienceScope

Genome Club The zebrafish may soon join the elite list of organisms honored by having their entire genome sequenced. The Wellcome Trust's Sanger Centre is expected to make the little striped swimmer the target of a new large-scale sequencing project, Philip Ingham, a developmental geneticist at the U.K.'s University of Sheffield, announced last week at the Cold



Spring Harbor Laboratory in New York. Ingham told a meeting of developmental biologists—who value the species for its transparent embryos—that he is "99% certain" that Wellcome trustees will approve the project.

As the Sanger Centre winds down its work on the human genome in October, Ingham said, it will have the capacity to start sequencing the fish. He estimated that the center could complete a rough draft of the 1.8-billion-base-pair genome in 2 years. As with human data, the center plans to release its newest fish sequences nightly to a public database. "I am ecstatic," said geneticist Stephen Johnson of Washington University in St. Louis. "If Sanger does it, we are going to get a fantastic product."

Russian Roulette The U.S. government must step up efforts to prevent former Soviet weapons scientists from selling their services to hostile nations, experts say. Meeting in Washington last week, members of an outside task force reviewing the Department of Energy's (DOE's) beleaguered nonproliferation programs took the department to task for not taking the threat seriously enough. "Future generations are going to look back on this period and wonder why we didn't do more," said former representative Butler Derrick (D–SC), now a lobbyist.

The State Department estimates that DOE, State, and Defense Department assistance programs, funded to the tune of about $175 million this year, have helped fewer than 15,000 of Russia's 50,000 nuclear, biological, and chemical weaponeers find civilian work. To improve on that record, the task force plans to give DOE advice on how to persuade Congress—which is skeptical that the conversion programs work—to go for a big boost in the 2002 budget.

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