

Interleukin-12 indicates survival prospects for melanoma patients

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Higher blood levels of an immune system protein predict poor survival prospects for melanoma patients with advanced disease, researchers at The University of Texas M. D. Anderson Cancer Center report today at the annual meeting of the American Association for Cancer Research.

Their finding that elevated levels of interleukin-12 (IL-12) are a marker of poor prognosis also points to a molecular explanation for a long-known risk factor for melanoma patients - older age.

Among 150 patients with Stage III melanoma, the study found that the highest levels of IL-12 are associated with a nearly 5-fold risk of death. Although older stage III patients also had an elevated risk of death, age was not a prognostic factor independent of IL-12.

"Melanoma in some cases can be vulnerable to attack by a patient's immune system," said senior researcher Jeffrey Lee, M. D., professor in M. D. Anderson's Department of Surgical Oncology. "What we've found could be evidence of a dysfunctional immune response that actually fuels the growth of melanoma."

Blood-born IL-12 provides both an accessible prognostic marker and a key connection to other signaling proteins; IL-12 as well as these related proteins already have been targeted by antibody therapies in certain autoimmune disorders, Lee said.

The research team examined age, stage of disease, and IL-12 levels in

658 melanoma patients - 445 with stage I or II disease, 150 with stage 3 and 63 at stage IV.

"First, we found that IL-12 levels increase with age," says first author and study presenter Yun Shin Chun, M.D. The mean levels of the protein increased at every age level above age 40. (See Chart)

Age, disease stage and IL-12 levels were then analyzed separately as prognostic factors. Increases in all three were associated with poor overall survival.

"When we analyzed these three factors together, only stage of disease and IL-12 levels were independent predictors of overall survival," Chun said. Age dropped completely out of the picture. Stage of disease was the most powerful prognostic factor.

Both IL-12 and IL-23 are cytokines, proteins that tell cells and other proteins what to do. Cytokines like IL-12 and IL-23 are particularly vital to immune system function. The general level of a person's immune function declines with age, Lee said, as do the levels of most cytokines. The rise of IL-12p40 with age is a relative anomaly.

Chun, Lee and colleagues are investigating IL-12's connection to the tumor promoting IL-23 and about 30 other cytokines in high-risk melanoma patients. Some of the suspect cytokines, including IL-12 and IL-23, already are targeted by therapies used autoimmune disease, Lee noted.

Source: University of Texas M. D. Anderson Cancer Center

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