Exploring the utility of myelin oligodendrocyte glycoprotein antibody epitopes in predicting a relapsing disease course

Ganesha Liyanage[1,2], Fiona Tea[1], Joseph A. Lopez[1,3], Alicia Zou[1,3], Vera Merheb[1], Fiona X. Z. Lee[1], Aleha Pillay[1], Nicholas Segran[1], Sudarshini Ramanathan[1], Russell C. Dale[1], Fabienne Brilot[1,2,3] and the Australasian and New Zealand MOG Study Group

[1] Brain Autoimmunity Group, Kids Neuroscience Centre, Kids Research at the Children's Hospital at Westmead, Sydney, Australia
[2] School of Medical Sciences, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia
[3] Specialty of Child and Adolescent Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia

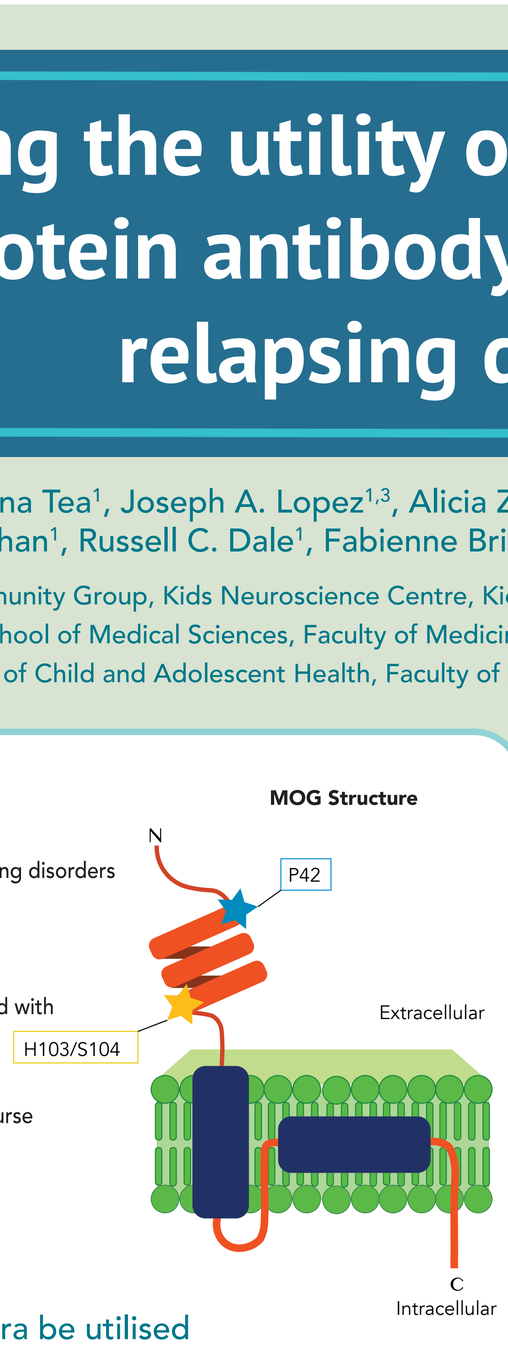
Background

Autoantibodies against myelin oligodendrocyte glycoprotein (MOG) have been used to define a novel class of CNS demyelinating disorders

The two key MOG antibody epitopes are Proline42 (P42) and Histadine103/Serine104 (H103/S104)

Approximately 50% of adult patients relapse, and this is associated with a greater level of disability compared to patients with a monophasic disease course

Currently, there is no method of predicting a relapsing disease course

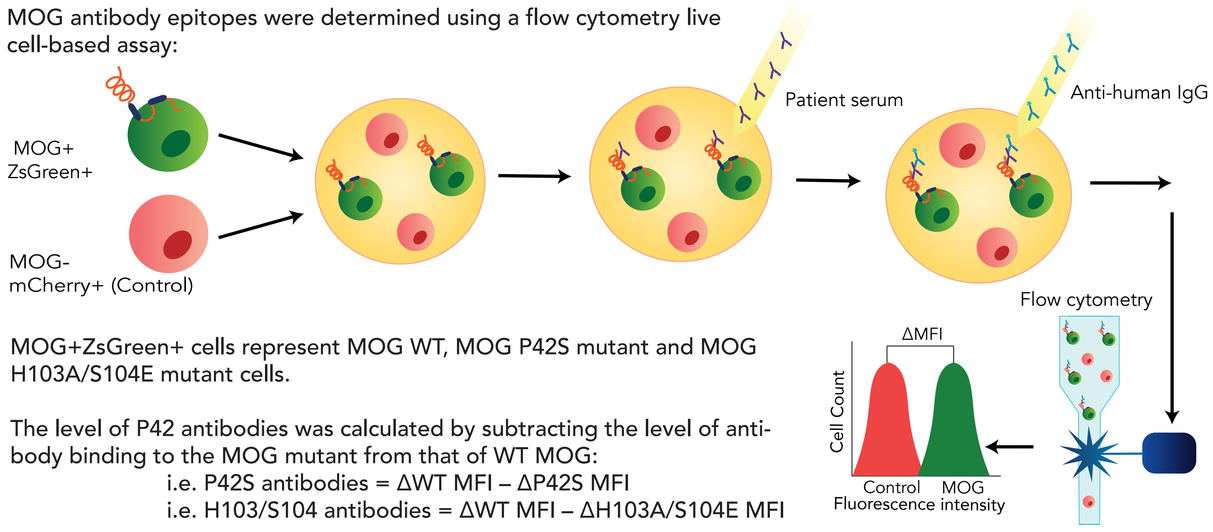


Research question

Can MOG antibody epitopes of patient sera be utilised to predict a relapsing disease course in MOG antibody-associated demyelinating disorders?

Methods

MOG antibody epitopes were determined using a flow cytometry live cell-based assay:



MOG+ZsGreen+ cells represent MOG WT, MOG P42S mutant and MOG H103A/S104E mutant cells.

The level of P42 antibodies was calculated by subtracting the level of antibody binding to the MOG mutant from that of WT MOG:
i.e. P42S antibodies = ΔWT MFI – ΔP42S MFI
i.e. H103/S104 antibodies = ΔWT MFI – ΔH103A/S104E MFI

The thresholds for P42 binders and H103/S104 binders was calculated by adding 3 SDs to the mean of 24 healthy controls.

Results

The most commonly recognised MOG antibody epitope was P42 followed by H103/S104

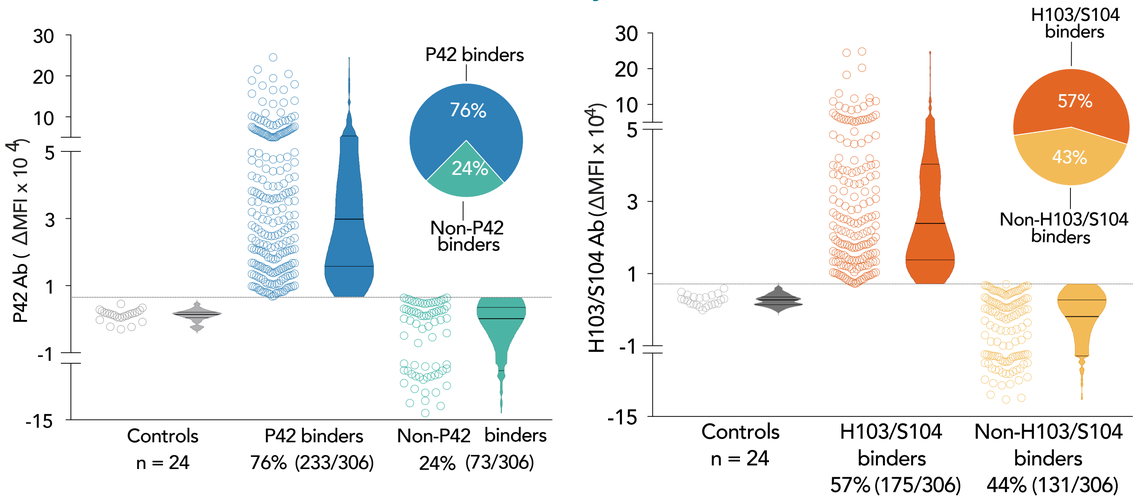
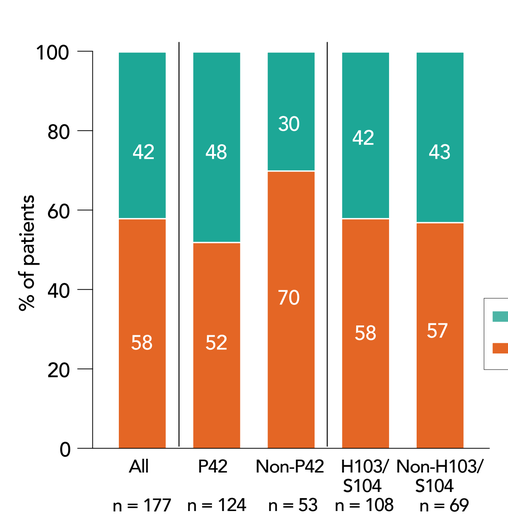


Figure 1. The P42 epitope was recognised by the majority of patients, followed by the H103/S104 MOG epitope. Sera from 306 MOG antibody positive patients were incubated with MOG WT and MOG P42 mutant cells (left), and with MOG H103/S104 mutant cells (right). The flow cytometry live cell-based assay was then performed. The dotted line represents the epitope threshold (mean of 24 controls + 3 SDs). 76% of the cohort recognised the P42 epitope and 57% of patients recognised the H103/S104 epitope.

Overall, a non-P42 epitope was associated with a relapsing course
This was enriched in patients with a non-P42 and non-H103/S104 epitope



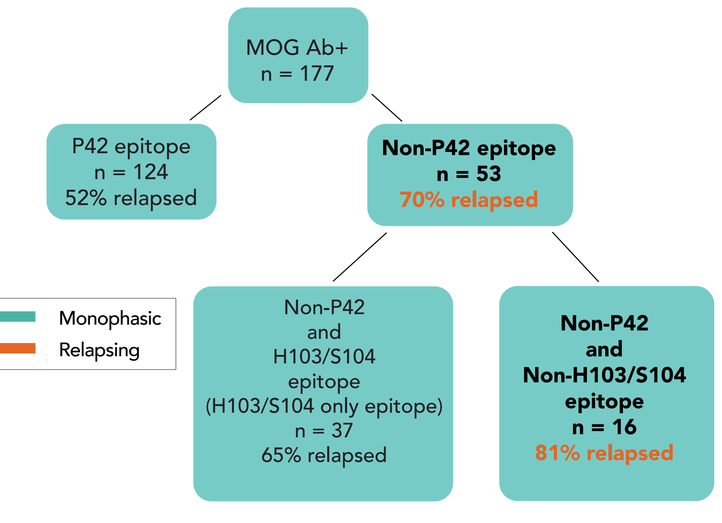


Figure 2. Associations between MOG antibody epitopes and a relapsing disease course across the cohort. 70% of patients with a non-P42 epitope relapsed (left). This was enhanced in patients with a non-P42 and non-H103/S104 epitope, where 81% of patients relapsed (right).

Among patients with unilateral optic neuritis (UON), 94% of patients with a non-P42 epitope exhibited a relapsing course

There was no association between an epitope and a relapsing course in patients with bilateral optic neuritis (BON)

A non-H103/S104 epitope may help predict a relapsing course for patients with transverse myelitis (TM)

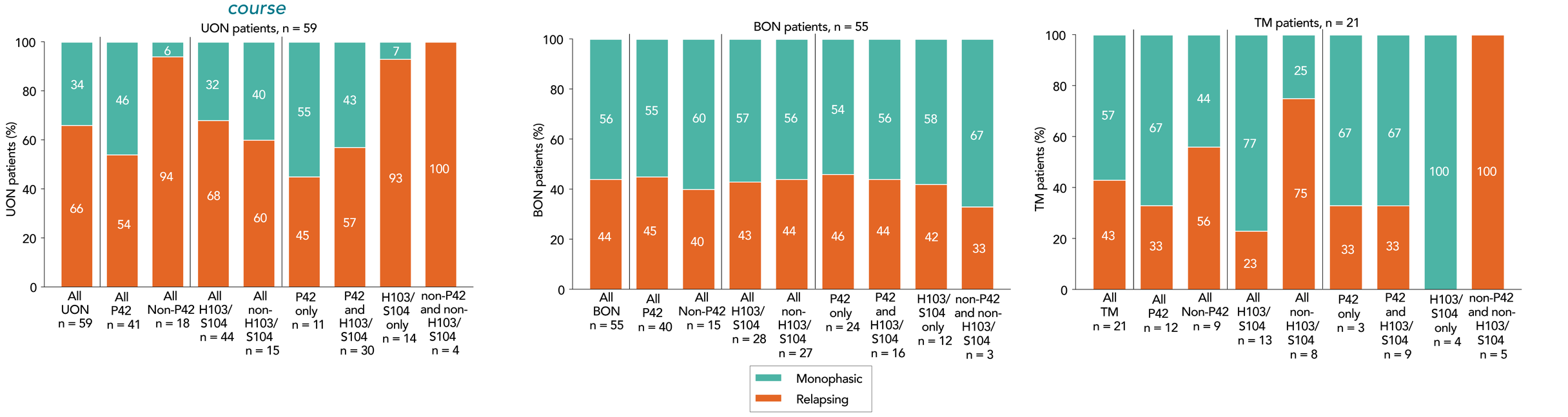


Figure 3. Associations between MOG antibody epitopes and a relapsing disease course within phenotypes. Non-P42 epitope patients with unilateral optic neuritis (UON) were more likely to exhibit a relapsing disease course, while those with bilateral optic neuritis (BON) did not show an increased likelihood of relapse in any of the epitope groups. Patients with transverse myelitis (TM) were more likely to exhibit a relapsing course in the non-H103/S104 epitope group, and this was enhanced for those with a non-P42 and non-H103/S104 epitope.

Conclusions

Overall, there is an association between a non-P42 MOG antibody epitope and a relapsing disease course

Within phenotypes, a non-P42 epitope is strongly associated with a relapsing course in patients with UON, but not BON

Preliminary evidence suggests that for patients with TM, a non-H103/S104 epitope may be associated with a relapsing course

This supports the prognostic utility of MOG antibody epitopes in predicting a relapsing disease course, which will enable clinicians to identify susceptible patients and modify treatment to prevent a relapse.

Acknowledgements

Kids Neuroscience Team at Kids Research

Westmead Research Hub Flow Cytometry Facility

All the patients and clinicians

Australian Research Training Program

Contact details:

Ganesha Liyanage

2nd Year PhD Student

Email: ganesha.liyanage@sydney.edu.au