Defective in vitro T Cell Colony Formation in Patients with Membranous Nephropathy

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Dear Sir,

The etiology and pathogenesis of idiopathic membranous nephropathy (MN) is not fully understood, but immunological mechanisms are thought to be involved [1]. We have recently shown that MN patients with the nephrotic syndrome (NS) have an impaired response of cell-mediated immunity (CMI) [2]. Our previous study [3, 4] also illustrated an alteration in concanavalin A-induced suppressor cell activity in the majority of MN patients with NS. The purpose of the present work was to assess the T lymphocyte colony formation in a selected group of MN in order to further elucidate the existence of a CMI disorder in this nephropathy (fig. 1). The T colony formation was studied in 9 adult patients with MN. Colony-forming assays were performed by a one-step culture method with some modifications [5]. In 13 normal subjects, the average number of T colony-

forming cells (TCFC) was 551.5 ± 90.5 (SD). By contrast, in MN patients with NS, the mean number of TCFC was 388.5 ± 151.9 , a value significantly less than normals ($p < 0.05$). During complete remission, TCFC levels were similar to those of normal subjects.

Compared with random determinations, serial studies of TCFC in individual patients were much more informative. Figure 2 shows the course of a 59-year-old woman who presented with NS. Her renal biopsy specimen showed MN. She showed persistently low TCFC during 3 months of the follow-up period, while the E rosetting

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Fig. 1. Photomicrograph of a lymphoid colony grown in agar medium from venous blood, T lymphocyte-enriched population stimulated with PHA-P.

Fig. 2. Serial study of TCFC and other parameters of CMI in a 59-year-old woman, H.A., with MN. A one-step single-layer soft agar culture system was employed. The cultures were prepared in triplicate 35-mm plastic Petri dishes. These contained 1 ml of 0.33% agar in RPMI-1640 media supplemented with 1×10^6 cells, 5% heat-inactivated fetal calf serum, and 1% (v/v) PHA-P. 7 days after planting, groups of more than 50 cells were scored as colonies using an inverted microscope.

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capacity and responsiveness to phytohemagglutinin (PHA) was within normal range.

This article describes a new cellular assay system of lymphocyte cooperation. To our knowledge, this is the first report that describes alterations in the T lymphocyte colony formation in MN patients. The precise mechanism of impaired T lymphocyte colony-forming capacity in MN remains unclear. We believe that decreased TCFC in vitro more or less reflects an in vivo activity. The present results might suggest an imbalance in the cellular cooperation or a T cell defect in the synthesis or secretion of T colony-stimulating factor in MN patients with NS. We propose that the assay system reported here represents an improved method for the measurement of CMI in patients with renal disease because it requires fewer donor cells, is technically simpler, and is more sensitive than previously described methods.

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