SOUTHWESTERN NEWS

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INCREASED FREQUENCY OF LUNG CANCER IN HIV-INFECTED PATIENTS MAY BE DUE TO DNA INSTABILITY

DALLAS — May 20, 1998 — Instability of DNA (deoxyribonucleic acid) may be the cause of the higher incidence of lung cancer in patients with the human immunodeficiency virus (HIV) compared with the frequency rate in the general population.

Researchers at UT Southwestern Medical Center at Dallas found that alterations in microsatellite DNA – short, tandemly repeated DNA sequences that are found throughout the genome – occur six times more frequently in HIV-associated lung tumors than in sporadic lung tumors (i.e. tumors from the general population). This finding of increased incidence of microsatellite alterations or changes in the number of simple DNA repeats -- published in the May 20 issue of the *Journal of the American Medical Association* -- also may apply to the development of many other HIV-associated tumors.

HIV-positive subjects are at great risk for the development of a large variety of tumors; approximately half of them will develop one or more tumors. Most of these are non-Hodgkin's lymphomas or Kaposi's sarcomas. But as HIV-positive individuals live longer, a wider variety of cancers are being added to a list that already includes primary central nervous-system lymphomas and cervical carcinomas. Lung cancer also should be included since a recent report by Dr. Mark Parker, a UT Southwestern assistant professor of radiology, showed that HIV-infected individuals had a 6.5 times greater risk of developing lung cancer.

In the UT Southwestern study Drs. Ignacio Wistuba, an instructor in the Nancy B. and Jake L. Hamon Center for Therapeutic Oncology Research, and Dr. Adi Gazdar, professor of pathology and associate director of the Hamon Center, and their colleagues examined 11 lung cancers arising in HIV-positive subjects and compared the genetic changes in them with those in 35 sporadic tumors. They used microdissection to isolate small numbers of malignant and benign

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lung cells uncontaminated by surrounding tissue. Molecular changes in these cells were analyzed at eight different chromosomal regions frequently altered in lung-cancer tumors.

"We were surprised to find that the number of microsatellite alterations was greatly increased in the HIV-associated group, while the loss of genetic material, which commonly occurs in lung cancer, was similar in both groups," said Gazdar, holder of the W. Ray Wallace Distinguished Chair in Molecular Oncology Research.

The reason why HIV-infected patients are so susceptible to tumor development is unknown. However, many blame the loss of immune surveillance and the involvement of infectious agents such as the Epstein-Barr virus, which has been implicated in the development of non-Hodgkin's lymphoma.

"We believe that if these alterations in microsatellite DNA appear early during the multistage development of lung cancer, we may have a useful method for assessing cancer risk in HIV-positive persons," Wistuba said.

Other UT Southwestern investigators contributing to this study were postdoctoral fellow Dr. Carmen Behrens, instructor of pathology Dr. Arvind Virmani and former technician Bilue Thomas, all from the Hamon Center; Dr. Sara Milchgrub, UT Southwestern associate professor of pathology; and Dr. John Minna, director of both the W.A. "Tex" and Deborah Moncrief Jr. Center for Cancer Genetics and the Hamon Center. He holds the Max L. Thomas Distinguished Chair in Molecular Pulmonary Oncology, the Sarah M. and Charles E. Seay Distinguished Chair in Cancer Research and the Lisa K. Simmons Distinguished Chair in Comprehensive Oncology.

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