CORRELATION BETWEEN MORBIDITY OF CANCERS AND TRANSFORMING GROWTH FACTOR- β (TGF- β)

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INTRODUCTION

TGF- β , which is distributed widely within the body, is said to influence the growth regulation of normal epithelial cells, healing of wounds, interstitial growth, and infiltration of cancer cells, and to exert a marked immunosuppressive function on the immune system^{1), 2), 3), 4)}.

In the present study, TGF- β in cancer tissues obtained during surgery for esophageal or pulmonary malignancies was measured to elucidate a correlation with the progression of cancers. In addition, the effects of TGF- β on induction of killer activity in lymphocytes were studied.

MATERIALES AND METHHODS

Cultured cancer cell lines (KATO III, PC-9, TE 9, TE 10, LCT-1) and tissues removed surgically from patients (five esophagal cancers and five lung cancers) were used in the study. Supernatants of cultures of cell lines were treated with acid by dialyzing them against 0.17 M acetic acid. Samples of TGF- β were extracted from cancer tissues with acid/

ethanol.

TGF- β was measured using the method of Roberts et al⁵⁾. Samples were added to NRK-49F cells, which were cultured in double-layer soft agar plates, and the numbers of colonies of NRK-49F cells produced in the mixture were counted. At the same time, the numbers of colonies of NRK-49F cells were counted when a fixed amount of TGF- β was added as the serial dilution. This allowed a comparison of the numbers of colonies in the samples to determine the quantity of TGF- β .

Also studied were the effects of adding TGF- β on the increased NK and LAK activities of human lymphocytes caused by IL-2.

RESULTS

TGF- β in the supernatants of cultures of cancer cell lines were found in larger quantities in KATO III and PC-9. There was no colony production in LCT-1 and TE 10 (Table 1). In cancer tissues, samples from three cases of esophageal cancer produced TGF- β levels of 10 ng/ml or higher. There were no

Table 1 TGF activities in conditioned media of the cell lines

Cell line	TGF- β activity (ng/ml)
KATO III	5
PC-9	4.5
TE 9	2.5
LCT I	<2.5
TE 10	<2.5

apparent differences in the degree of advancement of cancer between cases with large quantities of TGF- β and those with relatively low quantities of TGF- β .

In five cases of lung cancers, almost all samples produced TGF- β levels of 2.5 ng/ml or lower. Most lung cancers were without metastasis to lymph nodes. One of the recurrent lung cancer produced recognizable colonies with a TGF- β level of 4 ng/ml (Table 2).

Adding TGF- β suppressed killer activity in lymphocytes which were induced by IL-2. The suppression was particularly significant with TGF- β at 5 ng/ml. It was highly conceivable that the TGF- β was produced in cancer cells and cancer tissues, affecting interstitial tissues or immunocytes around cancer lesions and growth and infiltration of cancer cells.

production of TGF- β is believed to vary depending upon type of cancer cells, host organs, and the stage of cancers.

REFERENCE

1) Ura H., Obara T. et al.: Effects of Transforming Growth Factor- β Released

Table 2 TGF activities in esophageal or lung cancer cases

Organ	TGF- β activity (ng/ml)	p-stage
K. N. esophagus (primary cancer)	9	a ₃ n ₁ m ₀ p ₀ stage IV
H. F. esophagus (metastatic lymphnode)	10<	a ₃ n ₄ m ₀ p ₀ stage IV
T. E. esophagus (metastatic lymphnode)	10<	a ₃ n ₂ m ₀ p ₀ stage VI
S. S. esophagus (primary cancer)	10<	a ₂ n ₃ m ₀ p ₀ stage IV
H. N. esophagus (primary cancer)	< 2.5	a ₂ n ₂ m ₀ p ₀ stage III
K. H. lung (primary cancer)	< 2.5	t ₁ n ₀ m ₀ stage I
S. K. lung (primary cancer)	< 2.5	t ₁ n ₀ m ₀ stage I
M. E. lung (primary cancer)	< 2.5	t ₂ n ₀ m ₀ stage I
H. A. lung (recurrent cancer)	4	
T. M. lung (primary cancer)	< 2.5	t ₂ n ₀ m ₀ stage I

from Gastric Carcinoma Cells on the Contraction of Collagen-Matrix Gels Containing Fibroblasts. CANCER RESEARCH. 51. 3550-3554, 1991.

2) Cromack D. T., Sporn M. B. et al: Transforming Growth Factor- β Levels in Rat Wound Chambers. JOURNAL OF SURGICAL RESEARCH. 42. 622-628, 1987.

3) Tsunawaki S., Sporn M. et al.: Deactivation of Macrophages by Transforming growth factor- β . NATURE 334. 260-262, 1988.

4) Welch D. R., Fabra A. et al.: Transforming Growth Factor β Stimulates Mammary Adenocarcinoma Cell Invasion and Metastatic Potential. Proc. Natl. Acad. Sci. USA 87. 7678-7682, 1990.

5) Roberts A. B., Lamb L. C. et al.: Transforming Growth Factors: Isolation of Polypeptides from Virally and Chemically Transformed Cells by Acid/Ethanol Extraction. Proc. Natl. Acad. Sci. USA 77. 3494-3498, 1980.

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