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A NEW BIOMARKER FOR SYSTEMIC LUPUS ERYTHEMATOSUS: SIMULTANEOUSLY CALCULATING THE RATIO OF C4d TO CR1 ON ERYTHROCYTES BY CR1-2B11

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BACKGROUND/AIMS: Measurement of E-C4d/E-CR1 may be a potential biomarker to monitor disease activity in SLE patients, and may lead to earlier and more prompt therapeutic intervention. Moreover, it may have significant impact on the accuracy and timing of diagnosis of SLE. We recently developed a new monoclonal antibody, CR1-2B11, which should be useful for the accurate quantitation of erythrocyte CR1. This study was undertaken to determine E-C4d/E-CR1 ratio and its clinical association with SLE using CR1-2B11.

METHODS: We conducted a cross-sectional study of 67 patients with SLE, 64 patients with other diseases, and 72 healthy controls. Levels of C4d and CR1 on the surface of erythrocytes were measured by indirect immunofluorescence and flow cytometry for determination of its ratio in each study group.

RESULTS: The ratio was significantly higher in the SLE group (4.633 ± 5.10 versus 0.292 ± 2.23 in the other diseases group; $p < 0.0001$). Patients with SLE also had a higher ratio than that of healthy controls (4.633 ± 5.10 versus 0.116 ± 0.10; $p < 0.0001$). Moreover, we also observed a decline in ratio from active disease status to stable condition after treatment (19.23 to 1.01, 5.47 to 1.25, and 13.16 to 2.40, respectively).

DISCUSSION/CONCLUSIONS: These data explore the real value of E-C4d/E-CR1 in SLE, introducing E-C4d/E-CR1 ratio as a possible biomarker to predict lupus disease activity using CR1-2B11 and helping in making therapeutic stratagies to handle disease activity as well as diagnosing SLE in early stages.

Key words: Erythrocyte, C4d, Complement receptor 1

Table 1. Baseline characteristics of the 203 study participants in Tri-Service General Hospital during fiscal year 2005

	Controls (n = 72)	Patients with other diseases (n = 64)	SLE patients (n = 67)
Age, mean ± SD (range) years	29.31±11.56 (18-73)	35.17±16.56 (18-83)	33.36±11.58 (18-63)
Race, % Han	95.7%	98.6%	99.2%
Sex, % women	75.6%	64.7%	89.6%

Table 2. Comparison of E-C4d and E-CR1 levels among SLE patients, patients with other diseases and healthy controls and the E-C4d/E-CR1 ratio difference between groups*

Group	E-C4d MFI[#] mean ± SD, median (range)	E-CR1 MFI[#] mean ± SD, median (range)	E-C4d/E-CR1[†] mean ± SD, median (range)
SLE patients (n = 67)	9.01 ± 5.26, 7.35 (3.13-28.89)	5.00 ± 1.72, 4.56 (2.36-12.95)	4.63±5.10, 3.20 (0.22~21.75)
Patients other diseases (n=64)	3.78 ± 0.60, 3.63 (2.99-5.20)	6.59 ± 1.75, 6.44 (2.96-12.51)	0.29±2.23, 0.24 (0.02~1.42)
Controls (n=72)	3.39 ± 0.78, 3.16 (2.58-6.67)	8.33 ± 2.24, 8.19 (4.53-16.12)	0.12±0.10, 0.10 (0.02~0.57)

* E= erythrocyte; MFI = mean fluorescence intensity; SLE = systematic lupus erythematosus.

[#] Median values were significantly different for pairwise comparisons among the 3 groups by Mann-Whitney Tests, all *p* values < 0.001.

[†] E-C4d/E-CR1 = (C4d MFI minus isotype-matched control MFI) ÷ (CR1 MFI minus isotype-matched control MFI). All ratio differences between the SLE patients and the patients with other diseases as well as the healthy controls were significant at $p < 0.0001$, by Wilcoxon's rank-sum test.