

Claims

Claim 1. An *in vitro* method of detecting phosphorylation of a Rubicon protein comprising:

isolating proteins from a sample;

contacting the isolated proteins with an antibody that ~~hybridises~~ binds to a phosphorylated ~~Threonine~~ at 166 of a Rubicon protein to form a complex;

detecting the complex wherein detection of the complex that varies from a predetermined value indicates that the sample comes from a subject having a disease associated with Leucine-rich repeat kinase 2 (LRRK2) comprising Parkinson's disease, or chronic inflammation, or mycobacterial infections, wherein the antibody is capable of binding to SEQ ID NO. 2 at a titer at least 4 times higher than the antibody binds SEQ ID NO. 14.

Claim 2. The *in vitro* method according to claim 1, wherein the disease associated with Leucine-rich repeat kinase 2 (LRRK2) is Parkinson's disease.

Claim 3. The *in vitro* method according to claim ~~3~~ 1 or 2, wherein the antibody is a chimeric humanised antibody or a monoclonal antibody.

~~4. The *in vitro* method according to claim 3, wherein the antibody is a monoclonal antibody.~~

Claim ~~5~~ 4. The *in vitro* method according to any one of the preceding claims, wherein the complex is detected with an enzyme linked immunosorbent assay.

~~6. The *in vitro* method according to any one of the preceding claims, wherein the subject having a disease associated with Leucine-rich repeat kinase 2 (LRRK2) is treated with a compound able to block interaction of LRRK2 with Threonine 166 and/or Serine 189 of the Rubicon protein.~~

~~7. The *in vitro* method according to any one of the preceding statements, wherein the compound comprises a treatment antibody.~~

~~8. The *in vitro* method according to claim 7, wherein the treatment antibody is a chimeric humanised antibody.~~

~~9. The *in vitro* method according to claim 7, wherein the treatment antibody is a monoclonal antibody.~~

~~10. The *in vitro* method according any one of the preceding claims, further comprising removing blocking proteins prior to contacting the isolated proteins with the antibody.~~

~~11. The *in vitro* method according to claim 10, wherein the blocking proteins comprise albumin.~~

~~Claim 125.~~ An antibody which is capable of binding to ~~Rubicon~~-phosphorylated at ~~Threonine 166 and/or phosphorylated at Serine 189~~ of a Rubicon protein wherein the antibody is capable of binding to SEQ ID NO. 2 at a titer at least 4 times higher than the antibody binds SEQ ID NO. 14.

~~Claim 136.~~ The antibody according to claim ~~125~~, comprising at least one variable region incorporating a CDR selected from amino acid sequences i) to vi):

i) LC-CDR1: RSSQSLVHSNGNTYLH (SEQ ID NO. 4);

- ii) LC-CDR2: KLSNRFS (SEQ ID NO. 5);
- iii) LC-CDR3: SQSTHVPLT (SEQ ID NO. 6);
- iv) HC-CDR1: NYGVS (SEQ ID NO. 7);
- v) HC-CDR2: TINSNGGSKYYPDSVKG (SEQ ID NO. 8);
- vi) HC-CDR3: DVWLRRQWYFDV (SEQ ID NO. 9); and

a functional variant with 99% amino acid sequence identity to any one of amino acid sequences i) to vi).

Claim 147. The antibody according to claim ~~125~~, comprising amino acid sequences set forth in SEQ ID NO. 10 and SEQ ID NO. 11 or SEQ ID NO. 12 and SEQ ID NO. 13:

- ~~i) LC-CDR1: RSSQSLVHSNGNTYLH (SEQ ID NO. 4);~~
- ~~ii) LC-CDR2: KLSNRFS (SEQ ID NO. 5);~~
- ~~iii) LC-CDR3: SQSTHVPLT (SEQ ID NO. 6);~~
- ~~iv) HC-CDR1: NYGVS (SEQ ID NO. 7);~~
- ~~v) HC-CDR2: TINSNGGSKYYPDSVKG (SEQ ID NO. 8);~~
- ~~vi) HC-CDR3: DVWLRRQWYFDV (SEQ ID NO. 9); or~~

a functional variant with 99% amino acid sequence identity to any one of amino acid sequences set forth in SEQ ID NO. 10, SEQ ID NO. 11, SEQ ID NOS. 12 and SEQ ID NO. 13i) to vi).

Claim 158. The antibody according to any one of claims ~~12-5~~ to ~~147~~, wherein the antibody is a chimeric humanised antibody or is a monoclonal antibody.

~~16. The antibody according to any one of claims 12 to 14, wherein the antibody is a monoclonal antibody.~~

Claim 179. The antibody according to any one of claims ~~12-5~~ to ~~168~~, for use in the detection or treatment of a disease associated with Leucine-rich repeat kinase 2 (LRRK2) comprising Parkinson's disease, or chronic inflammation, or mycobacterial infections.

Claim 1810. The antibody for use according to claim ~~179~~, wherein the disease associated with Leucine-rich repeat kinase 2 (LRRK2) is Parkinson's disease.

Claim 1911. An inhibitor of Rubicon interaction with Leucine-rich repeat kinase 2 (LRRK2) comprising an ~~compound~~ antibody able to block interaction of LRRK2 with ~~Threonine 166 and/or Serine 189~~ of the Rubicon protein wherein the antibody comprises amino acid sequences set forth in SEQ ID NOS. 4 to 9 or a functional variant with 99% amino acid sequence identity to any one of amino acid sequences set forth in SEQ ID NOS. 4 to 9.

Claim 120. The inhibitor according to claim 1911, wherein the ~~compound~~ antibody comprises ~~an antibody~~.

~~21. The inhibitor according to claim 20, wherein the antibody is a monoclonal antibody or~~

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~~22. The inhibitor according to claim 20, wherein the antibody is a chimeric humanised antibody.~~

Claim 213. The inhibitor according to ~~any one of claims 19-11 to 2212~~, for use in the treatment of a disease ~~associated with Leucine-rich repeat kinase 2 (LRRK2) wherein,~~ the disease -

~~24. The inhibitor for use according to claim 23, wherein the disease associated with Leucine-rich repeat kinase 2 (LRRK2) is Parkinson's disease.~~

Claim 2514. Use of an antibody according to any one of claims ~~11-5 to 15-8~~ or an inhibitor according to ~~any one of claims 19-11 to 2212~~, in the manufacture of a medicament for the treatment of a disease associated with Leucine-rich repeat kinase 2 (LRRK2) comprising Parkinson's disease, or chronic inflammation, or mycobacterial infections.

Claim 2615. Use according to the claim ~~2514~~, wherein the disease associated with Leucine-rich repeat kinase 2 (LRRK2) is Parkinson's disease.

~~27. A method of treating a subject in need having a disease associated with Leucine-rich repeat kinase 2 (LRRK2) comprising:~~

~~administering a compound able to block interaction of LRRK2 with Threonine 166 and/or Serine 189 of the Rubicon protein.~~

~~28. The method according to claim 27, wherein the compound comprises an antibody according to claim 12.~~

~~29. The method according to claim 28, wherein the antibody is a chimeric humanised antibody.~~

~~30. The method according to claim 28, wherein the antibody is a monoclonal antibody.~~

Claim 316. A kit comprising an antibody according to any one of claims ~~12-6 to 169~~, and detection reagents for detecting a disease associated with Leucine-rich repeat kinase 2 (LRRK2) comprising Parkinson's disease, or chronic inflammation, or mycobacterial infections.

Claim 3217. The Kit according to claim ~~3114~~, wherein the disease associated with Leucine-rich repeat kinase 2 (LRRK2) is Parkinson's disease.