Newly found gene linked to cancer biology

When molecular biologists announced last month they had discovered the gene causing neurofibromatosis — the disease made famous in the movie "The Elephant Man" — they told colleagues and reporters they had no idea how the gene caused the disfiguring neurological disease (SN: 7/28/90, p.61). They weren't lying. They simply didn't know that some of their co-workers, who had skipped the Washington, D.C. press conference, had just solved the riddle.

While television cameras focused on two of the gene's discoverers — University of Utah's Raymond L. White and Francis S. Collins of the University of Michigan in Ann Arbor — White's co-worker Robert Weiss remained hunched over a keyboard in Salt Lake City. He was engaged in a painstaking computer search that compared the newly discovered gene's predicted amino-acid sequence with the amino-acid sequences of thousands of known proteins. Suddenly, almost unbelievably, a match came up: The protein causing neurofibromatosis, the computer declared, is very closely related to proteins already under intense scrutiny by other researchers for their role in cancer.

That discovery, described in the Aug. 10 CELL, has elated researchers in both the neurofibromatosis (NF) and cancer fields. Typically, scientists fail to find any significant sequence similarity between a newly identified, disease-causing protein and well-known proteins, says Robert Weinberg, a molecular biologist working with cancer genes at the Massachusetts Institute of Technology in Cambridge. Without such a match, researchers might spend years just figuring out what their newly discovered gene or protein really does. "It could well have been the case that this dismal paradigm would have been true for NF as well," he says.

As it turns out, the disease-causing protein, called NF1, belongs to a family called guanosine-triphosphatase-activating proteins, or GAPs. Cancer researchers are fascinated by the GAP family because these proteins appear critical as regulators of cell division. For example, one variety of GAP normally deactivates a gene product called ras. If ras can avoid deactivation by GAP, it can trigger uncontrolled cell proliferation, including a number of human cancers.

The computer match-up suggests that NF1, like other GAPs, suppresses abnormal cell division, putting the NF gene in a class of tumor-suppressor genes known as anti-oncogenes. Patients with neurofibromatosis have a mutated version of the NF gene — one whose product apparently cannot halt cell division triggered by ras or a ras-like protein. The resulting uncontrolled growth appears as cancer-like masses around the peripheral nerves of people bearing the mutant gene.

"GAP is one of the better-understood molecules" involved in regulating cell division, says Michael Wigler, who studies cellular signaling mechanisms at the Cold Spring Harbor Laboratory on Long Island. "A lot of drug companies have been working on ras and GAP, and it may well be that NF people will be the first to benefit from that work."

Jackson B. Gibbs, who investigates GAPs at Merck Sharp & Dohme Laboratories in West Point, Pa., agrees cautiously that the newly identified NF-GAP link "might have pharmaceutical implications." For example, he says, a drug that can modify ras-GAP interaction might prove useful for neurofibromatosis patients.

In any case, scientists say, the discovery is sure to boost collaboration among researchers working with cancer and neurofibromatosis, accelerating progress in both arenas. "We've just taken a crash course in oncology," says NF-gene co-discoverer David Viskochil of the University of Utah. He says his group is racing to identify NF1's precise function. However, he adds, "everybody else who has ras systems going has got a head start on us. We're playing catch-up now. We're scrambling."

Globally, neurofibromatosis affects one in 3,500 people, including an estimated 100,000 individuals in the United States. Although the disease is commonly associated with Joseph Merrick — the severely deformed 19th-century Londoner depicted in "The Elephant Man" — researchers today believe Merrick actually suffered from a much rarer disorder called Proteus syndrome. — *R. Weiss*

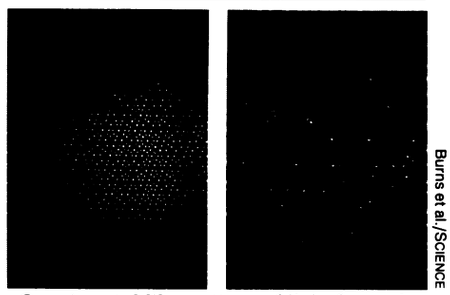
'Quasicrystals' made from 'optical matter'

On atomic and molecular scales, orderly exchanges and interactions of electrons underlie matter's compulsion to organize into specific chemical structures. Chemistry, some say, is the science of this electron behavior.

Last September, three physicists from the Rowland Institute for Science in Cambridge, Mass., reported they had discovered a previously unrecognized laser-induced binding force. They suggested it might provide a new way to manipulate micron-scale particles — thousands of times larger than atoms — into precise and regular patterns (SN: 9/30/89, p.212). Since these interactions depend on photons, not electrons, the researchers provocatively referred to the simple structures as "optical matter."

Now, in a more extensive report, the same group reports using the laser technique to organize hundreds of tiny plastic spheres into two-dimensional, crystal-like structures — some of the first examples of optical matter. "We suggest that such organized structures can be considered a new form of matter," write Michael M. Burns, Jean-Marc Fournier and Jene A. Golovchenko in the Aug. 17 SCIENCE.

To make optical matter, the researchers shine a laser through a set of optical devices and mirrors, splitting the single beam into several individual ones. Then they steer the beams through a chamber containing micron-scale polystyrene beads suspended in water. By choosing how many beams to use, and by controlling both the angles at which the beams enter the cell and the angles the beams form with respect to each other, the researchers can sculpt specific optical interference patterns. These patterns of low and high light intensity serve as templates that mimic the molecular patterns of different crystal lattices. Like theatergoers filling an auditorium, the particles file into the sites of maximum light intensity.



Burns et al./SCIENCE

Quasicrystal-like pattern of light formed by five laser beams (left) and the resulting assembly of spheres.

With five beams entering the chamber like "a pyramid of light," the scientists have even configured particles into a flat, single-layer quasicrystal structure — a bizarre molecular arrangement that violates rules of crystallographic symmetry yet characterizes a class of real crystals.

The researchers have yet to reliably induce spheres into regular three-dimensional arrangements, nor have they found a way to preserve the organization after the laser is turned off, Burns notes.

In addition to this patterning effect, intense optical fields can induce binding between particles, the researchers find. Unlike electron bonding, which can link only adjacent atoms, optical binding links particles separated by any of several discrete distances. And this could give materials scientists a new way of assembling particles, or even biological cells, for potential applications ranging from light filters to cellular grids for growing artificial skin, Burns says.

For the moment, however, optical matter remains in the realm of basic research. "We're discovering subtleties and complexities in the interaction of light and matter," Burns says. — *I. Amato*