Tumor Histology and the Immunoregulatory T Lymphocyte Subsets in Lung Cancer Patients*

NOBUKO KUMANO, SADAHIRO KOINUMARU, SHUJI SUZUKI, TETSUKO ISHIKAWA, KOTARO OIZUMI and KIYOSHI KONNO

Department of Internal Medicine, the Research Institute for Tuberculosis and Cancer, Tohoku University, Sendai 980

KUMANO, N., KOINUMARU, S., SUZUKI, S., ISHIKAWA, T., OIZUMI, K. and KONNO, K. *Tumor Histology and the Immunoregulatory T Lymphocyte Subsets in Lung Cancer Patients*. Tohoku J. exp. Med., 1986, **150** (4), 483-484 — The immunoregulatory T lymphocyte subsets (CD4⁺, CD8⁺) in 39 patients with primary lung cancer were analyzed as for the possible correlation with tumor histology. Compared to the healthy controls ($n=36$), cancer lymphocytes were generally characterized by a higher proportion of CD8⁺ subset ($p<0.01$) with no difference in either CD4⁺ subset or CD3⁺ cells. There was, however, a significant difference ($p<0.05$) between one extreme of epidermoid carcinoma with the highest CD8⁺ and the lowest ratio (CD4⁺/8⁺) and the other end of adenocarcinoma with the lowest CD8⁺ and the highest ratio. Large cell and small cell carcinomas were of the intermediate values. A spectrum of the subset marker profiles was thus found in association with tumor histology. A diversity in the host immune status was suggested in primary lung cancer, although clinical implication remains to be clarified. ——— T lymphocytes; lung cancer; tumor histology

The peripheral T lymphocyte surface markers (CD3⁺, CD4⁺, CD8⁺) were analyzed in 39 patients with primary lung cancer (14 adeno-, 16 epidermoid, 4 large cell, and 5 small cell carcinomas) with particular reference to the tumor histology. Prior chemotherapy and/or radiation therapy, if any, were discontinued at least 2 weeks before lymphocyte analysis. The indirect immunofluorescence assays were performed as described previously (Kumano et al. 1985).

The results are summarized in Table 1. Compared to the healthy controls, the mean percentages of CD8⁺ cells were generally higher ($p<0.01$) in agreement with previous observations (Dillman and Koziol 1983; Kumano et al. 1985). More notably was found a significant difference ($p<0.05$) between one extreme of epidermoid carcinoma with the highest CD8⁺ and the lowest ratio (CD4⁺/8⁺) and the other end of adenocarcinoma with the lowest CD8⁺ and the highest ratio. Large cell and small cell carcinomas were found in between, although the number of cases was limited. Either CD4⁺ or CD3⁺ (data not shown) was in a normal range regardless of tumor histology. Difference between these two extremes was also demonstrable in the distribution of the ratios. Whereas a convergent

Received September 25, 1986; accepted for publication November 27, 1986.

*A part of this paper was presented at the 14th International Congress of Chemotherapy, Kyoto, 1985, and at the 26th Annual Meetings of The Japan Lung Cancer Society, Sendai, 1985.

TABLE 1. *Tumor histology and T lymphocyte subsets in lung cancer patients*

Group	No. (M/F)	Mean age (years)	Stage (I, II/ III, IV)	Relative percentage (mean ± s.d.)		
				CD4 ⁺	CD8 ⁺	Ratio (CD4 ⁺ /8 ⁺)
Lung cancer patients						
Adeno	14 (5/ 9)	65 ± 8	1/13	57.2 ± 13.9	29.6 ± 13.5†	2.66 ± 1.98†
Epidermoid	16 (13/ 3)	69 ± 8	3/13	50.0 ± 10.3	42.3 ± 14.9†**	1.41 ± 0.82†
Large cell	4 (3/ 1)	64 ± 11	0/ 4	55.4 ± 4.2	33.2 ± 12.9	1.86 ± 0.71
Small cell	5 (3/ 2)	62 ± 11	1/ 4	53.7 ± 11.3	37.1 ± 15.5	1.85 ± 1.32
<i>Overall</i>	<i>39 (24/15)</i>	<i>66 ± 9</i>	<i>5/34</i>	<i>53.6 ± 11.2</i>	<i>36.9 ± 14.7**</i>	<i>1.90 ± 1.42</i>
<i>Healthy controls§</i>						
<35 years	13 (9/ 4)	29 ± 5		42.1 ± 9.6	30.6 ± 5.3	1.44 ± 0.49
>36 years	23 (14/ 9)	47 ± 7		53.4 ± 6.4	25.4 ± 3.9	2.15 ± 0.42
<i>Overall</i>	<i>36 (23/13)</i>	<i>41 ± 11</i>		<i>4.93 ± 9.4</i>	<i>27.3 ± 5.1</i>	<i>1.90 ± 0.55</i>

Significantly different as evaluated by Student's *t*-test: ***p* < 0.01 vs healthy controls (>36 years or overall); † *p* < 0.05 between adeno and epidermoid.

§Five decade age groups ranging from approximately 20 to 60 years were studied as will be reported elsewhere in more detail.

trend in a lower range was the case of epidermoid carcinoma, a considerable scattering over a wide range (0.63 to 7.12) was noted in adenocarcinoma. The extremely high ratios in the latter were attributable to the low-CD8⁺ and the high-CD4⁺, while the low ratios substantially resulted from the high-CD8⁺.

An elevated ratio in adenocarcinoma (*n* = 7) and a decreased ratio in squamous cancer (*n* = 10) were reported by Ginns et al. (1982). On the other hand, immunohistochemical study at the site of tumor (Watanabe et al. 1983) revealed the dense infiltration of T lymphocytes in adenocarcinoma, but not in squamous cell carcinoma. A severe failure in the cytotoxic capacity of the peripheral lymphocytes was also observed in association with particular histologic type, epidermoid carcinoma (Figarella et al. 1984). We described here a histology-associated spectrum found in the marker profiles of the circulating T lymphocytes, a diversity in the host immune status being suggested in patients with primary lung cancer. Further study is necessary to understand the possible correlation of the marker profiles with the cell functions as well as with the clinical features.

References

- 1) Dillman, R.O. & Koziol, J.A. (1983) Statistical approach to immunosuppression classification using lymphocyte surface markers and functional assays. *Cancer Res.*, **43**, 417-421.
- 2) Figarella, E.F., Morillo, F., Blanca, I. & Bianco C.N.E. (1984) Failure of cell-mediated effector mechanisms in lung cancer. *J. nat. Cancer Inst.*, **73**, 1-6.
- 3) Ginns, L.C., Goldenheim, P.D., Miller, L.G., Burton, R.C., Gillic, L., Colvin, R.B., Goldstein, G., Kung, P.C., Hurwitz, C. & Kazemi, H. (1982) T-lymphocyte subsets in smoking and lung cancer. Analysis by monoclonal antibodies and flow cytometry. *Amer. Rev. resp. Dis.*, **126**, 265-269.
- 4) Kumano, N., Suzuki, S., Oizumi, K., Konno, K., Himori, T., Mitachi, Y. & Wakui, A. (1985) Imbalance of T cell subsets in cancer patients and its modification with bestatin, a small molecular immunomodifier. *Tohoku J. exp. Med.*, **147**, 125-133.
- 5) Watanabe, S., Sato, Y., Kodama, T. & Shimosato, Y. (1983) Immunohistochemical study with monoclonal antibodies on immune response in human lung cancers. *Cancer Res.*, **43**, 5883-5889.