Expression of IL-22 and in the CNS of experimental autoimmune encephalomyelitis mice

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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[1].

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

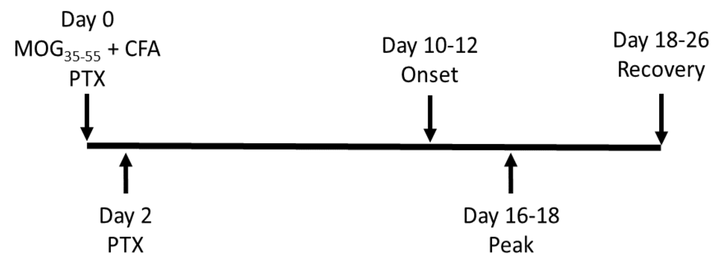
Aim

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_{35-55} 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

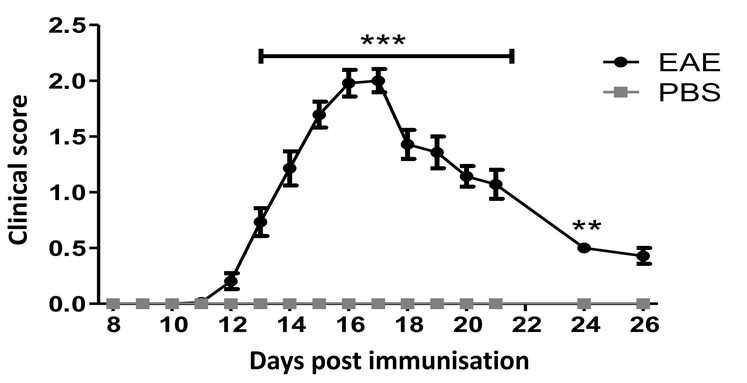


Figure 1 MOG induced EAE follows a monophasic disease course: Following immunisation, mice were scored daily. Clinical scores expressed as an average ± S.E.M. EAE, n=6-39; PBS, n=6-23. **P<0.005, ***P<0.001 versus PBS

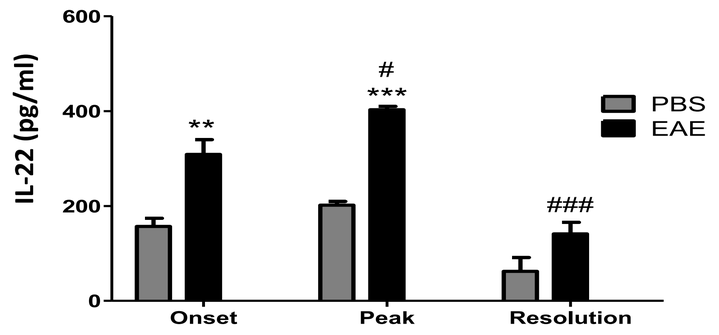


Figure 2 Serum expression of IL-22 correlates with EAE disease progression: Serum expression of IL-22 was determined by ELISA. EAE, n=6; PBS, n=5. **P<0.01, ***P<0.001 versus PBS, #P<0.05 versus EAE onset, ###P<0.001 versus EAE peak.

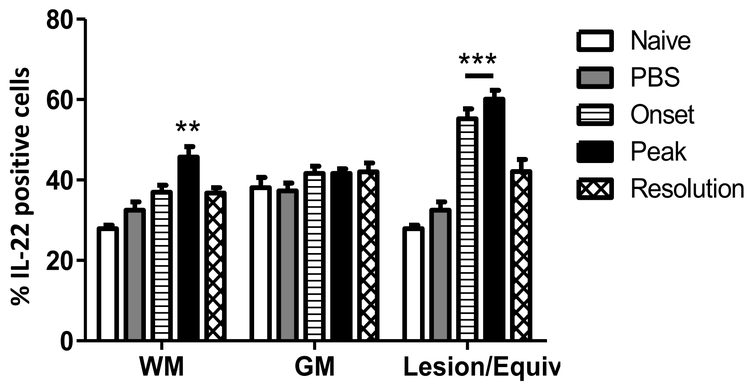
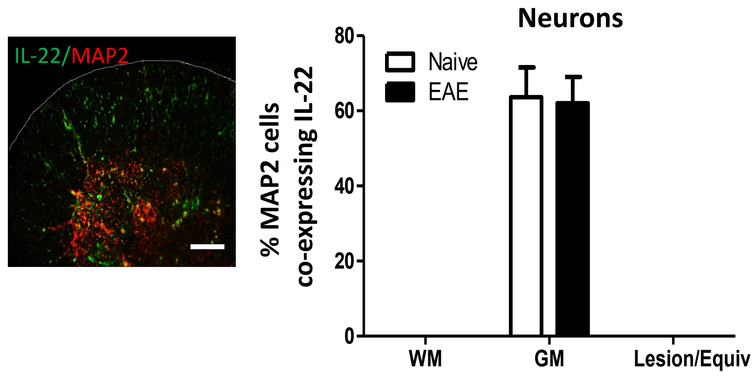


Figure 3 IL-22 expression in spinal correlates with EAE disease progression: Spinal cord sections were stained for expression of IL-22. Expression quantified using ImageJ. n=6 for all groups. **P<0.01, ***P<0.001 versus PBS control.



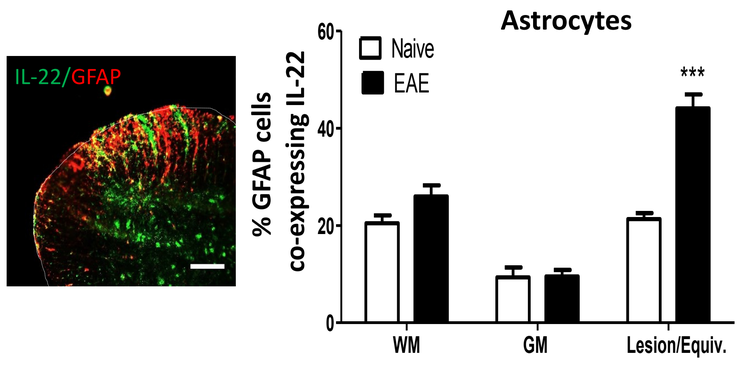


Figure 4 IL-22 co-localises with neurons and astrocytes: Double fluorescence staining was used to determine co-localisation of IL-22 with neurons and astrocytes. Expression quantified using ImageJ. n=6 for all groups. Scale bar= 100 µm. ***P <0.001 versus naïve.

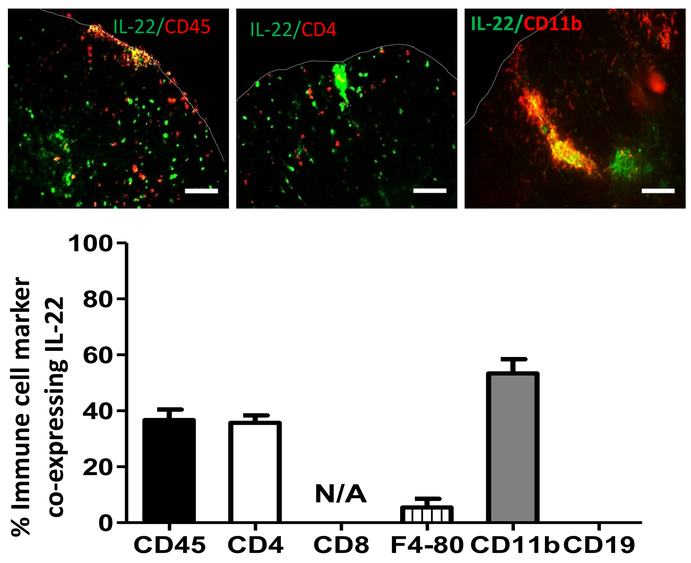


Figure 5 IL-22 co-localises with several immune cells. Double fluorescence staining was used to determine co-localisation of IL-22 with various infiltrating immune cells. All sections used were peak EAE. Expression quantified using ImageJ. n=5 for each group. Scale bar= 50µm.

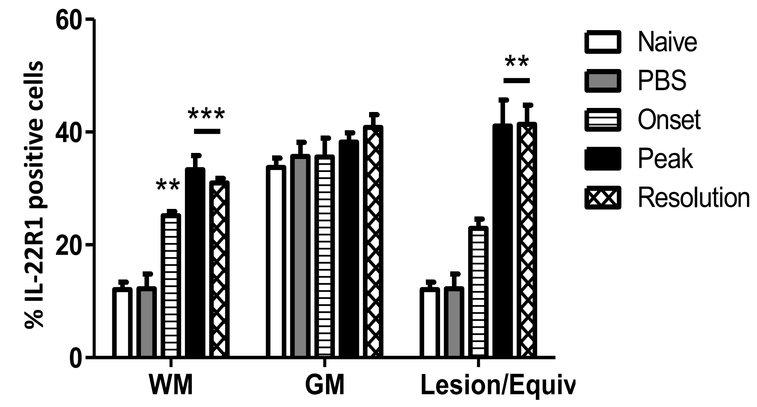


Figure 6 IL-22R1 expression in spinal cord is elevated during EAE within white matter and lesion areas: Spinal cord sections were stained for expression of IL-22R1. Expression quantified using ImageJ. n=6 for all groups. *P<0.05, **P<0.01, ***P<0.001 versus PBS control.

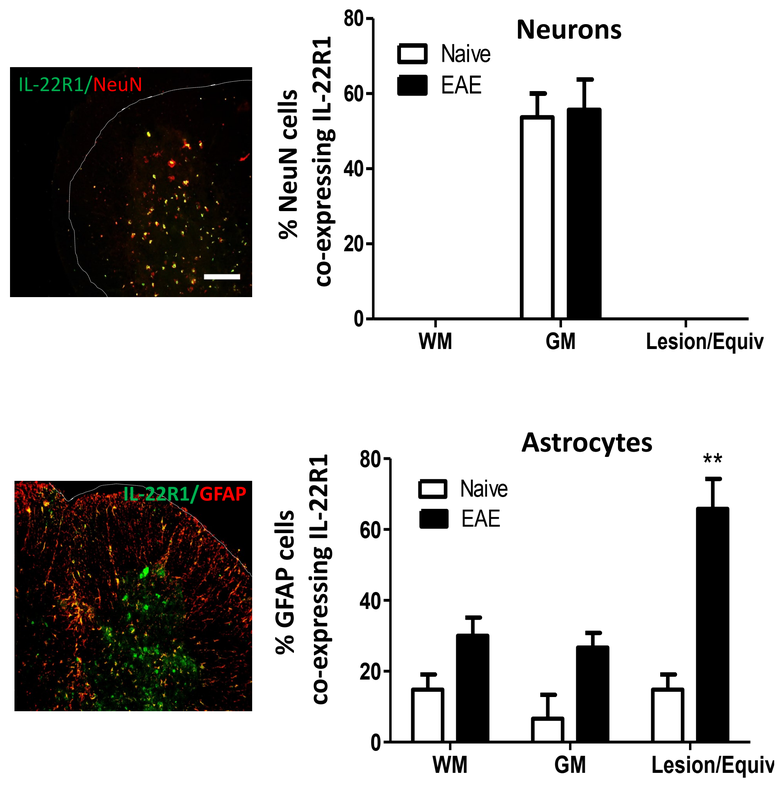


Figure 7 IL-22R1 co-localises with neurons and astrocytes: Double fluorescence staining was used to determine co-localisation of IL-22R1 with neurons and astrocytes. Expression quantified using ImageJ. n=3 for all groups. Scale bar= 100 µm.

Reference
(1) Dudakov *et al.*, 2015. *Annu Rev Immunol*. **33**: 747-85
(2)Kebir *et al.*, 2007. *Nature Med*. **13**: 1173-75
(3) Perriard *et al.*, 2015. *J. Neuroinflamm*. **12**: 119 - 26

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Conclusion

Our data shows that:

- Serum IL-22 elevated during EAE in a similar manner to MS patients during active disease.[3]
- 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.**