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Investigation of the role of CTLA-4 +49A/G (rs231775) polymorphism in non-small cell lung cancer and T cell immunity

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Cytotoxic T-lymphocyte associated protein 4 (CTLA-4) was the first immune checkpoint molecule to be used as a drug target and led the way in the field of immunooncology. CTLA-4 increases the activation threshold of T-cells and reduces immune responses to weak antigens, such as self and tumour antigens. In our study, 56 patients were diagnosed with NSCLC, and a control group of 98 healthy volunteers was included. CTLA-4 +49A/G gene polymorphism and serum CTLA-4 levels were assessed. However, we found that CTLA-4 +49A/G gene polymorphism was associated with lymphovascular invasion (LVI) (P=0.049). The ratio of the heterozygous AG variant was 42.9% in patients with LVI, while it was 14.3% without LVI. This could indicate that the CTLA-4 +49A/G heterozygote AG variant increases the risk of LVI. In addition, we detected with the CTLA-4 +49A/G heterozygote AG variant had the worst mean overall survival at 56 weeks in the NSCLC patient group (X±SE=56.00±11.52, 95%CI 33.41-78.58, P=0.048). Furthermore, the patient group had significantly higher CTLA-4 serum levels (X±SE=121.57±11.89 pg/mL) compared with the control group (X±SE=79.09±3.09 pg/mL)(P=0.02). Our study data serve as a guide for future studies to elucidate the pathogenesis of NSCLC and evaluate the therapeutic significance of CTLA-4.

Keywords: CTLA-4, Lung cancer, NSCLC, T cell immunity