1-2). Defective Signal Transduction Via TCR-CD3 Complex in Patients with Systemic Lupus Erythematosus

Tsutomu TAKEUCHI, Kensei TSUZAKA, Ming PANG and Tohru ABE

The Department of Internal Medicine, Saitama Medical Center, Saitama medical School, Saitama

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Systemic lupus erythematosus (SLE) is a prototype autoimmune disease characterized by multiorgan involvement and abundant production of a variety of autoantibodies with unknown etiology (1). A substantial number of observations on immune aberrations have been reported in patients with SLE, suggesting a central role of T cells in the pathogenesis of SLE (2).

Previous reports indicate that altered SLE T cell responses to antigens in the context of major histocompatibility complex (MHC) or crosslinking T cell receptor (TCR) can be corrected by phorbol ester plus ionomycin, which bypass the early signaling molecules. These results introduce a hypothesis that the functional defects of SLE T cells lie in the early signaling pathways between TCR and protein kinase C (3).

In order to pinpoint these defects, we examined the tyrosine phosphorylation of cellular proteins, the earliest biochemical event in signal transduction (4), via TCR-CD3 complex on peripheral blood T cells from SLE patients.

In our study, we showed that tyrosine phosphorylation and expression of TCR zeta were significantly decreased in SLE T cells. Among those patients, we found deletion of exon 7 in

TCR zeta chain in two cases. Since exon 7 spans the GTP/GDP binding site and the N-terminal tyrosine in the third ITAM domain of the TCR zeta chain, this deletion may lead to critical functional alterations in signal transduction (5, 6). We discussed the role of this aberrant TCR zeta chain in the immune abnormalities of SLE (5, 6).

References

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