Anti-leukemic immunity against U937 cells in uremic patients*

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To examine anti-tumor immunity in uremic patients undergoing regular hemodialysis, we designed this study using in vitro mononuclear cell (MNC) cultures, with human leukemic U937 cells as the target. MNC were collected and cultured from uremic subjects and age- and gender-matched healthy controls. Conditioned media from the cultures (MNC-CM) were collected after stimulation with various concentrations of phytohemagglutinin (PHA). The proliferation-inhibiting and differentiation-inducing activities of the PHA-MNC-CM on U937 cells were evaluated. The growth inhibition activity of uremic patients' PHA-MNC-CM was lower than that of controls. The differentiation-inducing effects were evaluated by morphological scoring, superoxide production, and monocyte-associated antigen expression (CD14 and CD68). All three parameters demonstrated that the differentiation-inducing effect of MNC-CM increased with increasing doses of PHA. These effects, however, were significantly less in uremic patients compared to controls at higher doses of PHA. The levels of TNF-α and IFN-γ in PHA-MNC-CM increased in a PHA dose-dependent manner and were much higher in the controls. We conclude that the capacity of MNC from uremic hemodialysis patients to produce anti-leukemic immunity is significantly lower than that of healthy controls.

Key words: Uremia, leukemic U937 cell, proliferation, differentiation.

The increased incidence of malignancy in patients with end-stage renal disease on hemodialysis has been studied in numerous investigations [18, 19]. Results of several *in vitro* assays suggest that cellular immunity is impaired in patients with renal failure. These include a decrease in absolute T lymphocyte counts [14, 24], suppression of the blastogenic response of uremic cells in one-way-mixed lymphocyte cultures [17], a decrease in CD4+ cells [7], inhibition of natural killer activity [15], a decrease in proliferative response to the T cell mitogens PHA and con A [23, 24], and reduction in release of activation-dependent cytokines such as interleukin-2 (IL-2) [10, 20] and interferon-γ (IFN-γ)[9, 28].

In a previous investigation, we found that mononuclear cell conditioned medium (MNC-CM) was capable of triggering differentiation and growth inhibition in the U937 cell line [3, 4, 5]. We compared anti-tumor cellular immune function in hemodialysis patients with that of controls by evaluating the *in vitro* effects of cytokines released by peripheral blood mononuclear cells (MNC) on this transformed cell line.

Material and methods

Subjects. Ten patients (6 females and 4 males) who were clinically stable on chronic hemodialysis at Mackay Memorial Hospital for at least 4 years (range 48–120 months) and who had not been hospitalized within the previous six months were recruited (Tab. 1). To exclude confounding by age and gender, we recruited age- and gender-matched volunteer subjects. The average age of dialysis patients was 64.4 and that of controls, 63.8. The study was approved by the hospital's Human Research Review Committee. In-

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