Genetic variation associated with survival advantage in African-Americans with HIV

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From the start of the HIV epidemic, it appeared that some of the people who were infected with the virus were able to ward off the fatal effects of the disease longer than others. Recent studies have begun to unravel the cause of this phenomenon, and new research suggests that African Americans with the disease have a unique survival advantage if they have both a low white blood cell count (known as leukopenia) and a genetic variation that is found mainly in persons of African ancestry. This study was prepublished online on July 20, 2009, in *Blood*, the official journal of the American Society of Hematology.

The research showed that African Americans with HIV who possess both a variation in the gene for the Duffy antigen receptor for chemokine (DARC) and leukopenia have slower HIV-to-AIDS progression rates than HIV-infected European Americans with leukopenia. Previous studies showed that the same DARC variant conferred protection for persons of African ancestry against a particular form of malaria, and that persons of African descent have, on average, lower white blood cell (WBC) counts than persons of European ancestry. Leukopenia is one of several blood conditions observed frequently in patients with HIV-1 infection, but its impact on disease course is relatively unknown.

“Even though leukopenia is tied to both African ancestry and faster disease progression, we found that compared with European Americans, African American patients with HIV who have leukopenia do not necessarily experience this expected outcome,” said lead author Sunil

Ahuja, MD, of the Veterans Administration (VA) Research Center for AIDS and HIV-1 Infection and the University of Texas Health Science Center in San Antonio.

This study evaluated data from the Air Force subset of the U.S. Military's HIV Natural History Study and included genetic and clinical data from 1,132 participants. The researchers tested for the presence of the DARC variation and evaluated patients' WBC counts from diagnosis and throughout the course of the disease to determine the impact of different levels of WBC counts on survival rates. The prevalence of leukopenia at the time of diagnosis was significantly higher in African Americans (28 percent) than in European Americans (15 percent) or other ethnicities (13 percent). The average WBC counts were also significantly lower during the course of the disease in African Americans with HIV than in other ethnicities.

The researchers found that leukopenia was generally associated with a faster disease progression from HIV to AIDS, independent of known predictors of AIDS development. "On average, leukopenic European Americans progressed nearly three times faster than their non-leukopenic African or European counterparts," explained Hemant Kulkarni, MD, first author of this study. "However, leukopenic African Americans had a slower disease course than leukopenic European Americans, even though twice as many African Americans in the study had leukopenia."

The investigators found that the DARC variation, not race, explained the differences in WBC counts in African Americans with HIV. Among those who were leukopenic, only those with the DARC variation experienced a significant survival benefit. Additionally, this survival advantage became increasingly pronounced in those with progressively lower WBC counts, suggesting that the interaction between DARC and WBC counts was the primary influence on slowing HIV disease

progression in African Americans.

“The results of this collaborative study highlight the importance of accounting for other factors, such as the white blood cell count, to uncover the full effects of genetic variations that may influence HIV disease course,” said Capt. Gregory Martin, MD, United States Navy, program director for the Infectious Diseases Clinical Research Program (IDCRP) and an expert on infectious diseases who was not involved with the study.

“White blood cells are intricately linked to inflammation, and inflammation is known to fuel HIV disease progression. Thus, future studies will need to decipher whether the interaction between the DARC variant and low white blood cell counts results in a reduced inflammatory state,” said Vincent Marconi, MD, of the IDCRP.

Source: American Society of Hematology