subjected to sterile filtration without significant loss of radiotracer due to adsorption to the filter.

Summary

In one aspect, there is provided an imaging agent which comprises an ^{18}F-radiolabelled c-Met binding cyclic peptide,

wherein said c-Met binding cyclic peptide is an 18 to 30-mer cyclic peptide of Formula I:

$$Z^1\text{-}[cMBP]\text{-}Z^2 \qquad (I)$$

where:

cMBP is of Formula II:

$$\text{-}(A)_x\text{-}Q\text{-}(A')_y\text{-} \qquad (II)$$

where Q is the amino acid sequence (SEQ-1):

-Cys^a-X^1-Cys^c-X^2-Gly-Pro-Pro-X^3-Phe-Glu-Cys^d-Trp-Cys^b-Tyr-X^4-X^5-X^6-

wherein X^1 is Asn, His or Tyr;

X^2 is Gly, Ser, Thr or Asn;

X^3 is Thr or Arg;

X^4 is Ala, Asp, Glu, Gly or Ser;

X^5 is Ser or Thr;

X^6 is Asp or Glu;

and Cys$^{a\text{-}d}$ are each cysteine residues such that residues a and b as well as c and d are cyclised to form two separate disulfide bonds;

A and A′ are independently any amino acid other than Cys, with the proviso that at least one of A and A′ is present and is Lys;

x and y are independently integers of value 0 to 13, and are chosen such that [x + y] = 1 to 13;

Z^1 is attached to the N-terminus of cMBP, and is H or M^{IG};

Z^2 is attached to the C-terminus of cMBP and is OH, OB^c, or M^{IG},

where B^c is a biocompatible cation;

each M^{IG} is independently a metabolism inhibiting group which

is a biocompatible group which inhibits or suppresses *in vivo*

metabolism of the cMBP peptide;

wherein cMBP is labelled at the Lys residue of the A or A′ groups with ^{18}F.

In another aspect, there is provided an imaging agent composition which comprises:

(i) the ^{18}F-radiolabelled c-Met binding cyclic peptide as defined herein;

(ii) an unlabelled c-Met binding cyclic peptide;

wherein: said c-Met binding cyclic peptide has the same amino acid sequence in (i) and (ii)

and wherein the unlabelled cMBP peptide is present in said composition at no more than 50 times the molar amount of said ^{18}F-labelled cMBP peptide.

In another aspect, there is provided a pharmaceutical composition which comprises the imaging agent as defined herein or the imaging agent composition as defined herein together with a biocompatible carrier, in a sterile form suitable for mammalian administration.

In another aspect, there is provided a precursor, useful in the preparation of the ^{18}F-radiolabelled c-Met binding cyclic peptide as defined herein, which comprises: (i) the c-Met binding cyclic peptide of Formula I as defined herein, wherein $Z^1 = Z^2 = M^{IG}$; or (ii) an amino-oxy functionalised c-Met binding cyclic peptide.

In another aspect, there is provided a method of preparation of the ^{18}F-radiolabelled c-Met binding cyclic peptide as defined herein, which comprises:

(i) provision of the precursor as defined herein;

(ii) when said precursor comprises an unlabelled c-Met binding cyclic peptide of Formula I wherein $Z^1 = Z^2 = M^{IG}$, reaction with either an ^{18}F-labelled activated ester, or an ^{18}F-labelled carboxylic acid in the presence of an activating agent, to give the ^{18}F-radiolabelled c-Met binding cyclic peptide conjugated *via* an amide linkage at the Lys residue of the cMBP of said cyclic peptide;

(iii) when said precursor comprises an amino-oxy functionalised c-Met binding cyclic peptide, reaction with either:

(a) an ^{18}F-labelled activated ester, or an ^{18}F-labelled carboxylic acid in the presence of an activating agent, to give the ^{18}F-radiolabelled c-Met binding

cyclic peptide conjugated *via* an amide linkage at the amino-oxy position of said functionalised peptide; or

(b) an ^{18}F-labelled aldehyde to give the ^{18}F-radiolabelled c-Met binding cyclic peptide conjugated *via* an oxime ether linkage at the amino-oxy position of said functionalised peptide.

In another aspect, there is provided a method of preparation of the imaging agent composition as defined herein, or the pharmaceutical composition thereof as defined herein, which comprises: (i) preparing the ^{18}F-radiolabelled c-Met binding cyclic peptide using the method as defined herein; (ii) chromatographic separation of the unlabelled c-Met binding cyclic peptide from the ^{18}F-radiolabelled c-Met binding cyclic peptide.

In another aspect, there is provided a method of imaging of the mammalian body *in vivo* to obtain images of sites of c-Met over-expression or localisation, which method comprises imaging said body to which the imaging agent as defined herein, the imaging agent composition as defined herein, or the pharmaceutical composition as defined herein, had been previously administered.

Detailed Description of the Invention.

In a first aspect, the present invention provides an imaging agent which comprises an ^{18}F-radiolabelled c-Met binding cyclic peptide, wherein said c-Met binding cyclic peptide is an 18 to 30-mer cyclic peptide of Formula I:

$$Z^1\text{-[cMBP]-}Z^2 \qquad \text{(I)}$$

where:

cMBP is of Formula II:

$$\text{-(A)}_x\text{-Q-(A')}_y\text{-} \qquad \text{(II)}$$

where Q is the amino acid sequence (SEQ-1):

-Cys^a-X^1-Cys^c-X^2-Gly-Pro-Pro-X^3-Phe-Glu-Cys^d-Trp-Cys^b-Tyr-X^4-X^5-X^6-

wherein X^1 is Asn, His or Tyr;

X^2 is Gly, Ser, Thr or Asn;

X^3 is Thr or Arg;

X^4 is Ala, Asp, Glu, Gly or Ser;

X^5 is Ser or Thr;

X^6 is Asp or Glu;

and Cys^{a-d} are each cysteine residues such that residues a and b as well as c and d are cyclised to form two separate disulfide bonds;

A and A′ are independently any amino acid other than Cys, with the proviso that at least one of A and A′ is present and is Lys;

x and y are independently integers of value 0 to 13, and are chosen such that [x + y] = 1 to 13;

Z^1 is attached to the N-terminus of cMBP, and is H or M^{IG};

Z^2 is attached to the C-terminus of cMBP and is OH, OB^c, or M^{IG},

where B^c is a biocompatible cation;

each M^{IG} is independently a metabolism inhibiting group which is a biocompatible group which inhibits or suppresses *in vivo* metabolism of the cMBP peptide;

wherein cMBP is labelled at the Lys residue of the A or A′ groups with ^{18}F.