

## Introduction

### Background

Interleukin (IL)-22, a T-helper (Th)-17 linked cytokine, has been associated with several autoimmune diseases. However, the role of IL-22 in multiple sclerosis (MS) has still be elucidated<sup>1</sup>.

While IL-22 is believed to aid in lymphocyte infiltration<sup>2</sup> of the CNS and elevated levels were observed in serum and lesion of MS patients, studies have highlighted potentially protective functions<sup>3</sup> within MS and experimental autoimmune encephalomyelitis (EAE) – an animal model of MS.

### Aim

This study aims to characterise the expression of IL-22 and its receptor subunit IL-22R1 in normal and EAE CNS tissue, and examine any potential correlation between expression level and disease severity.

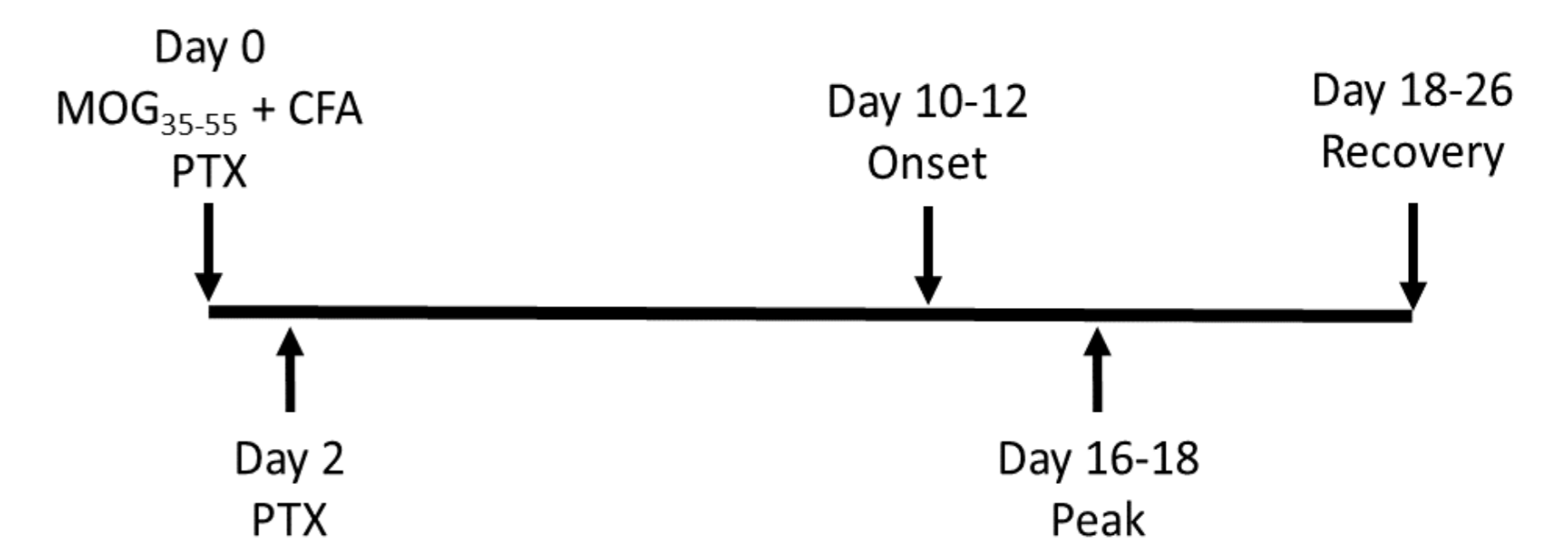
## Methods

### EAE Induction

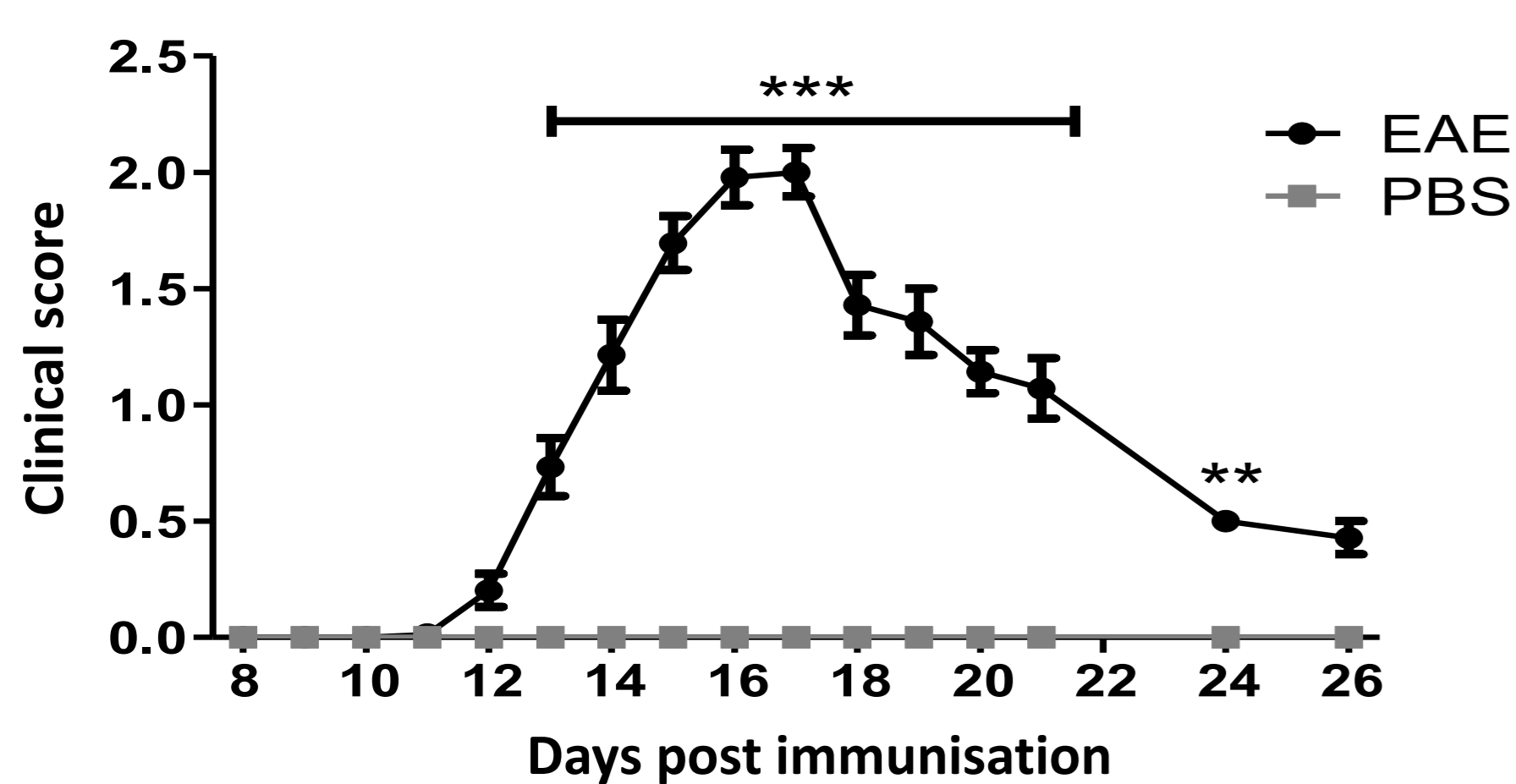
- C57BL/6 female mice were immunised subcutaneously with MOG<sub>35-55</sub> peptide or vehicle emulsified in complete Freund's adjuvant.
- Mice were weighed daily and scored based on tail/leg paralysis.

### Immunohistochemistry

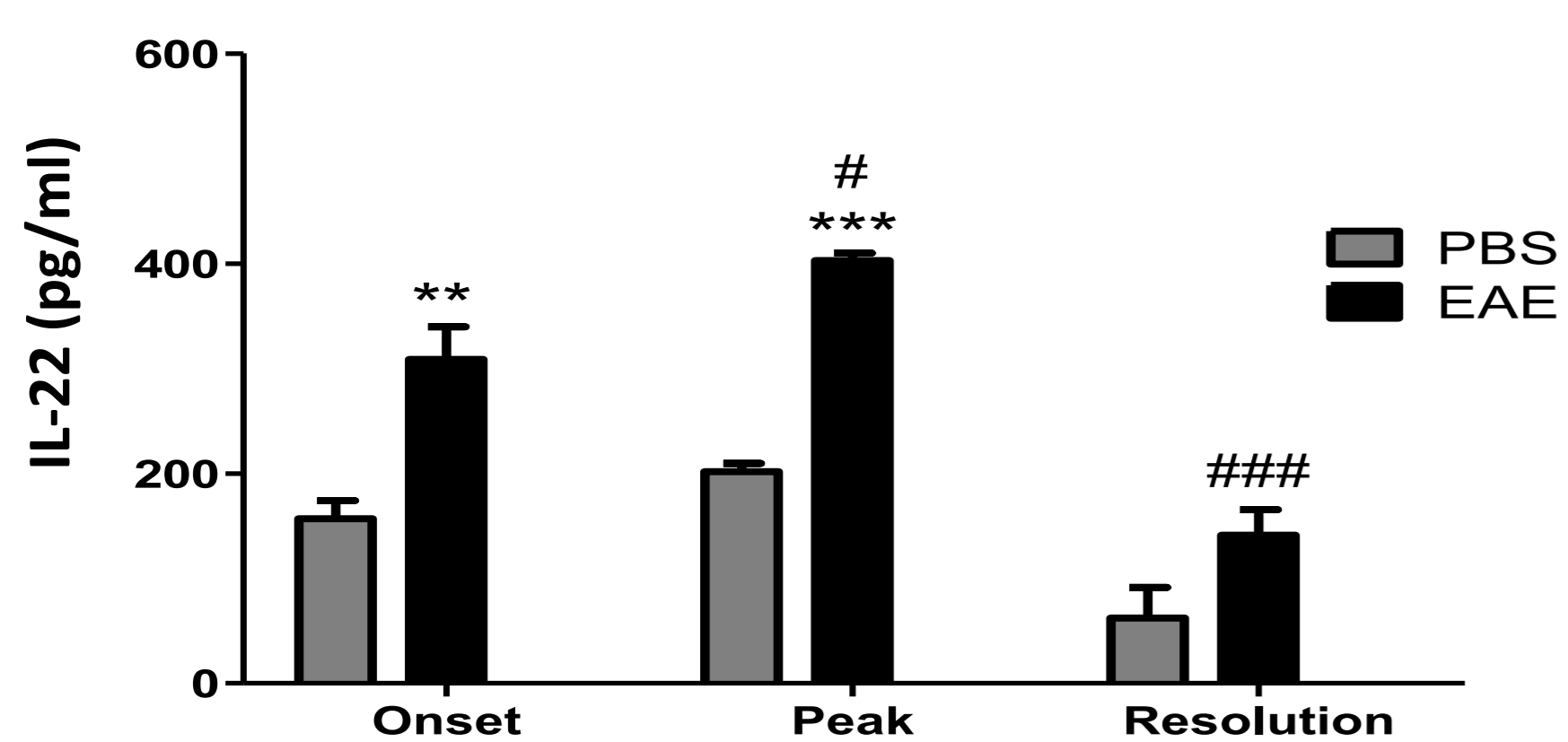
- Immunohistochemistry was used to determine IL-22 (Abcam; ab18499) and IL-22R1 (R&D; MAB42941) expression and co-localisation with CNS resident cells and infiltrating immune cells.



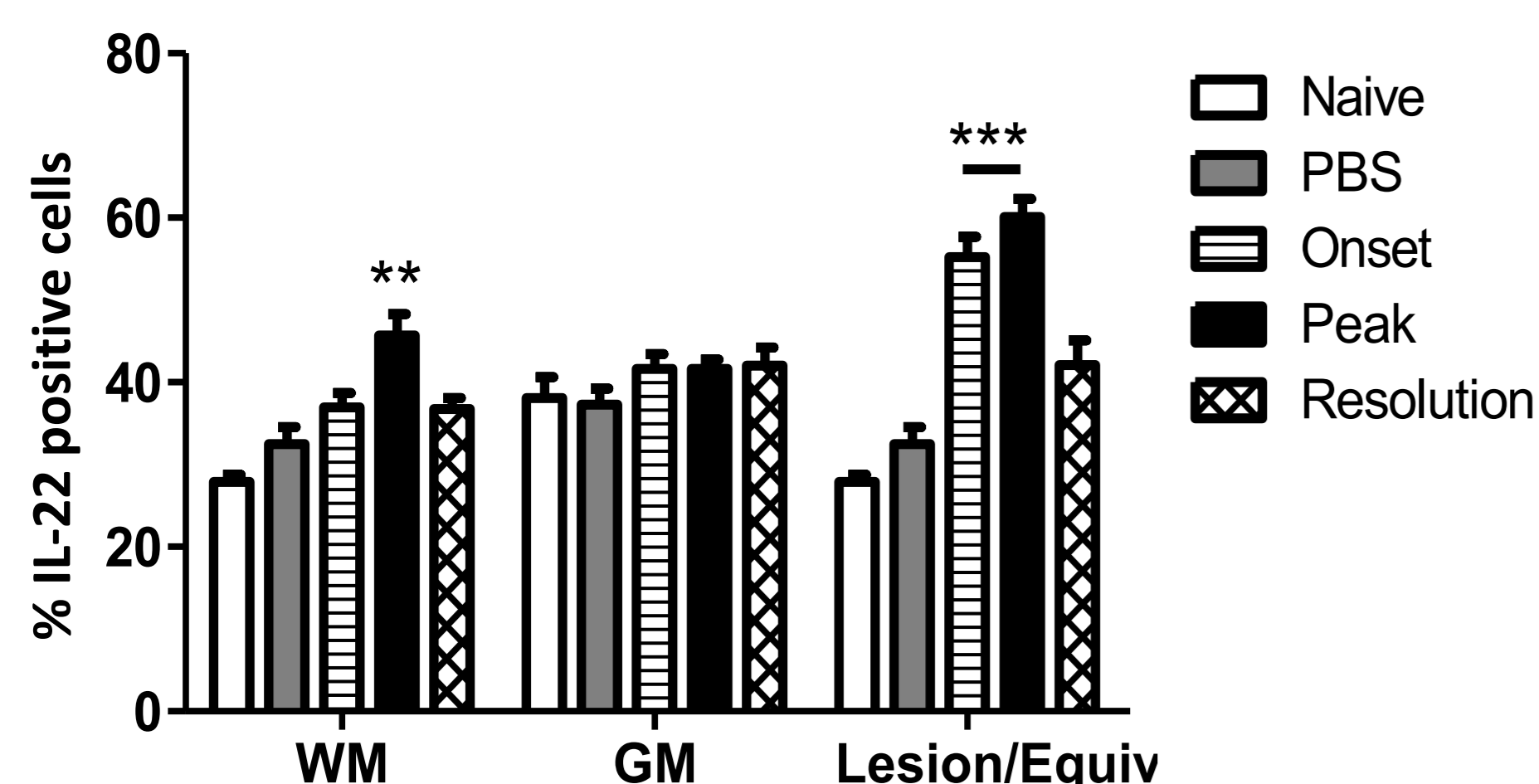
## Results



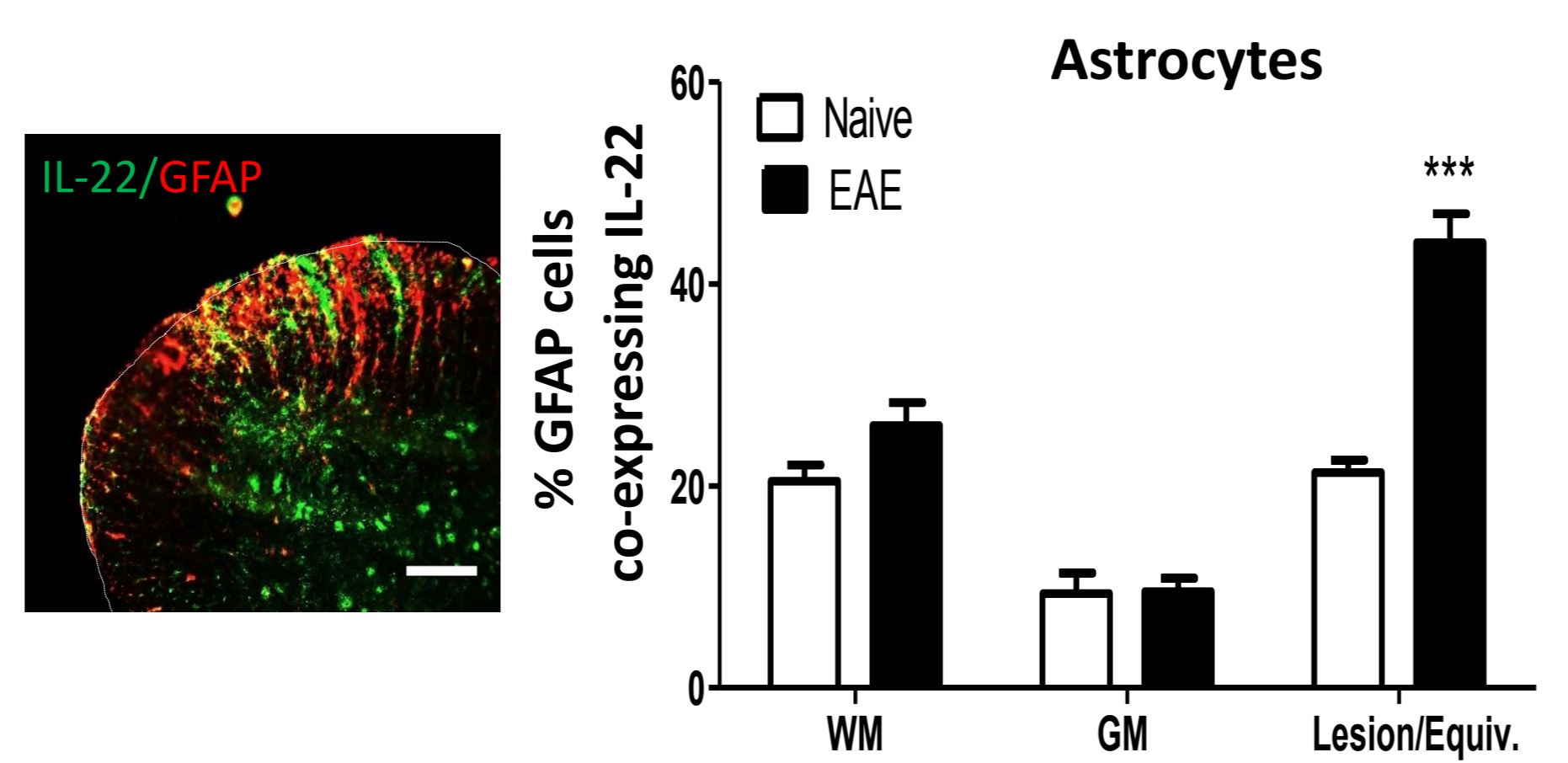
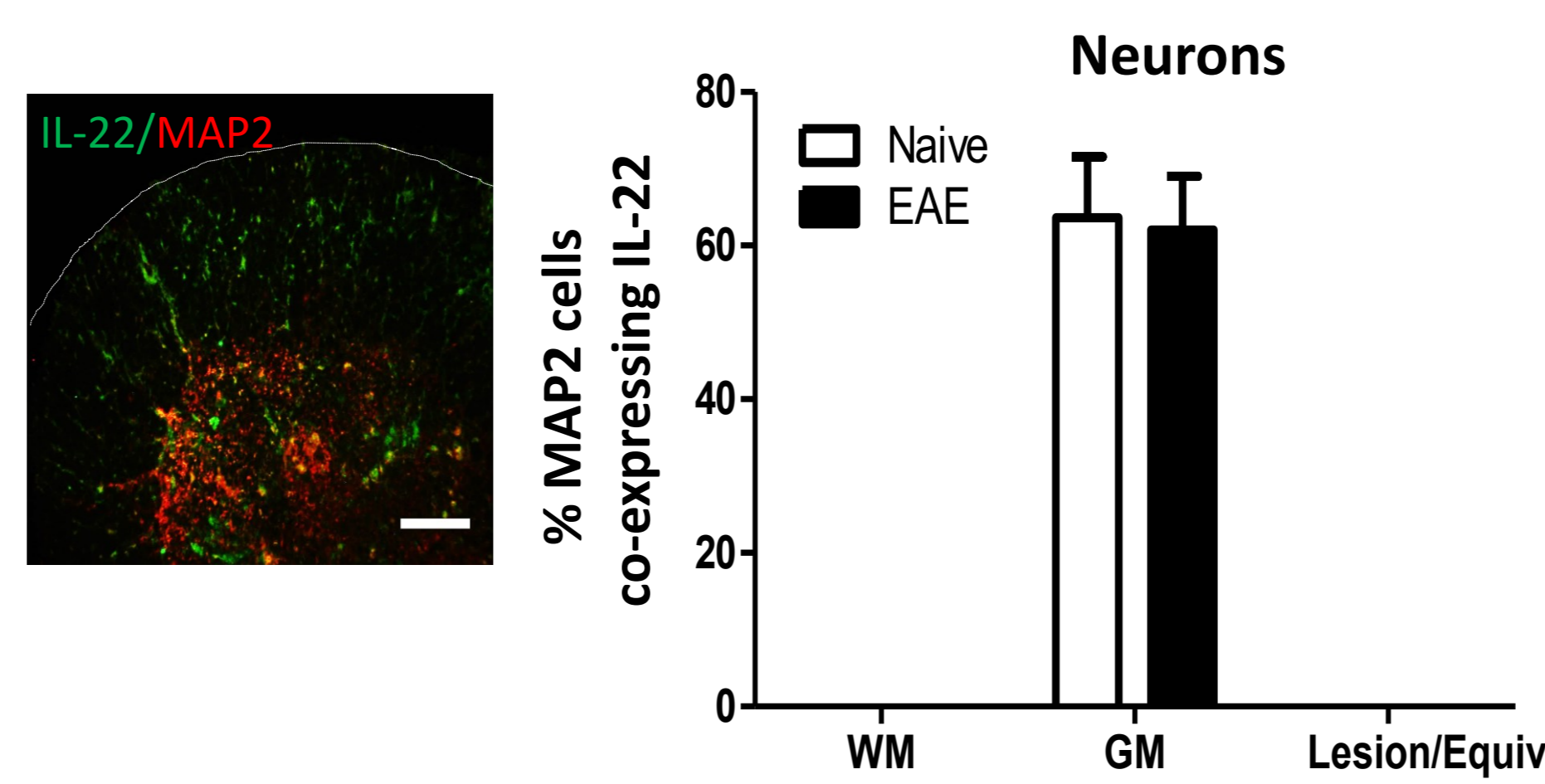
**Figure 1** MOG induced EAE follows a monophasic disease course: Following immunisation, mice were scored daily. Clinical scores expressed as an average  $\pm$  S.E.M. EAE, n=6-39; PBS, n=6-23. \*\*P<0.005, \*\*\*P<0.001 versus PBS



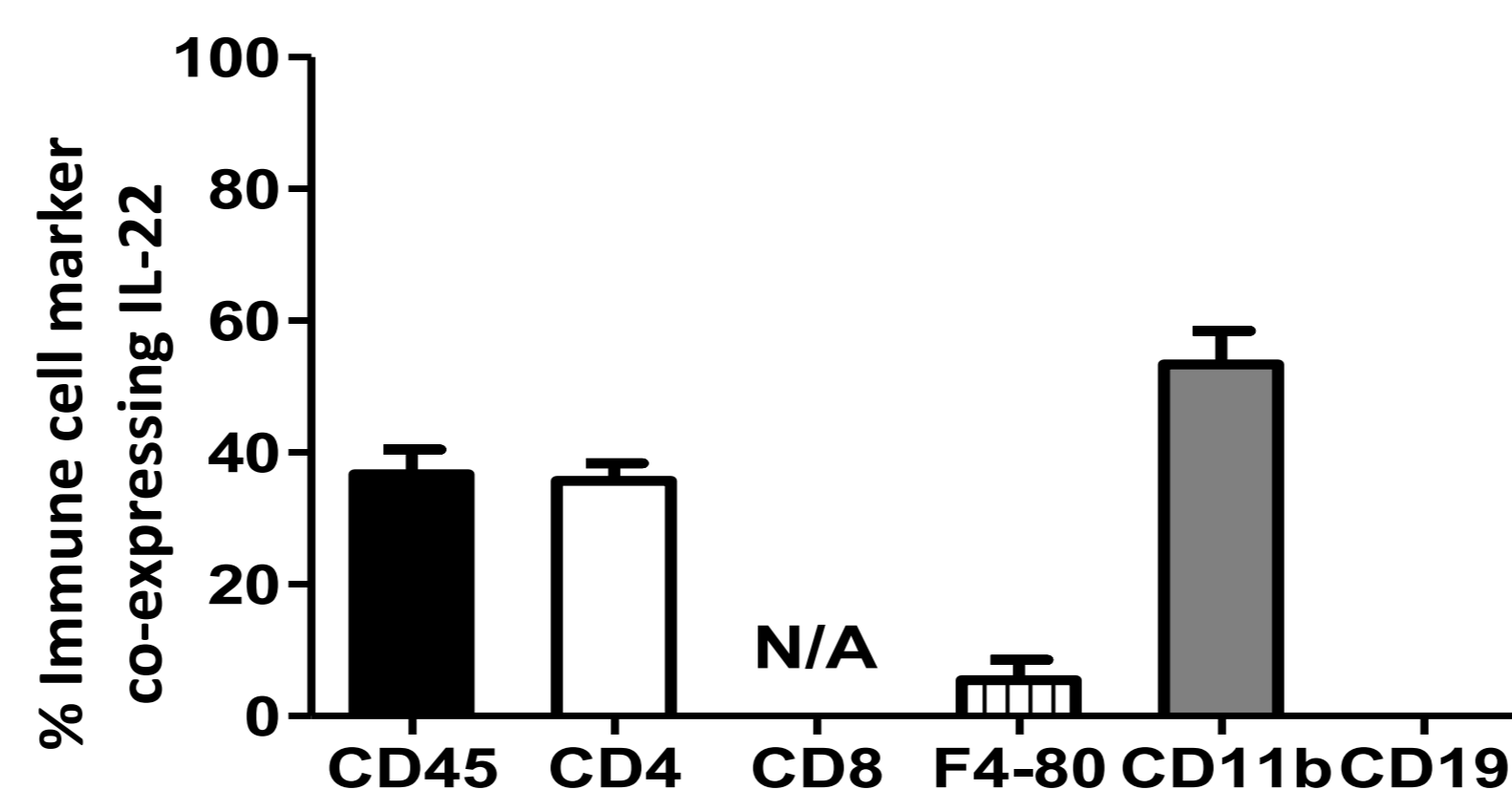
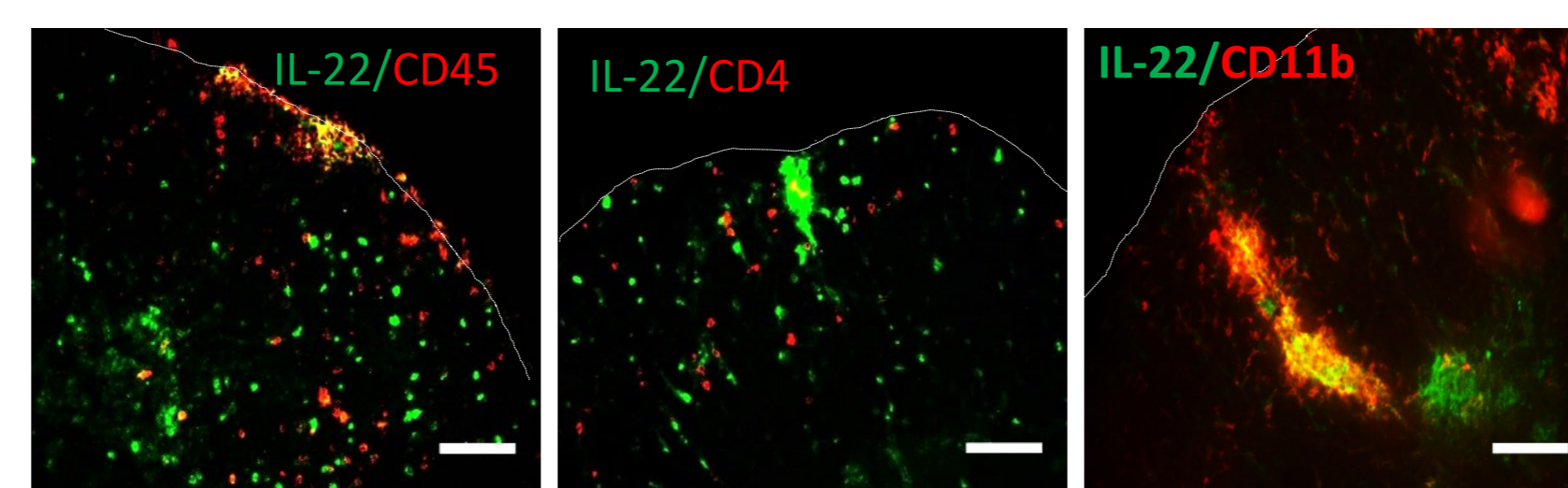
**Figure 2** Serum expression of IL-22 correlates with EAE disease progression: Serum expression of IL-22 was determined by ELISA. EAE, n=6; PBS, n=5. \*\*P<0.01, \*\*\*P<0.001 versus PBS, #P<0.05 versus EAE onset, ###P<0.001 versus EAE peak.



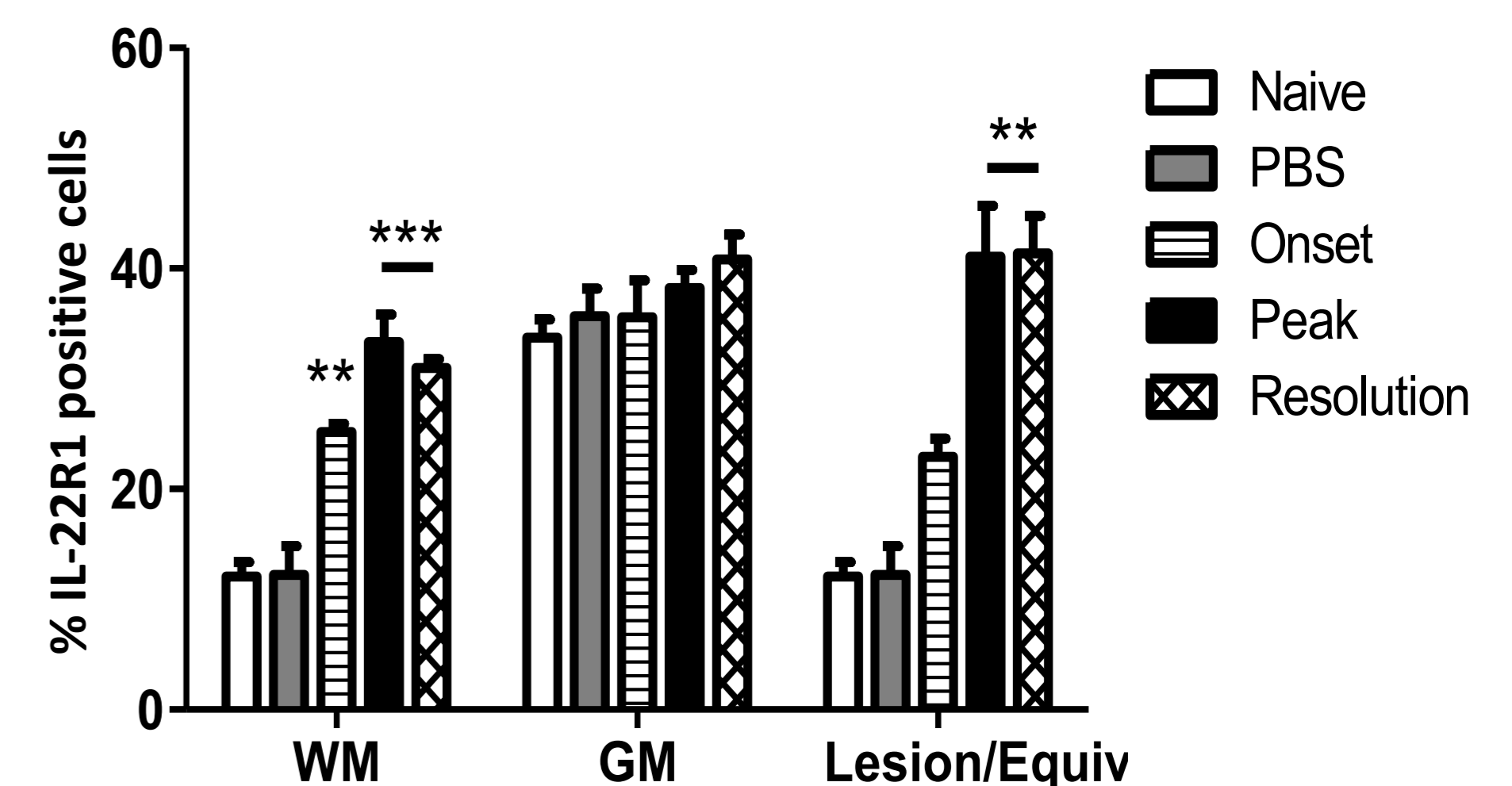
**Figure 3** IL-22 expression in spinal correlates with EAE disease progression: Spinal cord sections were stained for expression of IL-22. Expression quantified using ImageJ. n=6 for all groups. \*\*P<0.01, \*\*\*P<0.001 versus PBS control.



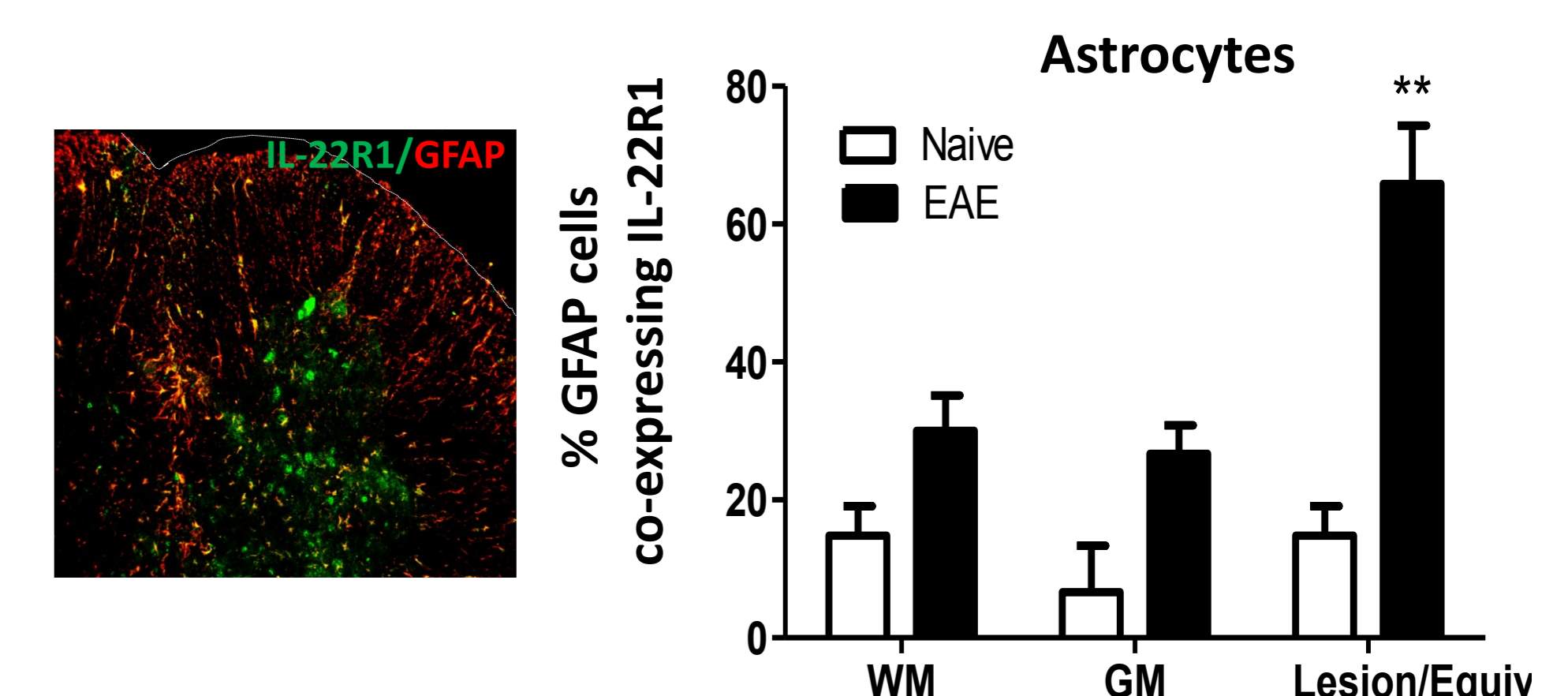
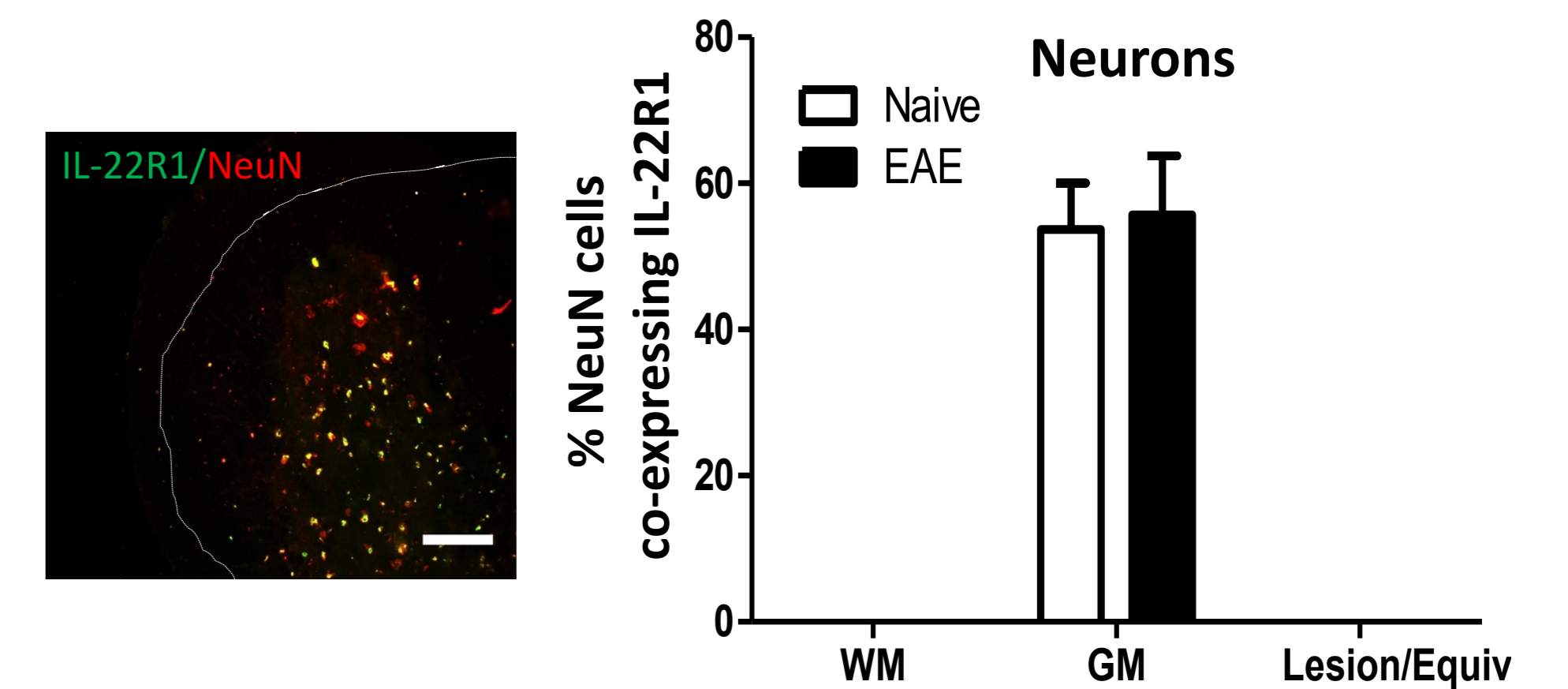
**Figure 4** IL-22 co-localises with neurons and astrocytes: Double fluorescence staining was used to determine co-localisation of IL-22 with neurons and astrocytes. Expression quantified using ImageJ. n=6 for all groups. Scale bar= 100  $\mu$ m. \*\*\*P <0.001 versus naive.



**Figure 5** IL-22 co-localises with several immune cells. Double fluorescence staining was used to determine co-localisation of IL-22 with various infiltrating immune cells. All sections used were peak EAE. Expression quantified using ImageJ. n=5 for each group. Scale bar= 50 $\mu$ m.



**Figure 6** IL-22R1 expression in spinal cord is elevated during EAE within white matter and lesion areas: Spinal cord sections were stained for expression of IL-22R1. Expression quantified using ImageJ. n=6 for all groups. \*P<0.05, \*\*P<0.01, \*\*\*P<0.001 versus PBS control.



**Figure 7** IL-22R1 co-localises with neurons and astrocytes: Double fluorescence staining was used to determine co-localisation of IL-22R1 with neurons and astrocytes. Expression quantified using ImageJ. n=3 for all groups. Scale bar= 100  $\mu$ m.

### Reference

- Dudakov *et al.*, 2015. *Annu Rev Immunol.* 33: 747-85
- Keber *et al.*, 2007. *Nature Med.* 13: 1173-75
- Perriard *et al.*, 2015. *J. Neuroinflamm.* 12: 119 - 26

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### Contact Details

If you have any further questions Please email me at [chelsey.wilson@strath.ac.uk](mailto:chelsey.wilson@strath.ac.uk)

## Conclusion

Our data shows that:

- Serum IL-22 elevated during EAE in a similar manner to MS patients during active disease.<sup>3</sup>
- IL-22 and IL-22R1 expression elevated in EAE spinal cord tissue, particularly within proximity of inflammatory lesions.
- Neurons express comparable levels of IL-22 and IL-22R1 in naïve and EAE mice however astrocytic expression of both is elevated during EAE specifically within the inflammatory lesions.
- Our data suggests IL-22 plays an important role in the development and progression of CNS inflammation however whether this function is mediated through astrocytes or other means has still to be determined.