protein turns on a variety of genes, and the researchers detected increased expression of certain of those genes.

The main role of p53 is to protect cells from damage by radiation and other insults. It first blocks cell division in order to allow cells to repair the damage, and if they can’t do that, p53 triggers a form of cell suicide known as apoptosis. Vassilev and his colleagues found that the Nutlins can inhibit cell division and trigger apoptosis. None of these effects occurred in cancer cells without a functional p53 gene, indicating that the compounds work by the postulated mechanism.

More importantly, when the researchers administered Nutlin-3 orally to mice bearing human tumor transplants, it inhibited tumor growth by 90%. It was “as good as or better than established drugs,” Vassilev says.

What’s more, the drug didn’t seem to produce harmful side effects in the animals. The work could be “very important for those tumors that have high levels of MDM2,” says Gigi Lozano of the M. D. Anderson Cancer Center in Houston, Texas. These include many sarcomas, which are relatively uncommon but very hard to treat, as well as some lung tumors, she says.

The work is “still at an early stage,” cautions David Heimbrook, who heads Hoffman-La Roche’s cancer drug discovery effort. “It’s very difficult to say when we would have something suitable for clinical testing.” One concern is safety. Although the mice tolerated Nutlin-3 without apparent ill effects, the long-term effects of an MDM2 blocker on normal cells remains to be established.

—JEAN MARX

**MICROBIOLOGY**

**The Pfiesteria Conundrum: More Study, Less Certainty**

**WOODS HOLE, MASSACHUSETTS**—More than a year after controversy erupted over whether a microbe called *Pfiesteria* has caused massive fish kills on the U.S. East Coast, questions about the research have deepened. The lab that tagged *Pfiesteria* as a potent fish killer faces ongoing skepticism in part because it has declined to share its “toxic” cultures with critics. And one lab that did receive cultures has failed to confirm that *Pfiesteria* has an unusually complex life cycle that includes an amoeboid form.

At a meeting here last month,* researchers heard some good news, however: Two rival groups began discussing plans to figure out together why only one of them has found evidence that *Pfiesteria* produces a fish-killing toxin.

Researchers say the collegial tone was a breakthrough in a field that has been riven by disputes about the work of *Pfiesteria* expert JoAnn Burckholder, who with North Carolina State University colleague Howard Glasgow first linked the dinoflagellate to fish kills. The same meeting 3 years ago was so contentious that some scientists walked out, says organizer Don Anderson. “The atmosphere was much better” this time, says Anderson, an algae expert at Woods Hole Oceanographic Institution in Massachusetts. Burckholder did not attend, however, because of an illness in her family.

In spite of the collegiality, however, attendees left without resolving a critical public health question: Does *Pfiesteria* pose a significant risk to wild fish and humans?

Burckholder and colleagues have blamed *Pfiesteria* for killing millions of fish since 1991 and sickening fishers and lab workers. But researchers have not yet fully characterized a toxin. Some have even suggested that fish deaths in the lab may not be caused by a toxin. Last year, a team led by fish pathologist Wolfgang Vogelbein of the Virginia Institute of Marine Science (VIMS) in Gloucester Point reported in *Nature* that...

Poisonous dispute. Scientists are still debating the toxicity of *Pfiesteria*, here feeding on fish epidermis.
Are Most Life-Friendly Stars Older Than the Sun?

Our solar system has lived in a hospitable part of the Milky Way for nearly 5 billion years. But most of the galaxy’s other inhabited systems—if they exist—would have had even longer to nurture life, according to a study on page 59. The analysis intrigues astronomers who dare ponder the conditions for complex life elsewhere, but others warn that we know too little about those conditions for the research to mean much.

The study explores the physical requirements for a “galactic habitable zone” (GHZ), a term coined in 2001 by astronomer Guillermo Gonzalez, now at Iowa State University in Ames, and colleagues. They identified the life-friendly zone as a narrow annulus of stars in the middle of our galaxy’s disk, the plane within which our sun revolves. Planetary systems closer to the crowded galactic center would face too much danger from exploding supernovas and passing stars that stir up comets, the team reasoned. And stars in the sparse outskirts wouldn’t contain enough heavy elements to spawn planets like Earth.

The logic made sense, says astronomer Charles Lineweaver of the University of New South Wales in Sydney, Australia. In the current study, he and two computational astrophysicists retraced the arguments taking a more rigorous approach. In particular, they applied a detailed model of how the key elements of terrestrial planets have built up in the galaxy since its birth, produced by the flash fusions of supernovas. They also considered what Lineweaver calls “Earth destroyers”: giant planets that migrate, formed by stars rich in heavy elements. Finally, the researchers included the time needed for complex organisms to arise. With no easy way to decide this slippery factor, they adopted Earth’s time scale of 4 billion years as typical. “We don’t assume that complex life exists, or that it is common or rare,” Lineweaver notes.

When they crunched the numbers, the researchers found that a habitable ring of stars emerged about 8 billion years ago and 25,000 light-years from the galaxy’s core—roughly the sun’s distance today. This zone has slowly spread toward and away from the galactic center since then, a spread not evident in the study by Gonzalez and his colleagues. All told, the authors conclude that the GHZ has embraced fewer than 10% of the stars ever born in the Milky Way.

Moreover, about three-quarters of the stars in the zone today are older than Earth—indeed, 1 billion years older, on average. “If you’re interested in whether extraterrestrial intelligence has evolved, this should be a sobering result,” Lineweaver says. “A billion years is a long, long time.”

Gonzalez lauds the work. “Our paper was not as quantitative as some of the chemical evolution of the galaxy,” he says. Other astronomers, however, think the galaxy’s influences on extraterrestrial biology are too myriad for a basic astrophysical analysis to grasp. “We hardly understand the origin of life, let alone the evolution of complex life,” says astronomer Mario Livio of the Space Telescope Science Institute in Baltimore, Maryland. “Until we do, it is extraordinarily difficult to talk about habitable zones.”

Astronomer Virginia Trimble of the University of California, Irvine, who considered the galaxy’s habitability in 1997, agrees. “Quantitative isn’t necessarily any better unless you can be sure you assigned the right numbers,” she says. For instance, if complex life typically takes twice as long to arise as it did on Earth, then older stars nearer the galactic center would be the best abodes—despite the supernovas and close neighbors. “I think the authors may have attached too much importance to the dangers of the environment there,” she notes.

Lineweaver encourages the debate. “When life is mentioned, astronomers have winced and haven’t talked about it. It’s been a taboo,” he says. “I’d like to convince the astrobiology community that there is credence to this approach.”

—ROBERT IRION