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Increased Levels of Soluble Interleukin-2 Receptors in Supernatants from Peripheral Blood Mononuclear Cells of Patients with Lung Cancer

Pietro Marino, Armando Preatoni, Gianfranco Buccheri, Domenico Ferrigno and Adriana Fruttero

INTERLEUKIN-2 (IL-2) stimulates immunity by acting on specific IL-2 cell surface receptors, expressed by activated but not resting immune cells [1]. It has been demonstrated that lymphocytes may produce a soluble form of IL-2 receptors(sIL-2r) [2]. We have reported increased sIL-2r serum levels in lung cancer patients [3] and increased sIL-2r serum levels were found in others neoplasms [4]. No data are available up to now on the amount of sIL-2r produced by tissue infiltrating lymphocytes (TIL) and scant data are available on the amount of sIL-2r produced by peripheral blood lymphocytes (PBL).

Using ELISA [2], we have investigated sIL-2r concentrations (Cellfree, T Cell Sciences Inc., Cambridge, Massachusetts) in serum and in non-stimulated supernatants of 100 μl peripheral blood mononuclear cells (PBMC) cultures and in phytohaemagglutinin (PHA) stimulated (20 μl, final concentration 1:100) PBMC for 3 days, derived from 20 patients with untreated lung cancer, or from 30 age- and sex-matched healthy subjects as control group. All samples derived from patients and controls were tested simultaneously.

In lung cancer patients, co-existing infections were excluded on the basis of clinical criteria along with the absence of leukocytosis and positive cultures of body fluids. Clinical staging was performed according to the TNM classification. Data are expressed as median value (range), and were analysed by the rank sum and Kruskall-Wallis tests and by Spearman rank correlation. Results are reported in Table 1.

A good correlation was found between sIL-2r levels in non-stimulated supernatant and stage of disease (metastatic vs. non-metastatic) ($r = 0.6$, $P < 0.05$), as well as between non-stimulated supernatant and sIL-2r serum levels ($r = 0.7$, $P < 0.01$). These preliminary results on the sIL-2r in supernatants of non-stimulated or PHA-stimulated PBMC cultures have shown an increased sIL-2r concentration, although not significantly, in lung cancer patients compared with controls. In particular, the median value of sIL-2r supernatant concentration in metastatic patients was significantly higher in comparison to non-metastatic patients ($P < 0.05$). As far as sIL-2r serum levels, significant higher sIL-2 serum levels were found in cancer patients with respect to controls ($P < 0.01$), but no differences were found between metastatic and non-metastatic patients. These last data confirm our previous results [5]. Interestingly, good correlation was found between sIL-2r serum levels and non-stimulated supernatant, whereas it was absent with stimulated surnatant.

The discrepancy found in metastatic patients between sIL-2r serum levels, which are not increased, and raised concentration in the supernatant could be explained by a reduced catabolic ability of the *in vitro* cell culture system.

However, further studies are needed in order to clarify the complex interactions existing among neoplastic tissue, TIL, and sIL-2r production and catabolism.

Table 1. Median values of sIL-2r in healthy subjects and in lung cancer patients

Cases	*n*	Supernatant (non-stimulated) (U/ml)	Supernatant (stimulated) (U/ml)	Serum level (U/ml)
Healthy subjects	30	90 (45–950)	124 (85–1100)	398 (197–1595)
Cancer patients	20	124 (50–1518)	216 (116–1543)	721* (521–2735)
With metastases	10	858† (98–922)	1087‡ (135–1260)	772 (660–1211)
Without metastases	10	106 (50–1518)	206 (116–1543)	721 (521–2735)

Median (range).
* $P < 0.01$ vs. healthy subjects; † $P < 0.05$ vs. non-metastatic patients; ‡ $P < 0.05$ vs. non-metastatic patients.

Correspondence to P. Marino.
P. Marino and A. Preatoni are at the Dipartimento di Medicina Interna, Università, Ospedale S. Paolo, via Di Rudini, 8, 20142 Milano; G. Buccheri and D. Ferrigno are at the Ospedale Pneumologico "A Carle"; and A. Fruttero is at the Servizio di Anatomia Patologica, Ospedale "S. Croce", Cuneo, Italy.
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