LETTER TO THE EDITOR

Pretreatment serum CRP and response to interleukin 2

Sir – Broom *et al.* (1992) have reported an interesting observation on the inverse correlation between pretreatment serum C-reactive protein (CRP) and response to interleukin 2 (IL-2) in patients with metastatic colorectal cancer. We would like to report a similar observation in metastatic renal carcinoma.

Serum CRP levels were measured the day before starting therapy in 121 patients with metastatic renal carcinoma treated with IL-2 between 1987 and 1991 and who were evaluable for response. None of these patients had evidence of infection at the time of sample. Three different IL-2-containing regimens were used: 56 patients received continuous intravenous (i.v.) IL-2, 28 bolus i.v. IL-2 with interferon alpha (IFN) and LAK cells and 37 subcutaneous IL-2 and IFN (Blay *et al.*, 1992). As previously reported, serum CRP levels were highly correlated to serum IL-6 in these patients (Blay *et al.*, 1992).

Patients who experienced progressive disease after IL-2 had significantly higher pretreatment CRP levels than other patients ($P < 0.001$, Table I). Only one of the 37 (3%) patients with pretreatment serum CRP over 50 mg l^{-1} achieved response to IL-2 compared with 20 of the 84 (24%) remaining patients (two-tailed Fisher's exact test: $P = 0.007$). These results demonstrate that pretreatment serum CRP levels are inversely correlated to the response to IL-2 in metastatic renal carcinoma.

These results indicate that serum CRP is inversely correlated to the response to IL-2 in two different tumour models (Broom *et al.*, 1992). Several interpretations could account for these observations. The increase in serum CRP could be related to the production of proinflammatory cytokines by tumour cells, such as IL-6, and thus be an index of tumour burden. However, no correlation between IL-6

and tumour mass was observed in patients with metastatic renal cancer (Blay *et al.*, 1992). Alternatively, serum CRP could by itself interfere with the immunological mechanisms involved in the anti-tumour activity of IL-2. CRP has been reported to play an important role in the cytotoxic activity of NK cells (Hamoudi & Baum, 1991). CRP is also involved in the binding of complement to CD3^+ cells *in vivo* in patients receiving IL-2, a phenomenon that contributes to endothelial injury during IL-2 treatment (Thijs *et al.*, 1990; Vachino *et al.*, 1991). Conceivably, high levels of circulating CRP in these patients before IL-2 administration could interfere with the biological mechanisms responsible for the antineoplastic activity of IL-2 *in vivo*.

The observation that baseline serum CRP is inversely correlated to response to IL-2 in different tumours has important potential consequences for the selection of candidates for IL-2 therapy. The exact role of CRP in these observations remains to be elucidated.

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Table I Pretreatment serum CRP levels and clinical response to IL-2 in patients with metastatic renal carcinoma

	CRP (mg l^{-1}) median (s.e.m.)	Patients with CRP $< 50 \text{ mg l}^{-1}$ number (%)	Patients with CRP $> 50 \text{ mg l}^{-1}$ number (%)
Objective response ($n = 21$)	20 (6.5)	20 (24%)	1 (3%)
Stable disease ($n = 39$)	19 (6.1)	32 (38%)	7 (19%)
Progressive disease ($n = 61$)	44 (5.3)*	32 (38%)	29 (78%)
Total		84 (100%)	37 (100%)

*Progressive disease vs others: Mann-Whitney U -test: $P < 0.001$.

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