the precise thicknesses of its layers, the specific semiconductors used, and the mechanical strain between adjacent layers, turn it into so-called quantum well in which electric charges approaching from the layers above and below it get trapped and recombine to emit red light.

Bounding the cavity are complex "mirrors" made up of alternating sublayers of aluminum arsenide and aluminum gallium arsenide. The mirrors reflect and amplify the emitted light and pave a low resistance pathway into the cavity for electrons and "holes"—mobile positive charges. The electrical current that drives the laser enters through metal electrodes that are deposited onto the very top and bottom of the multilayered structure.

This intricate device has already caught the eye of such electronics giants as Hewlett Packard, Honeywell, Xerox, and others, some of which have expressed interest in collaborating with Sandia to develop it into a full-fledged technology. There are good reasons for their interest, as laser maker Connie Chang-Hasnain of Stanford University points out. The new VCSEL's unique combination of features, she says, "opens up a lot of applications." One possibility, suggests Robert Thornton of the Xerox Palo Alto Research Center (PARC), is that the new VCSELs could end up muscling in on existing niches for red lasers such as the scanners at grocery checkout counters, which now rely on bulky, power-eating helium-neon gas lasers. Moreover, Schneider speculates, the new VCSEL could earn the status of an "enabling technology," one that eases the way for a host of other technologies.

Plastic optical fibers, for example, get lip service as a cheaper alternative to glass fibers for short-haul (intraoffice or intracity) optical communications but are still awaiting a suitable light source. So far, even edge-emitting lasers haven't produced the wavelengths best suited to plastic fibers in a beam of high enough quality. The new surface emitter, however, may fit the bill, says Schneider. "It is conceivable that on one 2-inch wafer, we could grow at least 10,000 little devices, each one putting out enough power" to pump light through a fiber, Schneider says.

Before technologies based on the new laser start to proliferate, Schneider concedes, there are bugs to work out. For one, the flow of electrons into the quantum wells is uneven, enabling the new VCSELs to lase only about 40% of the time even though their light looks continuous to the eye. For printing and scanning, he adds, continuous lasing is a must. Also, all of that exquisite layering takes skill, patience, and expensive equipment, Chang-Hasnain says. But with a host of potential applications pending, nobody is going to turn the lights out on these new little lasers any time soon.

–Ivan Amato

CANCER RESEARCH

New Tumor Suppressor Gene Captured

Step by step, base pair by base pair, researchers have finally closed in on the gene that causes von Hippel-Lindau (VHL) disease, a rare but deadly condition that predisposes affected individuals to a surprising variety of cancers, including those of the eye, the kidney, and the brain. On page 1317, an international team of scientists from the National Cancer Institute (NCI) in the United States, Cambridge University in England, and France's Centre d'Etude du Polymophisme Humain report that they have nabbed the elusive gene.

"They definitely have it and it's very exciting. It means real help for the von Hippel-Lindau families," says Wayne State University molecular geneticist David Smith, who was also racing to find the gene. Smith and others believe the discovery will lead to better diagnosis and improved monitoring of patients with the disease, and perhaps to new therapies as well.

The new gene is "an important one to know about. It's really nice to have it join the club."
—Alfred Knudson

What's more, the work confirms that the VHL gene is a tumor suppressor gene. As their name suggests, these genes, currently numbering fewer than a dozen, normally inhibit tumor cell growth, and it's their loss or inactivation that predisposes to cancer. The VHL gene is "an important one to know about. It's really nice to have it join the club," says Alfred Knudson of Fox Chase Cancer Research Center in Philadelphia, whose work more than two decades ago laid the foundation for current tumor suppressor gene research.

Winning the race to the VHL gene was a matter of hard work, a strong collaborative effort between clinicians and basic scientists, and a few strokes of luck, says one of the paper's authors, Michael Lerman of NCI's Frederick Cancer Research and Development Center. By doing classical genetic linkage studies in VHL families, researchers in 1988 first mapped the disease gene to a small region at the tip of the short arm of chromosome 3 and have since further narrowed the suspect area. After cloning that section of DNA, it quickly became a matter of pulling out the genes there and testing each one to see if it was consistently deleted or mutated in VHL patients. If so, it would mean the researchers had their tumor suppressor gene.

The VHL collaboration had at least one false alarm. They found a gene, which encoded a calcium pump and looked like a good candidate because it's active in the tissues where VHL cancers arise. But within weeks the team found a VHL patient whose deleted area on chromosome 3 did not include the calcium pump gene—almost definitive proof it was not the VHL gene. But fortune smiled on the gene hunters as they quickly located a second VHL patient who had a deletion within the first patient's missing region, and then a third patient whose deletion was inside the second's.

Like a Russian doll that gets smaller and smaller, these serendipitous nested deletions further narrowed the location of the VHL gene, explains coauthor Berton Zbar of NCI. Then, by analyzing the cloned DNA from the region defined by the deletions, the collaborators spotted two new candidate genes, one of which proved to be their quarry. It, too, was active in the tissues where VHL cancers strike, and the gene had changed very little in the course of evolution, a finding that suggests that it performs a very basic cellular function.

The clincher, however, has been extensive mutational analysis. For example, the group has found parts of the gene missing in "spontaneous" cases of VHL, instances where neither parent carries the disease gene but their child is afflicted. This indicates that these cases were caused by a newly arising deletion. A group led by NCI's Marston Lineham also detected mutations of the gene in cell lines from a sporadic type of kidney cancer, which is common in VHL patients.

The job of the VHL collaboration is certainly not over. Parts of the VHL gene remain to be sequenced, but the sequence obtained so far shows that the gene encodes a protein with no similarities to other tumor suppressors. "It already looks like it will be a new type of tumor suppressor gene," notes Lerman. The bad news is that the sequence provides few clues to the novel gene's function.

Researchers should have the gene's full sequence within the year, and a 100% accurate diagnostic test for VHL should soon follow. Researchers also hope they will be able to correlate specific mutations on the gene with the distinct forms of cancer that strike different VHL families. This could greatly improve patient monitoring by suggesting which tumors to look for most carefully, explains Zbar. Right now, notes Smith, those with the VHL gene contain "a ticking time bomb, and they don't know where it will go off." Having gene in hand, however, will help researchers defuse that danger.

–John Travis