

Anti-leukemic immunity against U937 cells in uremic patients*

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Received August 27, 2002

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 trig-

gering 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-

*This study was supported by grant MMH-8807 from Mackay Memorial Hospital.

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