

[00026] The antibodies and antigen-binding fragments thereof of the disclosure may be used in a method to treat, diagnose or image synucleinopathies, such as Parkinson's disease ((PD), including idiopathic and inherited forms of Parkinson's disease), Diffuse Lewy Body Disease (DLBD), Lewy body variant of Alzheimer's disease (LBV), Gauchers Disease (GD), Combined Alzheimer's and Parkinson disease (CAPD), pure autonomic failure and multiple system atrophy.

[0026a] In one aspect of the disclosure, there is provided a monoclonal antibody capable of specifically binding to human alpha-synuclein, wherein said antibody binds an epitope within amino acids 112-117 (**SEQ ID NO:9** (ILEDMP)) of human alpha-synuclein (**SEQ ID NO:10**), selected from the groups comprising,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:2**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:33**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:34**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:35**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**, or

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:20**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:21**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:22**;
- 5 (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:23**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:24**;
- and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:25**.

- 10 [0026b] In another aspect of the disclosure, there is provided a pharmaceutical composition comprising the monoclonal antibody as disclosed herein and a pharmaceutical acceptable carrier.

Brief Description of the Drawings

- 15 **[00027]** Fig. 1 shows immunization protocols for generation of hybridomas. The table outlines the differences of the immunogens and mouse strains used for the identification of GM37 and GM285. Different HCo17-Balb/c and HCo12/Balb/c mice were immunized independently (description of these mice are provided below). The hybridoma expressing GM37 was identified from mice immunized with full length alpha-synuclein containing amino acids 1-140 fibrils and boosted with truncated alpha-synuclein fragments 1-60 and 1-119 of full length (FL) alpha-synuclein (**SEQ ID NO**
- 20 **10**). The hybridoma expressing antibody GM285 came from an immunization protocol in which HCo12-Balb/c mice were immunized with full length monomeric alpha-synuclein, amino acids 1-140 followed by a boost with full length fibrillary alpha-synuclein (**Example 1**).

- 25 **[00028]** Fig. 2 (**PANEL A-C**) shows screening of GM37 for binding to alpha synuclein, alpha-synuclein homologs and orthologs.

A) Binding of antibody GM37 to alpha-synuclein using a no wash solution based ELISA (FMAT).

- 30 B) Using SPR (Fortebio) binding of antibody GM37 is specific for alpha-synuclein (Alpha Panel) and does not bind the other related synuclein family proteins, beta-synuclein (Beta Panel) and gamma-synuclein (Gamma Panel). Measurements were performed using SPR (Fortebio Octetred) GM37 shows similar binding to alpha-synuclein from cynomolgus monkey (Cyno Panel) and mouse (Mouse Panel). (**Example 1**).

- 35 C) Using SPR (Fortebio Octetred) binding of antibody GM285 is specific for alpha-synuclein and does not bind the other related synuclein family proteins, beta-synuclein and gamma-synuclein. Measurements were performed using SPR (Fortebio Octetred)

CLAIMS

1. A monoclonal antibody capable of specifically binding to human alpha-synuclein, wherein said antibody binds an epitope within amino acids 112-117 (**SEQ ID NO:9** (ILEDMP)) of human alpha-synuclein (**SEQ ID NO:10**), selected from the groups comprising:

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:2**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:33**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:34**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**,

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;

- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:35**;
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- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**, or

a monoclonal antibody comprising:

- (a) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:20**;
- (b) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:21**;
- (c) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:22**;
- (d) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:23**;
- (e) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:24**; and
- (f) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:25**.

2. The monoclonal antibody according to claim 1, selected from the group comprising:

a monoclonal antibody comprising a heavy chain consisting of a variable domain of **SEQ ID NO:7** and a light chain consisting of a variable domain of **SEQ ID NO:8**,

a monoclonal antibody, comprising a heavy chain consisting of a variable domain of **SEQ ID NO:30** and a light chain consisting of a variable domain of **SEQ ID NO:8**,

a monoclonal antibody, comprising a heavy chain consisting of a variable domain of **SEQ ID NO:31** and a variable domain of **SEQ ID NO:8**,

a monoclonal antibody, comprising a heavy chain consisting of a variable domain of **SEQ ID NO:32** and a variable domain of **SEQ ID NO:8**, and

a monoclonal antibody, comprising a heavy chain consisting of a variable domain of **SEQ ID NO:26** and a variable domain of **SEQ ID NO:27**.

3. A pharmaceutical composition comprising the monoclonal antibody according to any one of the previous claims, and a pharmaceutical acceptable carrier.