SUMMARY

The disclosure~~invention~~ provides anti-NRP1 antibodies and methods of using the same. In one embodiment, the disclosure~~invention~~ provides an isolated antibody that binds to neuropilin-1 (NRP1), wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:3, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:4, and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:5. In certain embodiments, the antibody further comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:8; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:9; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:10.

In one aspect, there is provided an isolated antibody that binds to neuropilin-1 (NRP1), wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:3, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:4, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:5, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:8, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:9, and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:10.

Also provided is an isolated antibody that binds to neuropilin-1 (NRP1), wherein the antibody comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:8; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:9; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:10.

In another embodiment, the disclosure~~invention~~ provides an isolated antibody that binds to neuropilin-1 (NRP1), wherein the antibody comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b). In some embodiments, the antibody comprises a VH sequence of SEQ ID NO:2. In certain embodiments, the antibody comprises a VL sequence of SEQ ID NO:7. Also provided is an isolated antibody that binds to neuropilin-1 (NRP1), wherein the antibody comprises a VH sequence of SEQ ID NO:2 and a VL sequence of SEQ ID NO:7.

In certain embodiments, the antibody of the disclosure~~invention~~ is an IgG1 antibody. In some embodiments the antibody is an antibody fragment that binds neuropilin, e.g., an antibody that lacks an Fc portion, an $F(ab')_2$, an Fab, or an Fv structure. In one~~another~~ aspect ~~the invention~~, there is provide~~s~~d an immunoconjugate comprising the antibody as described herein~~any of the antibodies of the invention~~.

In one aspect, there is~~The invention also~~ provide~~s~~d an isolated nucleic acid encoding the antibody as described herein~~any of the anti-NRP1 antibodies of the invention~~. In one embodiment, a vector comprising the nucleic acid is provided. In one embodiment, a host cell comprising the vector or comprising the nucleic acid is provided. In one aspect, there is provided a host cell comprising the nucleic acid as described herein. In one embodiment, the host cell is eukaryotic. In one embodiment, the host cell is a CHO cell. In one embodiment, a method of making an anti-NRP1 antibody is provided, wherein the method comprises culturing the host cell under conditions suitable for expression

of the nucleic acid encoding the antibody so that the antibody produced. In one aspect, there is provided a method of producing an antibody comprising culturing the host cell as described herein so that the antibody is produced. In some embodiments the method further comprises isolating the antibody produced by the methods.

In one aspect, there is provided a method of detecting the presence of NRP1 in a biological sample comprising contacting the biological sample with the antibody as described herein and detecting the presence of the bound antibody.

In one embodiment~~aspect~~, a method of detecting the presence of NRP1 in a biological sample is provided, the method comprising contacting the biological sample with an antibody of the disclosure~~invention~~ under conditions permissive for binding of the antibody to NRP1, and detecting the presence of the bound antibody, e.g., by detecting whether a complex is formed between the antibody and NRP1. In one aspect, there is provided~~Thus, provided herein is~~ an antibody as described herein~~of the invention~~ for use in detecting the presence of NRP1 in a biological sample. In some embodiments, the detection of the presence of NRP1 is by immunohistochemistry.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1A-D show results of immunohistochemistry using monoclonal anti-NRP1 antibody 7130. (1A: HEK-293 cells transfected with full length human NRP1 (positive control); 1B: HEK-293 cells transfected with empty vector (negative control); 1C: tissue section from kidney; 1D: tissue section from placenta).

Figure 2A-C show results of immunohistochemistry using monoclonal anti-NRP1 antibody 7130. (2A: tissue section from colorectal cancer (CRC) patient; 2B: tissue section from breast cancer (BC) patient; 2C: tissue section from non-small cell lung cancer (NSCLC) patient).

DETAILED DESCRIPTION OF EMBODIMENTS OF THE INVENTION

I. DEFINITIONS

An "acceptor human framework" for the purposes herein is a framework comprising the amino acid sequence of a light chain variable domain (VL) framework or a heavy chain variable domain (VH) framework derived from a human immunoglobulin framework or a human consensus framework, as defined below. An acceptor human framework "derived from" a human immunoglobulin framework or a human consensus framework may comprise the same amino acid sequence thereof, or it may contain amino acid sequence changes. In some embodiments, the number of amino acid changes are 10 or less, 9 or less, 8 or less, 7 or less, 6 or less, 5 or less, 4 or less, 3 or less, or 2 or less. In some embodiments, the VL acceptor human framework is identical in sequence to the VL human immunoglobulin framework sequence or human consensus framework sequence.