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**Title:** XAGE-1b and p53: Potential targets for immunotherapy of non-small cell lung cancer (NSCLC)

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**Body:** Induction of immune responses specifically against tumor-associated antigens by vaccination is a promising approach for cancer immunotherapy. XAGE-1b is a cancer-testis antigen that is aberrantly expressed in lung adenocarcinoma. p53 is a tumor suppressor protein that is over-expressed in NSCLC. We investigated local (primary tumor, tumor draining lymph node (TDLN)) and systemic (peripheral blood) immune responses against XAGE-1b and p53 in lung adenocarcinoma. Tissue and blood samples from 6 lung adenocarcinoma patients were obtained. Tumor-infiltrating lymphocytes (TIL) were isolated from tumor tissue by culturing for 3 weeks. Lymph node mononuclear cells (LNMC) were obtained from TDLN and cultured in 3 ways: medium alone (LN neg), stimulated once by XAGE-1b (LN XAGE) or p53 overlapping peptides (LN p53). Peripheral blood mononuclear cells (PBMC), TIL and the 3 LNMC cultures were analyzed for antigen-specificity by a 4-day proliferation assay and in supernatants taken at day 2 cytokine release was determined. In 1 out of 6 patients, XAGE-1b induced proliferation in LN XAGE and IFNγ release in LN XAGE and TIL. In another patient, XAGE-1b induced proliferation in PBMC and LN neg, but no IFN-γ release. In 3 out of 6 patients, a p53-induced proliferation was observed in LN p53, which was accompanied by IFN-γ release in 2 patients. In one patient, p53 induced TNF-α release in TIL. These preliminary data show T-cell immunity to XAGE-1b and p53 in lung adenocarcinoma indicating that these antigens are potential targets for immunotherapy. More patients are needed to define strength, breadth and phenotype of this antigen-specific response and its relation with antigen expression in the primary tumor.