Both, ^{68}Ga- and ^{177}Lu-RM2 show favorable pharmacokinetics as high tumor accumulation, fast clearance from non-tumor tissue and good retention in the tumor over a large time span in humans leading to a high contrast and good therapy results, respectively.

Nonetheless, certain Bombesin analogs are metabolically unstable in animals which limits the desired accumulation in tumor tissues.

On the other hand, it has to be mentioned that more stable GRPR derivatives show slower washout from the GRPR rich pancreas which has to be considered before the usage for therapy of humans due to a possible pancreatitis.

In other malignant indications, yet further markers and targets are of interest. These include Neuromedin-B receptor (Bombesin-1 receptor, NMBR), Bombesin receptor subtype 3 (BRS-3) and Cholecystokinin-2 receptor (CCK-2R).

In view of the above, the technical problem underlying the present invention can be seen in the provision of improved radiopharmaceuticals and radiodiagnostics, in particular in the field of cancer, improvements including pharmacokinetic properties.

This technical problem has been solved by the subject-matter disclosed below.

SUMMARY

In one aspect, the present disclosure provides a compound binding to an endogenous receptor, said compound comprising

(i) an oligopeptide comprising a dipeptide with Trp being the C-terminal amino acid of said dipeptide, wherein said Trp is replaced with an α-amino acid Xaa_2, whereby the stability in serum or plasma of the peptide bond connecting Xaa_2 to the N-terminally adjacent amino acid is increased as compared to the peptide bond connecting Trp to the N-terminally adjacent amino acid in an otherwise identical compound; and

(ii) a moiety capable of generating therapeutically effective radiation, said

moiety being covalently bound to said oligopeptide.

In another aspect, the present disclosure provides a compound of formula (I)

S — Y — Xaa_1 — Xaa_2 — L-Ala — L-Val — Xaa_5 — L-His — T (I)

wherein

S is a moiety capable of generating therapeutically active radiation;

Y is an optional linker;

Xaa_1 is (i) L-Gln, D-Gln, L-His, D-His or Gly, preferably L-Gln; or

(ii) an α-amino acid which increases stability in serum or plasma of the Xaa_1—Xaa_2 peptide bond as compared to Xaa_1 being Gln and Xaa_2 being Trp in an otherwise identical compound;

Xaa_2 is Trp or an α-amino acid which increases stability in serum or plasma of the Xaa_1—Xaa_2 peptide bond as compared to Xaa_1 being Gln and Xaa_2 being Trp in an otherwise identical compound;

provided that Xaa_1 is not any one of L-Gln, D-Gln, L-His, D-His and Gly, and Xaa_2 is not Trp, respectively, at the same time;

Xaa_5 is Gly, N-Me-Gly, D-Ala, β-Ala or 2-aminoisobutyric acid (Aib); preferably Gly; and

T is an optional terminal group.

In yet another aspect, the present disclosure provides a compound of formula (II)

S — Y — Xaa_3 — Xaa_4 — L-Ala — L-Val — Xaa_5 — L-His — T (II)

wherein

S is a moiety capable of generating a detectable signal;

Y is an optional linker;

Xaa_3 is (i) L-Gln, D-Gln, L-His, D-His or Gly, preferably L-Gln; or

(ii) an α-amino acid which decreases stability in serum or plasma of the Xaa_3— Xaa_4 peptide bond as compared Xaa_3 being Gln and Xaa_4 being Trp in an otherwise identical compound;

Xaa_4 is Trp or an α-amino acid which decreases stability in serum or plasma of the Xaa_3—Xaa_4 peptide bond as compared Xaa_3 being Gln and Xaa_4 being Trp in an otherwise identical compound;

wherein said α-amino acid at position Xaa_4 which decreases stability in serum

or plasma of the Xaa_3—Xaa_4 peptide bond is not a proteinogenic amino acid; provided that Xaa_3 is not any one of L-Gln, D-Gln, L-His, D-His and Gly, and Xaa_4 is not Trp, respectively, at the same time;

Xaa_5 is Gly, N-Me-Gly, β-Ala or 2-aminoisobutyric acid (Aib); preferably Gly; and

T is a optional terminal group.

In one aspect, the present disclosure provides a pharmaceutical composition comprising or consisting of a compound disclosed herein.

In another aspect, the present disclosure provides a diagnostic composition comprising or consisting of a compound disclosed herein.

DESCRIPTION

In a first aspect, the present invention relates to a compound binding to an endogenous receptor, said compound comprising (i) an oligopeptide comprising a dipeptide with Trp being the C-terminal amino acid of said dipeptide, wherein said Trp is replaced with an α-amino acid Xaa_2, whereby the stability in serum or plasma (preferably mammalian serum or plasma) of the peptide bond connecting Xaa_2 to the N-terminally adjacent amino acid is increased as compared to the peptide bond connecting Trp to the N-terminally adjacent amino acid in an otherwise identical compound; and (ii) a moiety capable of generating therapeutically effective radiation, said moiety being covalently bound to said oligopeptide.