LETTER to the EDITOR

IL-33, an Important Biomarker in Non-small-cell Lung Cancer?

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Dear Editor

We read with interest the article by Hu et al., published in Asian Pacific Journal of Cancer Prevention, showing that circulating IL-33 levels were higher in a non-small-cell lung cancer (NSCLC) group compared with the healthy volunteers and benign lung diseases groups, correlatingwith tumor stage (Hu et al., 2013). Using a cut-off level 68 pg/ml, IL-33 showed a good diagnostic performance for NSCLC. In addition, multivariate survival analysis showed that serum IL-33 was an independent prognostic factor in the entire NSCLC group. These findings suggest that IL-33 is a promising potential diagnostic and prognostic marker in NSCLC, and IL-33 may play an important role in NSCLS. However, Naumnik et al. (2012) showed that levels of IL-33 in serum and bronchoalveolar lavage fluid (BALF) did not differ markedly between NSCLC and the control group. No correlation was found between the serum level of IL-33 before therapy and the effect of chemotherapy. No correlation was found between the BALF concentration of IL-33 and the effect of chemotherapy as well (Naumnik et al., 2012).

IL-33 is the latest member of the IL-1 family, which includes IL-1α, IL-1β, IL-1 receptor antagonist, and IL-18. BALF level of IL-18 was lower in the NSCLC than that in the hypersensivity pneumonitis (HP) group, but higher than that in the sarcoidosis patients. Serum level of IL-18 was higher in the NSCLC than in the healthy subjects (Rovina et al., 2011; Naumnik et al., 2013). In addition, Fariadfar et al. showed that IL-18 gene polymorphism contributes to the lung cancer risk, particularly among squamous carcinoma patients (Farjadfar et al., 2009). Interestingly, IL-33 levels in the serum of gastric cancer patients were significantly elevated in comparison with that of healthy volunteers, and higher serum levels of IL-33 in gastric cancer patients were found to correlate with several poor prognostic factors like depth of invasion, distant metastasis and advanced stage (stage III/IV) (Sun et al., 2011). On the contrary, no significant difference in IL-33 serum levels was found in hepatocellular carcinoma patients compared to liver cirrhosis patients and healthy controls (Bergis et al., 2013). IL-33 levels did not correlate with overall survival, liver function parameters, the Model for End-Stage Liver Disease (MELD) score (Bergis et al., 2013). Recently, Gao, et al showed that transgenic expression of IL-33 attenuated tumor metastasis in the Lewis lung carcinoma (LLC) metastatic models, where the percentages and cytotoxicity of CD8+ T cells and NK cells and their infiltration into the tumor tissues were markedly increased by the transgenic expression of IL-33 in tumor-bearing mice (Gao et al., 2013). In addition, treatment with recombinant IL-33 could increase the cytotoxicity of CD8+ T cells and NK cells in vitro, and depletion of CD8+ T cells and NK cells using anti-CD8 or anti-asialo GM1 antibody abolished the pulmonary metastasis inhibition mediated by IL-33 (Gao et al., 2013).

Collectively, these data imply that whether IL-33 may be a potential biomarker like other IL-1 family members such as IL-18 in NSCLC, and the role of IL-33 plays in NSCLS should be studied with large-scale prospective investigations in the future.

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