

**Follistatin suppresses the production of experimental multiple-organ metastasis by small cell lung cancer cells in natural killer cell-depleted SCID mice.**

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**PURPOSE:** Follistatin (FST), an inhibitor of activin, regulates a variety of biological functions, including cell proliferation, differentiation, and apoptosis. However, the role of FST in cancer metastasis is still unknown. Previous research established a multiple-organ metastasis model of human small cell lung cancer in natural killer cell-depleted SCID mice. In this model, i.v. inoculated tumor cells produced metastatic colonies in multiple organs including the lung, liver, and bone. The purpose of this study is to determine the role of FST in multiple-organ metastasis using this model. **EXPERIMENTAL DESIGN:** A human FST gene was transfected into the small cell lung cancer cell lines SBC-3 and SBC-5 and established transfectants secreting biologically active FST. The metastatic potential of the transfectants was evaluated using the metastasis model. **RESULTS:** FST-gene transfection did not affect the cell proliferation, motility, invasion, or adhesion to endothelial cells *in vitro*. I.v. inoculated SBC-3 or SBC-5 cells produced metastatic colonies into multiple organs, including the lung, liver, and bone in the natural killer cell-depleted SCID mice. FST transfectants produced significantly fewer metastatic colonies in these organs when compared with their parental cells or vector control clones. Immunohistochemical analyses of the liver metastases revealed that the number of proliferating tumor cells and the tumor-associated microvessel density were significantly less in the lesions produced by FST transfectants. **CONCLUSIONS:** These results suggest that FST plays a critical role in the production of multiple-organ metastasis, predominantly by inhibiting the angiogenesis. This is the first report to show the role of FST in metastases.