Claims

1. A method for diagnosing the risk of cancer recurrence in a mammalian patient, comprising detecting the expression of macroH2A1.1 and/or macroH2A2 in a biological sample obtained from said patient, wherein a low or reduced expression of said macroH2A1.1 and/or macroH2A2 is indicative for an increased risk of cancer recurrence in said patient.

2. The method according to claim 1, wherein said expression is normalized to the expression of macroH2A1.2 in said sample and/or a control sample.

3. The method according to claim 1 or claim 2, wherein a correlation between the expression of macroH2A1.1 or macroH2A2 and the disease-free survival is $P < 0.05$, preferably $P < 0.01$, and more preferably $P < 0.006$.

4. The method according to any of claims 1 to 3, wherein said cancer is selected from the group of solid cancer, lung cancer, breast cancer, kidney cancer, liver cancer, head and neck cancer, prostate cancer, pancreatic cancer, stomach cancer, colon cancer, thyroid cancer, esophageal cancer, and brain cancer.

5. The method according to any of claims 1 to 4, wherein said biological sample is selected from the group of cells from a lung tumor, breast tumor, kidney tumor, liver tumor, head and neck tumor, prostate tumor, pancreatic tumor, stomach tumor, colon tumor, thyroid tumor, esophageal tumor, and brain tumor, whole blood, serum, plasma, urine, lymph fluid, pleural fluid, and brain liquor.

6. The method according to any of claims 1 to 5, further comprising detecting the expression of additional cancer markers, such as Ki-67.

7. The method according to claim 6, wherein said expression of said macroH2A1.1 and/or macroH2A2 in said sample inversely correlates with the expression of Ki-67.

8. The method according to any of claims 1 to 7, further comprising a diagnosis of senescent cells, in particular of cancer cells, in the tumor based on the expression of macroH2A1.1.

9. The method according to any of claims 1 to 5, further comprising a prediction of said cancer recurrence based on said diagnosis.

10. The method according to any of claims 1 to 9, wherein said sample is taken from the patient during surgery.

11. The method according to any of claims 1 to 10, wherein said detecting the expression comprises PCR, in particular rtPCR, immunohistochemical staining, in particular using a macroH2A1.1-specifc or macroH2A2-specifc antibody, and/or mRNA analysis.

12. A method for screening for an agent specific for macroH2A1.1 or macroH2A2, comprising contacting macroH2A1.1 or macroH2A with an agent potentially specific for macroH2A1.1 or macroH2A2, and determining, whether said agent specifically binds to macroH2A1.1 or macroH2A.

13. The method for screening according to claim 12, wherein said agent potentially specific for macroH2A1.1 or macroH2A2 is present in a compound library, a phage display library, in particular an sc-Fv phage display library, or in a library of antibodies.

14. The method for screening according to claim 12 or 13, wherein said agent potentially specific for macroH2A1.1 or macroH2A2 is a diagnostic agent and/or a therapeutic agent.

15. A diagnostic agent and/or therapeutic agent, screened according to the method of any of claims 12 to 14.

16. A method for producing a macroH2A1.1 or macroH2A2 specific antibody or macroH2A1.1 or macroH2A2 specific fragment thereof, comprising a step of
a) affinity purification of a serum or cell culture supernatant containing antibodies using macroH2A1.1 or macroH2A2 domains coupled to a chromatography column, or
b) screening an sc-Fv phage display library using macroH2A1.1 or macroH2A2 domains.

17. A macroH2A1.1 or macroH2A2 specific antibody, or macroH2A1.1 or macroH2A2 specific fragment thereof, produced according to the method according to claim 16.

18. The macroH2A1.1 or macroH2A2 specific antibody according to claim 17, which is selected from a monoclonal, polyclonal, human, humanized, and/or recombinant antibody, optionally comprising a label.

19. A diagnostic kit, comprising a diagnostic agent according to claim 15, and/or a macroH2A1.1 or macroH2A2 specific antibody, or macroH2A1.1 or macroH2A2 specific fragment thereof according to claim 17 or 18, optionally together with additional auxiliary agents for performing a method according to any of claims 1 to 11.

20. A method of treating cancer in a mammalian patient, comprising a method according to any of claims 1 to 11, and treating and/or preventing the recurrence of said cancer in a patient identified as having an increased risk of cancer recurrence in said patient.

21. The method of treating cancer in a mammalian patient according to claim 20, wherein said treatment comprises administration to said patient in need thereof an agent as screened according to the method of any of claims 10 to 12.

22. The method of treating cancer in a mammalian patient according to claim 20 or 21, further comprising monitoring the amount and/or proportion of senescent cells, in particular of cancer cells, in the tumor in response to said treatment, based on the expression of macroH2A1.1.

23. Use of an agent as screened according to the method of any of claims 12 to 14, and/or a macroH2A1.1 or macroH2A2 specific antibody, or macroH2A1.1 or macroH2A2 specific fragment thereof according to claim 16 or 17, or a kit according to claim 19 for the prevention, treatment and/or diagnosis of cancer, in particular for the prevention, treatment and/or diagnosis of cancer recurrence.

24. Use according to claim 23, wherein said cancer is selected from the group of solid cancer, lung cancer, breast cancer, kidney cancer, liver cancer, head and neck cancer, prostate cancer, pancreatic cancer, stomach cancer, colon cancer, thyroid cancer, esophageal cancer, and brain cancer.

CLAIMS

1. A method for diagnosing a proliferative or malignant tumor in a mammalian patient, comprising detecting the expression of macroH2A1.1 in a biological sample, such as, for example, blood, serum or plasma sample, obtained from said patient,
wherein a low or reduced expression of said macroH2A1.1 is indicative of a proliferative or malignant tumor in said patient,
and optionally further comprising normalizing the expression to the expression of macroH2A1.2 in said sample and/or a control sample.

2. A method for diagnosing a slowly proliferating, pre-malignant or benign tumor in a mammalian patient, comprising detecting the expression of macroH2A1.1 and/or macroH2A2 in a biological sample, such as, for example, blood, serum or plasma sample, obtained from said patient,
wherein a high or increased expression of said macroH2A1.1 and/or macroH2A2 is indicative of a slowly proliferating, pre-malignant or benign tumor in said patient,
and optionally further comprising normalizing the expression to the expression of macroH2A1.2 in said sample and/or a control sample.

3. A method for diagnosing senescent cells, including senescent cancer cells, in a mammalian patient, comprising detecting the expression of macroH2A1.1 in a biological sample, such as, for example, blood, serum or plasma sample, obtained from said patient,
wherein a high or increased expression of said macroH2A1.1 is indicative of senescent cells in said patient,
and optionally further comprising normalizing the expression to the expression of macroH2A1.2 in said sample and/or a control sample.

4. A method for diagnosing the risk of cancer recurrence in a mammalian patient, comprising detecting the expression of macroH2A1.1 in a biological sample, such as, for example, blood, serum or plasma sample, obtained from said patient,
wherein a low or reduced expression of said macroH2A1.1 is indicative for a patient at risk,
and optionally further comprising normalizing the expression to the expression of macroH2A1.2 in said sample and/or a control sample.

5. The method according to any of claims 1 to 4, wherein said cancer is selected from the group of solid cancer, lung cancer, breast cancer, kidney cancer, liver cancer, head and neck cancer, prostate cancer, pancreatic cancer, stomach cancer, colon cancer, thyroid cancer, esophageal cancer, and brain cancer, in particular breast or lung cancer.

6. The method according to any of claims 1 to 5, further comprising detecting the expression of additional cancer markers, such as Ki-67, wherein preferably said expression of said macroH2A1.1 and/or macro H2A2 in said sample inversely correlates with the expression of Ki-67.

7. The method according to any of claims 1 to 6, further comprising a diagnosis of senescent cells in cancer cells in the tumor, based on the expression of macroH2A1.1.

8. The method according to any of claims 1 to 7, wherein said detecting of the expression comprises PCR, in particular rtPCR, immuno-histochemical staining, in particular using a macroH2A1.1 specifc antibody, and/or mRNA analysis.

9. Use of a diagnostic kit, comprising a macroH2A1.1 or macroH2A2 specific antibody, or macroH2A1.1 or macroH2A2 specific fragment thereof together with additional auxiliary agents in the diagnosis of cancer, in particular of cancer recurrence, or the prevention and/or treatment of cancer, in particular of cancer recurrence.

10. Use according to claim 9, wherein said cancer is selected from the group of solid cancer, lung cancer, head and neck cancer, prostate cancer, pancreatic cancer, bone or lung cancer, stomach cancer, colon cancer, thyroid cancer, esophageal cancer, and brain cancer, preferably breast or lung cancer.