CXCL13 Levels and Autoantibody Epitope Specificities in LGI1-Autoantibody Syndromes

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Background and Aims
CXCL13 triggers B-cell homing to germinal-centres (GCs). Plasma CXCL13 levels are a marker of GC activity[1], and CSF CXCL13 levels are elevated in MS[2], NMDA-R-antibody encephalitis[3,4], and NMO[5]. Our objectives were to examine CXCL13 concentrations in LGI1-antibody patients, and the concept of GC-reactions in these patients[6]. Additionally, we explored patient serum binding patterns to two LGI1 domains: LRR and EPTP[7].

Methods
End-titrations against full-length LGI1, LRR and EPTP were quantified by live-CBA for 100 sera from 38 LGI1-antibody patients. Serum CXCL13 levels were determined by ELISA in 86 samples from 19 LGI1-antibody patients and HCs (n=20), and evaluated with Mann-Whitney and Spearman's correlation.

Results
98% sera bound both EPTP and LRR, with tight correlation in end-titres (r 0.9257;p<0.0001****) which did not change over disease course. LGI1-antibody patients showed higher serum levels of CXCL13 compared to HCs (p<0.0001). CXCL13 trends over time showed markedly high levels at onset and sharp rises during relapses.

Conclusions
LGI1-antibody patients showed high CXCL13 levels with dynamic longitudinal fluctuations. Autoantibodies with reactivity to both EPTP- and LRR-LGI1 domains were detected in equal proportions throughout disease, indicating their ongoing production. Overall, these findings suggest that sustained, ongoing GC-reactions may act as a dominant mechanism of autoantibody production in LGI1-antibody syndromes.

References

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