Scientists seek to fight cancer with cancer

Earlier this year, researchers injected two patients suffering from advanced melanoma with white blood cells modified to bear the genetic instructions for making a cancer-fighting protein. Now, they want to take their gene therapy experiment one step farther.

Study director Steven A. Rosenberg says his group plans to insert two cancer-fighting genes directly into tumor cells taken from additional volunteers with advanced melanoma — a highly lethal skin cancer — and then put the altered cells back into the patients. The proposed experiment, which he announced in Houston this week at a meeting of the American Society of Clinical Oncology, would mark the first use of genetically engineered cancer cells in humans.

Rosenberg, of the National Cancer Institute in Bethesda, Md., says he expects the altered tumor cells to prompt a stronger immune response against the cancer, in effect immunizing the patients against their own tumors. "We're trying to convince the cancer patient's body to generate a better and more effective antitumor response," he says.

The study is an outgrowth of a 1989 experiment in which Rosenberg and his co-workers treated melanoma patients with genetically modified cells called tumor-infiltrating lymphocytes (TIL). The researchers removed these cancer-fighting white blood cells from the patients' tumors, then supercharged the cells with interleukin-2 and added a "marker" gene as a label. When the supercharged TIL cells were reinjected into the patients, they homed in on and attacked tumors better than other lymphocytes from elsewhere in the body.

Last January, the team treated two melanoma patients with TIL cells engineered to carry a gene for tumor necrosis factor (TNF). Injections of this normal body protein have been shown to drastically reduce tumors in mice (SN: 2/2/91, p.69), but purified TNF is too toxic in humans to be injected in doses large enough to shrink their tumors. The researchers sought to circumvent this problem by using the altered TIL cells to release TNF only in tumors. Rosenberg says it's too early to present the results, but he reports that neither patient has shown serious side effects from the experimental treatment.

In the new experiment, he plans to eliminate the need for TIL cells by inserting genes for TNF or interleukin-2 directly into tumor cells removed from patients. The researchers will allow the engineered cells to multiply in a lab culture, then return them to the patients.

In mouse experiments, such altered tumor cells continued to multiply after reinjection, then died off as the mouse's immune system attacked them, Rosenberg says. But before the cells died, they enhanced the immune system's ability to recognize and kill all remaining tumor cells. Using this approach, "we have been able to immunize animals against their cancers," he reports.

The National Cancer Institute's bioethics review board has granted provisional approval to test the treatment in human patients. But Rosenberg must also win approval from three other National Institutes of Health committees and from the FDA — a process that could take more than six months.

J. Gordon McVie, scientific director of Britain's Cancer Research Campaign, calls the proposal to engineer tumor cells instead of TIL cells "absolutely brilliant." He adds, "We haven't got the foggiest idea which one will work better."

Rosenberg is already planning yet another gene therapy approach to cancer. He believes he has isolated a gene for a protein present on the tumor cells of all melanoma patients. Although the discovery awaits confirmation, he hopes one day to insert the gene for this "melanoma tumor antigen" into *Vaccinia* viruses, commonly used as the basis for vaccines.

With such a vaccine, he suggests, "someday it may be possible . . . to immunize [people] against cancer" so that they never develop melanoma. — *C Ezzell*

Nearby gas clouds pose cosmological puzzle

Astronomers have for the first time counted the hydrogen clouds neighboring our galaxy. Their analysis of quasar light, using detectors on the Hubble Space Telescope, reveals many more clouds than predicted. Because some hydrogen clouds represent material that has failed to coalesce into galaxies, the surprising abundance of nearby gaseous bodies may have far-reaching consequences for the structural development of the universe, researchers say.

Hydrogen clouds have been called the Rosetta stones of the universe, the key to understanding its history. Some clouds may date to the Big Bang, and some provide the raw material for galaxies. Though they offer clues to the evolution of the cosmos, these clouds emit little light and have never been seen. Instead they make their presence known by absorbing specific wavelengths as quasar light passes through on its way to Earth.

As observed near Earth, each cloud absorbs a different wavelength of light, depending on the cloud's location. Due to the expansion of the universe, clouds farther from Earth move faster and appear to absorb redder light wavelengths, which are detectable from the ground. The more slowly moving near-Earth clouds absorb a spectrum of ultraviolet light that can only be observed from space. Together, the clouds create a thicket of absorption lines — called the Lyman alpha forest — within the spectra of quasars.

Ground-based instruments measure absorption spectra from only the most distant clouds, looking back to a time when the universe was just 10 to 20 percent of its current age. Those limited observations, made during the past decade, showed that the high density of clouds creating the Lyman alpha forest began to thin rapidly with decreasing distance from the Milky Way. Researchers reasoned that if the thinning continued, regions near our galaxy should contain one or two clouds at most. Now, two Hubble instruments tell a different story.

Last week, at a science writers' workshop in Baltimore, Ray J. Weymann of the Carnegie Observatories, based in Pasadena, Calif., announced his team had found nine to 16 hydrogen clouds relatively nearby — 30 million to 1.6 billion light-years from our galaxy. They based their findings on the absorption of light emitted by the quasar 3C273, as determined by Hubble's Goddard High-Resolution Spectrograph.

This week, John N. Bahcall of the Institute for Advanced Study in Princeton, N.J., provided SCIENCE NEWS with new details about the detection of clouds using light from the same quasar, but analyzed by Hubble's Faint-Object Spectrograph. He says that five of the seven clouds found by his team and announced last month (SN: 5/4/91, p.285) are among those detected by Weymann's group. These include two clouds that lie a mere 30 million light-years from the Milky Way and appear associated with the Virgo cluster of galaxies.

The new findings alone won't prompt a revision of galaxy formation theories, Bahcall notes. "We've first got to further characterize the darn things [clouds]," he says — determining, for instance, whether they formed during the Big Bang or much more recently.

Using Hubble, Bahcall plans to search for metal elements in the clouds, which would indicate the clouds have formed some stars and may act as budding galaxies surprisingly late in the history of the universe. Other puzzles remain, he says, such as whether these clouds are gravitationally bound to galaxies. Their association with galaxies could account for the clouds' survival, possibly over billions of years, Bahcall explains. But if instead the clouds are independent, then extra hidden mass — perhaps a theorized material called cold dark matter (SN: 1/26/91, p.52) — may supply the gravity to confine each as separate entities, he adds. — *R. Cowen*