SUMMARY ~~OF THE INVENTION~~

[0009] The compositions of the disclosure~~invention~~ are a new class of imaging agents that are capable of binding specifically to HER2 or variants thereof.

[0009a] In a first aspect, there is provided an imaging agent composition comprising an isolated polypeptide comprising SEQ. ID. No 2, conjugated with an $Al^{18}F$-NOTA-chelator to form an $Al^{18}F$-NOTA-chelator conjugated polypeptide wherein the isolated $Al^{18}F$-NOTA-chelator conjugated polypeptide binds specifically to HER2 or variants thereof.

[0010] In one or more embodiments, the imaging agent composition comprises an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID. No 2 or a conservative variant thereof, conjugated with a ^{99m}Tc via a diaminedioxime chelator. The diaminedioxime chelator may comprise Pn216, cPn216, Pn44, or derivatives thereof. The isolated polypeptide binds specifically to HER2 or variants thereof.

[0011] In one or more embodiments, the imaging agent composition comprises an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID. No 2 or a conservative variant thereof, conjugated with ^{67}Ga or ^{68}Ga via a NOTA chelator. The isolated polypeptide binds specifically to HER2 or variants thereof.

[0012] In one or more embodiments, the imaging agent composition comprises an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID. No 2 or a conservative variant thereof, conjugated with an $Al^{18}F$-NOTA chelate. The isolated polypeptide binds specifically to HER2 or variants thereof.

[0013] In one or more embodiments, the imaging agent composition comprises an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID. No 2 or a conservative variant thereof, conjugated with ^{18}F via a linker. The linker comprises a group derived from an aminoxy group, an azido group, or an alkyne group. The isolated polypeptide binds specifically to HER2 or variants thereof.

[0014] In one or more embodiments, the imaging agent composition comprises an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID. No 2 or a conservative variant thereof, conjugated with ^{18}F via an isotopic fluorine exchange chemistry. The isolated polypeptide binds specifically to HER2 or variants thereof.

[0015] In one or more embodiments, methods of making an imaging agent composition as described herein are provided. In a second aspect, there is provided a method of making an imaging agent composition as defined herein comprising (i) providing an isolated polypeptide comprising SEQ. ID No. 2; (ii) reacting the polypeptide with a NOTA-chelator to form a NOTA-chelator conjugated polypeptide; and (iii) reacting the NOTa-chelator conjugated polypeptide with an $Al^{18}F$ moiety to form a $Al^{18}F$-NOTA-chelator conjugated polypeptide. An example of a method of the disclosure~~invention~~, for preparing an imaging agent composition, comprises (i) providing an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID No. 2 or a conservative variant thereof; and (ii) reacting a diaminedioxime chelator with the polypeptide to form a chelator conjugated polypeptide. In another example, the method comprises

(i) providing an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID No. 2 or a conservative variant thereof; (ii) reacting the polypeptide with a linker; and (iii) reacting the linker with an ^{18}F moiety to form a ^{18}F conjugated polypeptide. The linker may comprise an aminoxy group, an azido group, or an alkyne group.

[0015a] In a third aspect, there is provided a method of making an imaging agent composition as defined herein comprising (i) providing the isolated polypeptide comprising SEQ. ID No. 2; (ii) reacting the polypeptide with a NOTA-chelator, wherein the NOTA-chelator comprises a NOTA chelate moiety and a linker, to form a NOTA-chelator conjugated polypeptide; and (iii) reacting the NOTA-chelator conjugated polypeptide with an ^{18}F moiety or a source of ^{18}F.

[0016] In another example, the method comprises (i) providing an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID No. 2 or a conservative variant thereof; (ii) reacting the polypeptide with a NOTA- chelator to form, respectively, a NOTA-chelator conjugated polypeptide and (iii) reacting the NOTA- chelator conjugated polypeptide with an $Al^{18}F$ moiety to form, a $Al^{18}F$-NOTA chelator conjugated polypeptide..

[0017] In another example, the method comprises (i) providing an isolated polypeptide comprising SEQ. ID No. 1, SEQ. ID No. 2 or a conservative variant thereof; (ii) reacting the polypeptide with a silicon fluoride (e.g. [^{19}F]-silicon fluoride)-containing moiety to form a silicon fluoride conjugated polypeptide; and (iii) reacting the silicon fluoride conjugated polypeptide with an ^{18}F moiety to form an ^{18}F-silicon fluoride conjugated polypeptide.

[0017a] In a fourth aspect, there is provided a pharmaceutical composition comprising an imaging agent composition as defined herein and a pharmaceutically acceptable carrier.

FIGURES

[0018] These and other features, aspects, and advantages of the present invention will become better understood when the following detailed description is read with reference to the accompanying figures wherein:

[0019] FIGs. 1A and 1B are graphs of the surface plasmon resonance (SPR) of the binding affinity of two anti-HER2 polypeptides, Z477 (SEQ. ID No. 3) and $(Z477)_2$ (SEQ. ID No. 5), respectively, at eight different concentrations, to human HER2.

[0020] FIGs. 2A and FIG. 2B are graphs of the qualitative flow cytometry of C6 (rat glioma, control) and human anti-HER2 antibody to SKOV3 (human ovarian carcinoma) respectively. FIG. 2C shows a bar chart for Her2 receptors per cell for SKOV3 and C6 cell lines.

[0021] FIG. 3 is a bar graph of ELISA assays for Her2 with respect to a panel of tumor types SKOV3 2-1, SKOV3 3-1, SKOV3 3-4, with respect to SKOV3 cells, and blank.