

Epitope Characteristics of MOG Antibodies in MOG antibody-associated disease

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INTRODUCTION

To explore the epitope recognition profile of immunoglobulin G (IgG) antibodies targeting myelin oligodendrocyte glycoprotein (MOG) in MOG antibody-associated disease (MOGAD), a condition in which MOG IgG seropositivity is a key diagnostic marker,¹ we aimed to identify specific MOG epitopes recognized by circulating antibodies in MOGAD patients. Understanding these epitope recognition patterns is crucial for unraveling the underlying pathophysiology of MOGAD and may contribute to the development of more precise diagnostic and therapeutic strategies.

METHODS

MOG mutants (Rat MOG, N31D, H103A/S104E, P42S, P42S/H103A/S104E, R9G/H10Y, and R86Q) with species-specific and glycosylation variations were expressed in HEK293T cells. Conformational epitopes were screened using fixed and live cell-based assays

(CBA), with a tenfold reduction in titer compared to hMOG indicating epitope specificity. Linear epitopes were mapped using 17 overlapping 15-mer peptides spanning the full-length MOG protein, including point mutations, via immunoblotting. The flowchart of this study is attached at the end of the abstract (Figure 1).

RESULTS

Linear epitope detection on 40 samples was negative, as patient sera did not bind to the peptides. Of 126 samples tested by fixed-CBA, 74 failed to bind with fixed-hMOG, precluding further analysis. Among the 52 readable samples, discrepancies were observed between Fixed-CBA and live-CBA for conformational epitopes (Figure 2). Live-CBA analysis of 191 samples revealed the highest recognition at the H103/S104 and P42 epitope, with frequencies of 78 (40.84%) and 46 (24.08%), respectively. Twenty-five samples (13.01%) exhibited no epitope recognition. Age stratification showed that H103/S104 and P42 remained the dominant epitopes,

with younger patients showing increased recognition of N31 and R86. Recognition rates for N31 were 8.95% and 14.04% in patients > 18 and ≤ 18 years, respectively, and for R86, 13.43% and 15.79%. Among those > 11 and ≤ 11 years, N31 recognition was 8.33% and 20.00%, and R86 recognition was 12.82% and 20.00%, respectively (Figure 3).

Figure 1. Flowchart of the study design.

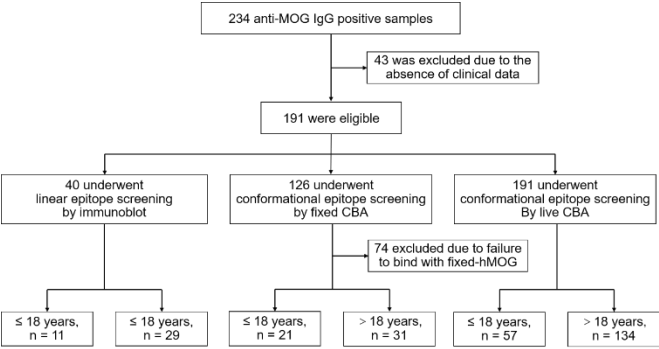


Figure 2. Comparison of epitope recognition frequency between Fixed-CBA and live-CBA.

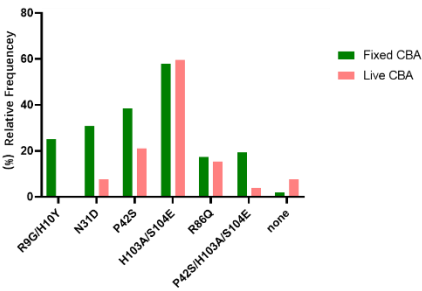
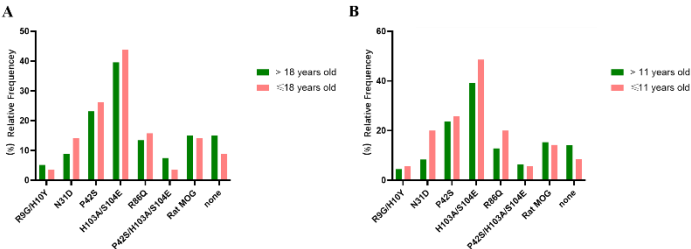


Figure 3. Comparative analysis of epitope recognition frequency across age stratifications.



Our study demonstrates that MOG antibodies primarily target conformational epitopes, with H103/S104 and P42 as key binding sites. Age-dependent differences were noted, with younger patients showing enhanced recognition of epitopes such as N31 and R86. These findings suggest that epitope specificity may vary with age, potentially influencing the clinical presentation of MOGAD. Ongoing studies will further investigate the relationship between antibody epitope specificity and clinical phenotypic variability, with the aim of improving diagnostic and prognostic capabilities in MOGAD.

LITERATURE

1. Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. Lancet Neurol. 2023 Mar;22(3):268-282. doi: 10.1016/S1474-4422(22)00431-8. Epub 2023 Jan 24.

DISCUSSION