

## The Significance of T Helper 1 Cell–Derived Cytokines in Patients With Systemic Lupus Erythematosus With Acquired Thrombotic Thrombocytopenic Purpura

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### To the Editor

We read with great interest the contribution by Muscal et al.<sup>1</sup> They reported the development of systemic autoimmunity such as systemic lupus erythematosus (SLE) and antiphospholipid antibodies in children with acquired thrombotic thrombocytopenic purpura (TTP). We would like to suggest some potential pathologic mechanisms on the development of concurrent SLE in relation to TTP.

Kakishita<sup>2</sup> found that TTP after bone marrow transplantation (BMT) could be predicted at an early stage by an increase in the level of plasma interleukin (IL)-12, postulating that TTP might be related to inflammation or autoimmunity. According to an animal experiment by Nakajima et al,<sup>3</sup> transfer of IL-12–stimulated splenocytes from 5-month-old B/W F1 mice to B/W F1 mice of the same age enhanced the production of IgG anti-dsDNA antibody, indicating that IL-12 serves a key role in the complexity of cytokine regulation in the pathogenesis of SLE autoimmunity. In another animal model by Huang et al,<sup>4</sup> MRL/MP-lpr/lpr (MRL/lpr) mice, developing a spontaneous autoimmune disease, also produced markedly higher concentrations of IL-12 than age-matched MRL/lpr+ or BALB/c mice, and daily injection of IL-12 increased serum levels of interferon  $\gamma$  (IFN- $\gamma$ ) and accelerated glomerulonephritis in the young MRL/lpr mice.

Recently, Tucci et al<sup>5</sup> demonstrated that higher serum IL-12 levels in SLE were associated with lupus nephritis, and a T helper 1 (T<sub>H</sub>1) phenotype with high IFN- $\gamma$  expression was correlated in parallel with the severity of renal damage. Shah et al<sup>6</sup> also reported that increased levels of IL-12 and

IFN- $\gamma$  were found in the culture supernatant of peripheral blood mononuclear cells of patients with SLE and positively correlated with the Systemic Lupus Erythematosus Disease Activity Index.

Therefore, there is a possibility that T<sub>H</sub>1-derived cytokines, such as IL-12 and IFN- $\gamma$ , might fulfill a critical role in the development of SLE in children, particularly children with TTP. However, further studies are necessary to elucidate the exact signaling transduction pathway of IL-12 and IFN- $\gamma$  and the subset of T<sub>H</sub> cells that is more prevalent in the disease process. The role of IL-21, a member of the type I cytokine superfamily, and IL-17, produced by CD4+/CD45RO+ memory T cells, in autoimmunity should also be further evaluated.

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