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(54) Titre : ANTICORPS MONOCLONAUX ANTI-CLAUDINE 1 POUR LA PREVENTION ET LE TRAITEMENT DU  
CARCINOME HEPATOCELLULAIRE  
 (54) Title: ANTI-CLAUDIN 1 MONOCLONAL ANTIBODIES FOR THE PREVENTION AND TREATMENT OF  
HEPATOCELLULAR CARCINOMA

(57) **Abrégé/Abstract:**

Use of anti-Claudin 1 monoclonal antibodies and pharmaceutical compositions thereof, for the prevention and/or treatment of hepatocellular carcinoma in patients suffering from liver disease, in particular liver disease that is not associated with HCV infection or in patients who have been cured from HCV infection. Methods of preventing and/or treating hepatocellular carcinoma by administration of such a monoclonal antibody, or a pharmaceutical composition thereof, are also described. Experimental results with the hepatocarcinoma cell line HuH-7.5.1 are given.

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(54) Title: ANTI-CLAUDIN 1 MONOCLONAL ANTIBODIES FOR THE PREVENTION AND TREATMENT OF HEPATOCELLULAR CARCINOMA

(57) Abstract: Use of anti-Claudin 1 monoclonal antibodies and pharmaceutical compositions thereof, for the prevention and/or treatment of hepatocellular carcinoma in patients suffering from liver disease, in particular liver disease that is not associated with HCV infection or in patients who have been cured from HCV infection. Methods of preventing and/or treating hepatocellular carcinoma by administration of such a monoclonal antibody, or a pharmaceutical composition thereof, are also described. Experimental results with the hepatocarcinoma cell line HuH-7.5.1 are given.



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## Claims

What is claimed is:

1. An anti-Claudin 1 antibody, or a biologically active fragment thereof, for use in the prevention or treatment of a non-HCV-associated hepatocellular carcinoma in a subject.
2. The anti-Claudin-1 antibody, or the biologically active fragment thereof, for use in the prevention of a non-HCV-associated hepatocellular carcinoma in a subject.
3. The anti-Claudin 1 antibody, or the biologically active fragment thereof, for the use according to claim 1 or claim 2, wherein the subject has never been infected with HCV or has been cured from HCV infection.
4. The anti-Claudin 1 antibody, or the biologically active fragment thereof, for the use according to any one of claims 1 to 3, wherein the non-HCV-associated hepatocellular carcinoma is associated with hepatitis B virus (HVB) infection, alcoholism, non-alcoholic fatty liver disease (NAFLD), hereditary hemochromatosis, alpha 1 antitrypsin deficiency, porphyria cutanea tarda, Wilson's disease, tyrosinemia, glycogen storage diseases, autoimmune hepatitis, primary biliary cirrhosis, or exposure to aflatoxins, or wherein the non-HCV-associated hepatocellular carcinoma is of unknown origin.
5. The anti-Claudin 1 antibody, or the biologically active fragment thereof, for the use according any one of claims 1 to 4, wherein the anti-Claudin 1 antibody is a monoclonal antibody.
6. The anti-Claudin 1 antibody, or the biologically active fragment thereof, for the use according to any one of claims 1 to 5, wherein the anti-Claudin 1 antibody is a monoclonal antibody secreted by a hybridoma cell line deposited at the DSMZ on July 29, 2008 under an Accession Number selected from the group consisting of DSM ACC2931, DSM ACC2932, DSM ACC2933, DSM ACC2934, DSM ACC2935, DSM ACC2936, DSM ACC2937, and DSM ACC2938.

7. The anti-Claudin 1 antibody or the biologically active fragment thereof, for the use according to any one of claims 1 to 6, wherein the anti-Claudin 1 antibody comprises the six complementary determining regions (CDRs) of a monoclonal antibody secreted by a hybridoma cell line deposited at the DSMZ on July 29, 2008 under an Accession Number selected from the group consisting of DSM ACC2931, DSM ACC2932, DSM ACC2933, DSM ACC2934, DSM ACC2935, DSM ACC2936, DSM ACC2937, and DSM ACC2938.
8. The anti-Claudin 1 antibody or the biologically active fragment thereof, for the use according to any one of claims 1 to 7, wherein the antibody is humanized, de-immunized or chimeric.
9. The anti-Claudin 1 antibody or the biologically active fragment thereof, for the use according to any one of claims 1 to 8, wherein the biologically active fragment interferes with liver cell signalling and reverses a patient-derived HCC risk signature.
10. A pharmaceutical composition comprising an effective amount of an anti-Claudin 1 antibody, or a biologically active fragment thereof, and at least one pharmaceutically acceptable carrier or excipient, for use in the prevention or treatment of a non-HCV-associated hepatocellular carcinoma in a subject.
11. A pharmaceutical composition comprising an effective amount of an anti-Claudin 1 antibody, or a biologically active fragment thereof, and at least one pharmaceutically acceptable carrier or excipient, for use in the prevention of a non-HCV-associated hepatocellular carcinoma in a subject.
12. The pharmaceutical composition for the use according to claim 10 or claim 11, wherein the subject has never been infected with HCV or has been cured from HCV infection.
13. The pharmaceutical composition for the use according to any one of claims 10 to 12, wherein the non-HCV-associated hepatocellular carcinoma is associated with Hepatitis B virus infection, alcoholism, non-alcoholic fatty liver disease (NAFLD), hereditary hemochromatosis, alpha 1 antitrypsin deficiency, porphyria cutanea tarda, Wilson's disease, tyrosinemia, glycogen

storage diseases, autoimmune hepatitis, primary biliary cirrhosis, or exposure to aflatoxins, or wherein the non-HCV-associated hepatocellular carcinoma is of unknown origin.

14. The pharmaceutical composition for the use according to any one of claims 10 to 13, wherein the anti-Claudin 1 monoclonal antibody is as defined in any one of claims 5 to 8.
15. The pharmaceutical composition for the use according to any one of claims 9 to 14 further comprising an additional therapeutic agent.
16. The pharmaceutical composition for the use according to claim 15, wherein the additional therapeutic agent is selected from the group consisting of anti-viral agents, anti-inflammatory agents, immunomodulatory agents, analgesics, antimicrobial agents, kinase inhibitors, molecules interfering with signalling, antibacterial agents, antibiotics, antioxidants, antiseptic agents, anti-cancer agents and combinations thereof.