at the University of California, San Francisco. The ability to produce the virus in quantity will help resolve questions surrounding it, Jaffe said, including its susceptibility in vitro to anti-viral drugs.

"But the big issue is that in AIDS malignancies we're seeing virus-associated diseases," said Harvard's Elliot Kieff, M.D., who spoke at the February working group meeting. "We see them playing out late in HIV infection, when the immune system has become so weak it can't fight the foreign proteins."

The apparent link between a weakening immune system and emerging malignancies raises the possibility that boosting certain components of the immune system could slow or prevent cancers. The components that most intrigue AIDS malignancy researchers are several cytokines and growth factors. Some, like interleukin 12, are thought to be dysregulated in both tumor development and HIV infection, said NCI's Gene Shearer, Ph.D., another speaker at the working group meeting.

Clinical Implications

The emerging understanding of AIDS malignancies and the immune system has important clinical implications, Kieff said. For instance, it might be possible to heighten the level of immunity to a specific virus. One way might be to immunize against a virus early, when the body is still able to mount an immune response. Another possibility, he said, would be to take a few normal T cells from patients, ones capable of recognizing virus-infected cells, and grow them in a laboratory. They then could be returned to the patient to fight the virus.

One of the upcoming consortium trials will test interleukin 2 and another in the pipeline will look at interleukin 12. Both are thought to have a role in the development of non-Hodgkin's lymphoma. A third trial will test a novel agent that may inhibit the growth of new blood vessels in Kaposi's sarcoma, thus limiting the spread of the malignancy. Angiogenesis has been an area of intense research interest in KS.

As investigators learn more about how AIDS malignancies respond to cytokine and viral inhibitors, they expect to learn a lot more about the biology of carcinogenesis and about HIV infection itself. The consortium will share laboratories with the AIDS Clinical Trial Group, a collaboration that both groups expect to be productive. And there is the possibility of large, phase III, randomized trials down the road in conjunction with the NCI-sponsored cooperative groups.

"We should have a chance to learn something about the larger issues in both HIV infection and cancer," Feigal said. "This is a really fertile area."

— Caroline McNeil

AIDS Malignancy Consortium Plans First Clinical Trials

Members of the newly formed AIDS Malignancy Consortium decided to begin with five trials, which are in the planning stage, according to Ellen Feigal, M.D., who coordinates the consortium at the National Cancer Institute.

An exploratory trial of 5-azacytidine in B-cell lymphomas associated with the Epstein-Barr virus. The drug may allow EBV antigens to be recognized and thus make them more vulnerable to the patient's immune system.

A phase II trial of interleukin 2 in patients with B-cell lymphomas. A previous trial showed that IL-2 may promote cellular immunity.

A phase II trial of retinoids in patients with Kaposi's sarcoma. A topical form of the drug applied to KS lesions was effective in a phase I trial; the hypothesis is that an oral version would be even more beneficial, because KS is a systemic disease. The retinoid may have a dual role in that it may inhibit programmed cell death (apoptosis) of T cells and it may downregulate certain cytokines thought to be important in the growth of KS.

A phase I trial of an angiogenesis inhibitor in KS patients. This trial will test whether a new investigational agent that inhibits the receptor for platelet-derived growth factor can prevent the new vessel growth that makes metastases possible.

A phase I/II trial of a protease inhibitor and interferon alpha in KS patients. The hypothesis is that the anti-viral combination will inhibit development of the lesions.

Other protocols, including a trial of interleukin 12 in B-cell lymphoma, are also in development, Feigal said.

— Caroline McNeil