

CLAIMS

1. A method for the *in vitro* diagnosis of esophageal cancer in a subject, comprising the steps of:
 - 5 a) contacting said biological sample from said subject with at least one progastrin-binding molecule,
 - b) detecting the binding of said progastrin-binding molecule to progastrin in said sample, wherein said binding indicates the presence of esophageal cancer in said subject.
- 10 2. The method of claim 1, wherein step b) further comprises determining the concentration of progastrin and wherein a concentration of progastrin at least 10 pM in said biological sample is indicative of the presence of esophageal cancer in said subject.
3. The method of claim 2, comprising the further steps of:
 - 15 c) determining a reference concentration of progastrin in a reference sample,
 - d) comparing the concentration of progastrin in said biological sample with said reference concentration of progastrin,
 - e) determining, from the comparison of step d), the presence of esophageal cancer.
- 20 4. The method of any one of claims 1 to 3, wherein said progastrin-binding molecule is an antibody, or an antigen-binding fragment thereof.
5. The method of any of claims 1 to 4, wherein said antibody, or antigen-binding fragment thereof, is selected among N-terminal anti-progastrin monoclonal antibodies and C-terminal anti-progastrin monoclonal antibodies.
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6. The method of any of claims 1 to 5, wherein said antibody binding to progastrin is a monoclonal antibody chosen in the group consisting of:

- 5 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°4, 5 and 6, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°7, 8 and 9, respectively,
- 10 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°10, 11 and 12, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°13, 14 and 15, respectively,
- 15 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively,
- 20 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°22, 23 and 24, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°25, 26 and 27, respectively,
- 25 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°28, 29 and 30,

respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N° 31, 32 and 33, respectively, and

- 5 - A monoclonal antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N° 34, 35 and 36, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N° 37, 38 and 39, respectively.
- 10 7. The method of any one of claims 1 to 6, wherein said biological sample is contacted with a first molecule, which binds to a first part of progastrin, and with a second molecule, which binds to a second part of progastrin.
- 8. The method of any one of claim 1 to 7, wherein biological sample is chosen among: blood, serum and plasma.
- 15 9. The method of any one of claims 1 to 8, wherein said biological sample is plasma, and wherein a concentration of progastrin of at least 10 pM is indicative of the presence of esophageal cancer in said subject.
- 10. A composition for use in the prevention or the treatment of esophageal cancer, wherein said composition comprises a progastrin-binding antibody, or an antigen-binding fragment thereof.
- 20 11. A composition for the use of claim 10, wherein said progastrin-binding antibody, or antigen-binding fragment thereof, is selected among humanized antibodies, single chain antibodies, camelized antibodies, IgA1 antibodies, IgA2 antibodies, IgD antibodies, IgE antibodies, IgG1 antibodies, IgG2 antibodies, IgG3 antibodies, IgG4 antibodies and IgM antibodies.
- 25 12. A composition for the use of any one of claims 10 or 11, wherein said progastrin-binding antibody, or an antigen-binding fragment thereof, is

selected among N-terminal anti-progastrin antibodies and C-terminal anti-progastrin antibodies.

13. A composition for the use of any one of claims 10 to 12, wherein said progastrin-binding molecule, or an antigen-binding fragment thereof, is a neutralizing antibody.

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14. A composition for the use of any one of claims 10 to 13, wherein said progastrin-binding molecule is a humanized antibody chosen among:

- An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°4, 5 and 6, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°7, 8 and 9, respectively,

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- An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°10, 11 and 12, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°13, 14 and 15, respectively,

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- An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°16, 17 and 18, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N°19, 20 and 21, respectively,

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- An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N°22, 23 and 24,

respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N° 25, 26 and 27, respectively,

- 5 - An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N° 28, 29 and 30, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of amino acid sequences SEQ ID N° 31, 32 and 33, respectively, and
 - 10 - An antibody comprising a heavy chain comprising at least one, preferentially at least two, preferentially three, of CDR-H1, CDR-H2 and CDR-H3 of amino acid sequences SEQ ID N° 34, 35 and 36, respectively, and a light chain comprising at least one, preferentially at least two, preferentially three, of CDR-L1, CDR-L2 and CDR-L3 of
 - 15 amino acid sequences SEQ ID N° 37, 38 and 39, respectively.
15. Use of a progesterin-binding antibody, or an antigen-binding fragment thereof, as in any one of claims 10 to 14 for the in vitro diagnosis of esophageal cancer.