

Correspondence

High levels of LIGHT and low levels of soluble herpesvirus entry mediator in sera of patients with atopic dermatitis

doi: 10.1111/j.1365-2230.2011.04079.x

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by infiltration of activated T cells.¹ Serum chemokine (C-C motif) ligand (CCL)17 levels are associated with activity of AD.² LIGHT (lymphotoxin-like inducible protein that competes with glycoprotein D for herpesvirus entry mediator on T lymphocytes), also known as herpesvirus entry mediator (HVEM) ligand, is a tumour necrosis factor (TNF) superfamily member known for its role in T-cell development.³ HVEM is a member of the TNF receptor superfamily involved in T-cell activation. Ligation of HVEM on immune cells (including T cells) by LIGHT leads to activation of their effector functions.⁴ We evaluated serum levels of LIGHT and soluble (s)HVEM in patients with AD.

The medical ethics committee of the University of Tokyo approved the study, and it was conducted according to the principles of the Declaration of Helsinki.

The study enrolled 39 patients with AD (27 men, 12 women; mean $\pm$ SD age 34.5 ± 10.9 years, range 10–53). Clinical severity of AD was evaluated according to the criteria of Ranikin and Langeland⁵ as mild ($n = 13$), moderate ($n = 13$) or severe ($n = 13$). Informed consent was obtained from patients and healthy controls. Immunoreactive LIGHT and sHVEM in sera were quantified by ELISA (Human LIGHT/TNFSF14 ELISA Kit and HVEM/TNFRSF14 Duo Set; both R & D Systems, Minneapolis, MN, USA). The control group consisted of 17 healthy volunteers (eight men, nine women; mean $\pm$ SD age 36.5 ± 15.4 years, range 12–59).

The Mann–Whitney *U*-test was used for comparison between the two groups. Correlation coefficients were determined by using the Spearman rank correlation test. $P < 0.05$ was considered significant.

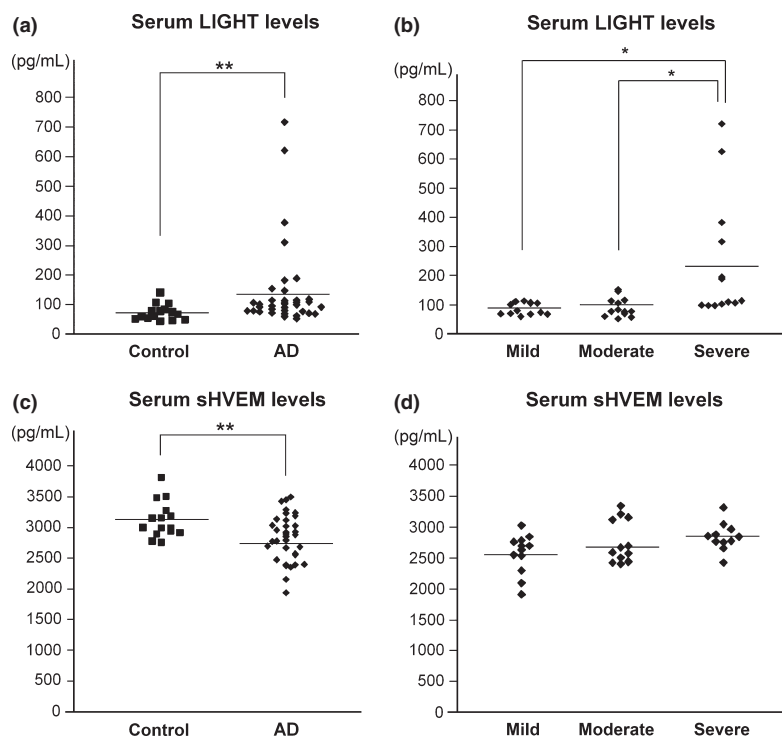


Figure 1 Serum levels of (lymphotoxin-like inducible protein that competes with glycoprotein D for herpesvirus entry mediator on T lymphocytes) and soluble herpesvirus entry mediator (sHVEM) in patients with atopic dermatitis (AD) and healthy controls. The severity of AD was divided into three groups: mild, moderate and severe. (a) Serum LIGHT levels in AD and healthy controls. (b) Serum LIGHT levels in mild, moderate and severe AD. (c) Serum sHVEM levels in AD and healthy controls. (d) Serum sHVEM levels in mild, moderate and severe AD. * $P < 0.05$, ** $P < 0.01$ by Mann–Whitney *U*-test.

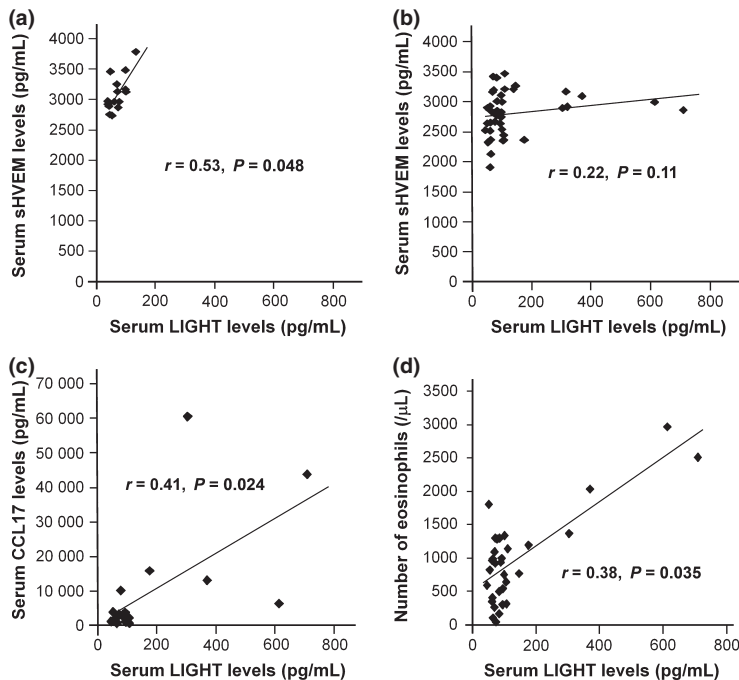


Figure 2 Correlations between serum LIGHT or sHVEM and serum CCL17 levels and eosinophil numbers. (a,b) Correlations between serum LIGHT and sHVEM levels (a) healthy controls and (b) patients with atopic dermatitis (AD). (c,d) Correlations between serum LIGHT and (c) CCL17 levels and (d) eosinophil numbers in patients with AD.

Serum LIGHT levels were significantly higher ($P < 0.01$) in patients with AD (132.2 ± 138.7 pg/mL) than in healthy controls (70.6 ± 26.4 pg/mL) (Fig. 1a). Patients with severe AD (230.8 ± 213.2 pg/mL) had significantly higher LIGHT levels than did patients with mild AD (82.9 ± 20.8 pg/mL; $P < 0.05$) (Fig. 1b) or moderate AD (86.5 ± 32.6 pg/mL; $P < 0.05$). By contrast, serum sHVEM levels were significantly lower in patients with AD (2786.6 ± 361.9 pg/mL) than in healthy controls (3097.5 ± 294.3 pg/mL; $P < 0.01$) (Fig. 1c). Serum sHVEM levels were not associated with severity of AD (Fig. 1d). Serum sHVEM levels were significantly correlated with serum LIGHT levels in healthy controls (Fig. 2a), but not in patients with AD (Fig. 2b). However, serum LIGHT levels in patients with AD were significantly correlated with serum CCL17 levels and eosinophil numbers in peripheral blood (Fig. 2c,d).

In conclusion, serum levels of LIGHT were increased and sHVEM decreased in patients with AD. The interaction between LIGHT and HVEM may contribute to the enhanced T-cell activation in AD, or sHVEM may act as a decoy to block LIGHT–HVEM interactions. In normal controls, serum sHVEM levels correlated with serum LIGHT levels, but this finding was not seen in patients with AD. Low serum sHVEM levels may reflect a defect in negative feedback, inducing impaired resolution of inflammation in patients with AD.

Acknowledgements

This study was supported by grants from the Ministry of Education, Culture, Sports and Technology and from the Ministry of Health, Labour and Welfare in Japan.

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Conflict of interest: none declared.

Accepted for publication 10 February 2011

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