

CLAIMS

1. ~~Use of an anti-IFNAR antibody in the manufacture of a medicament for treating a type I IFN mediated disease~~SLE in a subject, wherein a therapeutically effective amount of the anti-IFNAR antibody is to be administered to the subject, wherein the patient ~~is identified as having~~has an elevated interferon protein signature (IFNPS) characterised by elevated protein expression of EPHB2, BLC, LAG-3 and IP-10 in the serum compared to a subject not having ~~the type I IFN mediated disease~~SLE, -

2. ~~1. The use of claim 1, wherein the anti-IFNAR antibody is anifrolumab and or a functional derivative thereof.~~

3. ~~2. The use of claim 2, comprising administration of 300 mg anifrolumab, optionally wherein the method comprises intravenous administration of 300 mg anifrolumab every 4 weeks.~~

4. ~~3. The use of any preceding claim, wherein the treatment supresses the IFNPS.~~

5. ~~The use of any preceding claim, wherein the type I IFN mediated disease is SLE.~~

6. ~~4. The use of claim 15, wherein the treatment results in an improvement of the subject's SLE Disease Activity Index (SLEDAI).~~

7. ~~5. The use of claim 15 or 6, wherein the treatment results in an improvement of the subject's Cutaneous Lupus Erthematosus Disease Area and Severity Index (CLASI) activity score.~~

8. ~~The use of any of claims 1 to 4, wherein the IFN mediated disease is myositis.~~

9. ~~6. The use of any preceding claim, wherein the subject is identified as not having an elevated IFNGS signature compared to a subject not having the type I IFN mediated disease~~SLE.

10. ~~7. The use of any preceding claim, wherein the treatment decreases the elevated IFNPS signature.~~

11. ~~A pharmaceutical composition for use in the treatment of a type I interferon mediated disease in a subject, wherein the pharmaceutical composition comprises a therapeutically effective amount of an anti-IFNAR antibody and wherein the subject is identified as having an elevated IFN protein signature characterised by elevated EPHB2, BLC, LAG-3 and IP-10 protein expression.~~

12. ~~The pharmaceutical composition for the use of claim 11, wherein the anti-IFNAR antibody is anifrolumab.~~

13. The pharmaceutical composition for the use of claim 11, wherein the pharmaceutical composition comprises 300 mg anifrolumab.

14. The pharmaceutical composition for the use of claim 13, wherein the use comprises administration of 300 mg of anifrolumab every four weeks.

15. The pharmaceutical composition for the use of claims 11 to 14, wherein the treatment suppresses the IFNPS.

16. The pharmaceutical composition for the use of any of claims 11 to 15, wherein the type I IFN mediated disease is SLE.

17. The pharmaceutical composition for the use of claim 15, wherein the treatment results in an improvement of the subject's SLE Disease Activity Index (SLEDAI).

18. The pharmaceutical composition of the use of claims 16 or 17, wherein the treatment results in an improvement of the subject's Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score.

19. The pharmaceutical composition for the use of claim 10, wherein the IFN mediated disease is myositis.

20. The pharmaceutical composition for the use of any of claims 11-19, wherein the subject is identified as not having an elevated IFNGS signature compared to a subject not having the type I IFN mediated disease.

21.8. _____ An *in vitro* method for detecting elevated IFN activity in a sample isolated from a subject, the *in vitro* method comprising quantifying EPHB2, BLC, LAG-3 and IP-10 protein expression in the sample and comparing the protein expression in the sample with EPHB2, BLC, LAG-3 and IP-10 protein expression in a sample from a healthy donor.

22. A method of identifying a subject suitable for treatment of a type I interferon-mediated disease or disorder with a therapeutic agent that modulates type I interferon activity, said method comprising detecting an increased level of a first protein in a sample of the subject and an increased level of a second protein in a sample of the subject,

wherein the first protein is EPHB2,

wherein the second protein has a gene expression inducible by type I interferon and displays a Pearson correlation coefficient greater than 0.3 versus a type I interferon gene signature, and

wherein the increased level of the first protein and the increased level of the second protein is relative to:

- a) the level of the first protein and the level of the second protein, respectively, in a sample from a tissue or person not having the type I interferon-mediated disease or disorder, or
- b) the level of one or more control proteins in a sample of the subject.

23. An anti-type I interferon antibody or an anti-type I interferon receptor antibody that modulates type I interferon activity for use in the treatment of a type I interferon-mediated disease or disorder in a subject, wherein the subject has been identified by detecting an increased level of a first protein in a sample of the subject and an increased level of a second protein in a sample of the subject,

wherein the first protein is EPHB2,

wherein the second protein has a gene expression inducible by type I interferon and displays a Pearson correlation coefficient greater than 0.3 versus a type I interferon gene signature, and

wherein the increased level of the first protein and the increased level of the second protein is relative to:

- a) the level of the first protein and the level of the second protein, respectively, in a sample from a tissue or person not having the type I interferon-mediated disease or disorder, or
- b) the level of one or more control proteins in a sample of the subject.

24. Use of an anti-type I interferon antibody or an anti-type I interferon receptor antibody that modulates type I interferon activity in the manufacture of a medicament for treating a type I interferon-mediated disease or disorder in a subject, wherein the anti-type I interferon antibody or an anti-type I interferon receptor antibody is to be administered to the subject, wherein the subject has been identified by detecting an increased level of a first protein in a sample of the subject and an increased level of a second protein in a sample of the subject,

wherein the first protein is EPHB2,

wherein the second protein has a gene expression inducible by type I interferon and displays a Pearson correlation coefficient greater than 0.3 versus a type I interferon gene signature, and

wherein the increased level of the first protein and the increased level of the second protein is relative to:

- a) ~~the level of the first protein and the level of the second protein, respectively, in a sample from a tissue or person not having the type I interferon-mediated disease or disorder, or~~
- b) ~~the level of one or more control proteins in a sample of the subject.~~
- 5 25. ~~The method of claim 22, the use of claim 24, or the antibody for use according to claim 23, further comprising detecting an increased level of at least one other protein in a sample of the subject, wherein the at least one other protein has a gene expression inducible by type I interferon and displays a Pearson correlation coefficient greater than 0.3 versus a type I interferon gene signature; and wherein the increased level of the at least one other protein is~~
- 10 ~~relative to:~~
- a) ~~the level of the at least one other protein in a sample from a tissue or person not having the type I interferon-mediated disease or disorder, or~~
- b) ~~the level of one or more control proteins in a sample of the subject.~~
- 15 26. ~~A method of monitoring or prognosing a type I interferon-mediated disease or disorder progression in a subject comprising:~~
- i) ~~identifying a first protein expression level in an initial sample of the subject and at least one other protein expression level in an initial sample of the subject; and~~
- 20 ~~ii) identifying the first protein expression level in a further sample of the subject and the at least one other protein expression level in a further sample of the subject;~~
- ~~wherein an increase in the expression level of the first protein and an increase in the expression level of the at least one other protein in the further sample relative to the initial sample of the subject prognoses disease progression; or~~
- ~~wherein a decrease in the expression level of first protein and a decrease in the expression level of the at least one other protein in the further sample relative to the initial sample of the subject prognoses disease regression;~~
- 25 ~~wherein the first protein is EPHB2; and~~
- ~~wherein the at least one other protein has a gene expression inducible by type I interferon and displays a Pearson correlation coefficient greater than 0.3 versus a type I interferon gene signature.~~
- 30 27. ~~An anti-IFNAR antibody for use in therapy.~~