Decreased Galectin-1 expression and apoptotic activity in systemic lupus erythematosus

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Introduction:

Galectin-1 (Gal-1) is a lectin with immunomodulant activities. It has been suggested to contribute to the T and B-lymphocyte dysfunction observed in animal models of systemic lupus erythematosus (SLE). As the effects of Gal-1 have not been investigated on human samples, the aim of the authors was to compare the expression of Gal-1, and the apoptotic response to exogenous Gal-1 between T-cells of SLE patients and healthy subjects, and to determine the Gal-1 binding ability of activated T-cells, as an altered binding pattern may contribute to an impaired response to apoptotic signals.

Methods:

T-cells were separated from peripheral blood of 16 SLE patients, and were activated with PHA. The results were compared with those on samples from the same patient taken in (treatment-induced) remission(n=9), and from healthy controls (n=17). Intracellular Gal-1 expression at the mRNA level was measured with quantitative RT-PCR, and at the protein level with extra- and intracellular cytofluorimetry..In order to determine the response to exogenous Gal-1, activated T-cells were co-cultured with Gal-1-expressing and non-expressing HeLa tumour cells. After 16 hours of co-culture, the apoptosis rate of T-cells was assessed with fluorescent Annexin V-labelling by means of fluorescent microscopy. The cell surface binding of fluorescent-labelled Gal-1 was examined with flow cytometry.

Results:

Gal-1 mRNA exhibited significantly lower expression in SLE activated T-cells than int he controls (0.25 vs 0.38, p=0.02). After successful therapy, the amount of Gal-1 protein significantly increased as compared with that in the active disease state (3.17 vs 2.25, p=0.015). The presence of exogenous Gal-1 significantly increased the apoptotic rate of the healthy T-cells, whereas the apoptotic cell death rate of lupus T-cells was significantly lower (relative apoptotic rate: 12.2 vs 3.03, p=0.01). Gal-1 displayed different cell surface binding patterns in the two groups.

Conclusions:

T-lymphocytes from SLE patients produce less Gal-1 during active disease, and, in parallel, are resistant to the apoptotic effects of exogenous Gal-1. The reduced production and impaired regulatory activity of the immunosuppressant protein Gal-1 may play role in the pathogenesis of SLE. These results obtained with the use of T-cells from SLE patients corroborate the authors'observations on Jurkat cells which indicate that the emergence of Gal-1 intracellularly may sensitize the T-cells to the apoptotic effects of exogenous Gal-1.

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