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In the News

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- **Melanoma Vaccine Trials**
- **Outcomes Research Grants Available**
- **APL Protocol**

MELANOMA VACCINE TRIALS

The latest scientific findings on the origins, biology, and treatment of skin cancers were topics of discussion at the 19th Annual General Motors Cancer Research Foundation Scientific Conference, held June 10-11, 1997, at the National Institutes of Health in Bethesda, Md. A highlight of the two-day conference was an update on the clinical results of a melanoma vaccine developed by Steven A. Rosenberg, M.D., Ph.D., chief of the surgery branch at the National Cancer Institute.

Immunotherapy for melanoma and other cancers has used interleukin-2 (IL-2) to stimulate lymphocytes to fight tumors. IL-2 therapy has produced a response—sometimes a dramatic one—but in only 10 to 20 percent of patients.

"When we give interleukin-2, we're non-specifically stimulating all the lymphocytes in the body. While there are lymphocytes that can react against cancer, there also may be suppressor lymphocytes that can inhibit immune reactions," said Rosenberg.

"It appears that immunotherapy can probably be curative for the small percentage of patients who respond. And we have some patients who are twelve years out from our first trials of IL-2 who have never recurred," he said. "But what we need is a surgical strike just against the tumor antigen that the immune system recognizes as foreign to stimulate just the immune lymphocytes specifically reactive against the tumor."

That surgical strike may come from two antigens discovered by Rosenberg's group: MART-1, short for "melanoma antigen recognized by T-cells," and gp100, both common in melanoma. Immune cells called tumor-infiltrating lymphocytes (TIL) taken from patients with melanoma were used to clone genes encoding for MART-1, gp100, as well as other tumor antigens (including TRP-1, TRP-2, and tyrosinase) found in melanoma.

The research team at NCI was surprised to learn that MART-1, gp100, TRP-1, TRP-2, and tyrosinase are actually normal, nonmutated self-proteins that are presented on the surface of melanoma cells as well as on the surface of the pigment-producing cells called melanocytes that gave rise to the tumor. "It is probably those molecules that the immune system reacts against when patients get interleukin-2," speculated Rosenberg. "Somehow the growth of the melanoma has resulted in the breaking of tolerance, the normal ability of the body not to react against itself to these self-proteins. That may explain why IL-2 works in some people, but not in others."

Rosenberg's group has conducted early clinical trials of the MART-1 and gp100 peptide vaccines. Preliminary data from 51 patients with metastatic melanoma compared blood levels of immune cells before and after a series of four vaccinations and found a significant increase in cytotoxic T lymphocytes in 70 percent of the patients. In these preliminary studies, several patients had some decrease in the size of their melanoma lesions, and one patient had complete disappearance of disease.

In more recent studies presented at the conference, Rosenberg reported on a new generation of vaccines using tumor peptides from gp100 antigen that were modified to increase their immune strength. These vaccines induced far stronger immune reactions against the tumor than were seen in previous studies, and patients are now being enrolled in clinical trials to determine the therapeutic value of these vaccines.

In its new vaccine trials, the research team also used recombinant DNA technology to fashion vaccines encoding for MART-1 and gp100, using as a vector either adenoviruses or the same vaccinia viruses last used twenty-six years ago to deliver the inactivated

continued on page 30

continued from page 10

smallpox virus vaccine by making small pricks in the skin.

OUTCOMES RESEARCH GRANTS AVAILABLE

As part of its campaign to advance the science of health outcomes management, Hoechst Marion Roussel is offering research grants of nearly $500,000 to fund health economies and outcomes studies through its 1997 ACCORD (A Company-wide Commitment to Outcomes Research and Development) program. The 1997 grants will be awarded in amounts ranging from $5,000 to $100,000. Researchers can apply for full or partial funding of a research project.

The program encourages research projects that focus on health outcomes research in oncology, cardiovascular diseases, neuroscience, respiratory diseases, endocrinology, rheumatology, and infectious diseases. Consideration also is given to projects in other areas that further the science of health outcomes research.

Proposals will be accepted through August 15. Researchers and institutions interested in applying for ACCORD grants can receive a program brochure and application form by contacting ACCORD coordinator Mary Miller at Hoechst Marion Roussel, Mail Station J3-M1728, 10236 Marion Park Drive, Kansas City, MO 64137-1405; (816) 966-3780.

APL PROTOCOL

Aronex Pharmaceuticals, Inc., has announced a treatment use (compassionate plea) protocol for treatment of acute promyelocytic leukemia (APL) using intravenously administered liposomal tretinoin (Atragen™). Key inclusion criteria: patients with newly diagnosed or relapse APL who require treatment with tretinoin, who are, however, unable to be treated with oral ATRA; 2) patients who have failed treatment with oral ATRA and/or chemotherapy; and 3) pediatric and/or adult patients. For more information, please contact Jakki Whitehead at Aronex Pharmaceuticals, (281) 367-1666, ext. 314.

OMISSION

The names of two contributing authors were omitted in the article, "What Makes a Successful Cancer Information Center?," which appeared in the March/April *Oncology Issues*. They are Nancy Kuhrik, Ph.D., R.N., and Marilee Kuhrik, Ph.D., R.N., both associate professors at Jewish Hospital College of Nursing and Allied Health in St. Louis, Mo. In addition, the Jewish Hospital Auxiliary in support of Barnes-Jewish Hospital was incorrectly referred to as the Barnes-Jewish Hospital Auxiliary.