INTRODUCTION. The discovery of thalidomide and its renewal plays an important role in the treatment of various malignancies. While thalidomide has been well documented to have anti-inflammatory, anti-angiogenic and immunosuppressive properties, the mechanisms of action are not fully elucidated. ICAM-1 is an inducible surface glycoprotein associated with inflammatory and immune responses.(1) Our recent study has shown that ICAM-1 expression induced by TNF-α elicited alveolar epithelial carcinoma cell invasion (2). Preliminary data showed the inhibitory effect of thalidomide on TNF-α induced-alveolar carcinoma cell invasion. Therefore, the effect of thalidomide on ICAM-1 expression and on mouse xenograft model of lung cancer was examined, and the action mechanism was studied.

METHOD. A human alveolar epithelial carcinoma cell line A549 was used and ICAM-1 expression was detected by Elisa. Nude mice bearing s.c. human lung cancer (A549) xenografts were treated with the thalidomide. Tumors were excised and processed for detection of ICAM-1. In vivo metastasis to lung was examined by hematoxylin-eosin staining and counting the metastasis nodules. Degradation of cytosolic IkBα and translocation of NF-κB were measured by Western blot

RESULTS. Thalidomide induced a dose-dependent inhibition on A549 tumor cell invasion and on TNF-α induced-ICAM-1 expression in A549 cells. It also expressed prominent growth inhibition on A549 tumors implanted in nude mice. Level of ICAM-1 was found to be increased in tumors and reduced by
thalidomide. Vascular endothelial growth factor (VEGF) in tumors as well as metastasis nodules in lungs was also reduced by thalidomide. TNF-α induced-\(\text{IκB}\alpha\) degradation and translocation of NF-\(\kappa\)B to the nucleus were not affected by thalidomide.

**DISCUSSION.** Thalidomide is emerging as a treatment for cancer and inflammatory diseases. Different stages of clinical trials on its implications for malignant diseases have been conducted (3). It has been shown to be effective for hematological cancers especially multiple myeloma, and activity against solid tumors including renal-cell carcinoma, glioma, prostate cancer and colorectal cancer has been observed (3). In the present study, we found the anti-tumor effect of thalidomide on mouse xenograft model of lung cancer, and its anti-ICAM-1 effect contributes to the anti-tumor effect. \(\text{IκB}\alpha\) degradation and translocation of NF-\(\kappa\)B to the nucleus were not affected by thalidomide. Action mechanisms of its inhibition on ICAM-1 expression are in progress. These studies provide the framework for targeting NF-\(\kappa\)B-regulated gene by thalidomide in biologically based therapies for lung cancer.

**REFERENCES**