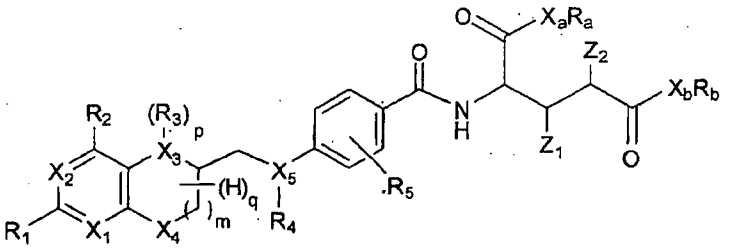
Claims

1. A compound having formula II



II

wherein

X_1 to X_5 are independently of each other C or N,

R_1 and R_2 are independently of each other H, Hal, -OR', -NR''R''', C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, and (C_1-C_{12} alkylamino)carbonyl, wherein R' is H or C_1-C_6 alkyl, and wherein R'' and R''' are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl,

R_3, R_4 are independently of each other H, formyl, trifluoroacetyl, iminomethyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-,

-CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl, or R_3 and R_4 form together a C_1 or C_2-bridge between X_3 and X_5,

R_5 is H, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, and (C_1-C_{12} alkylamino)carbonyl,

m is 0 or 1,

p is 0, 1 or 2,

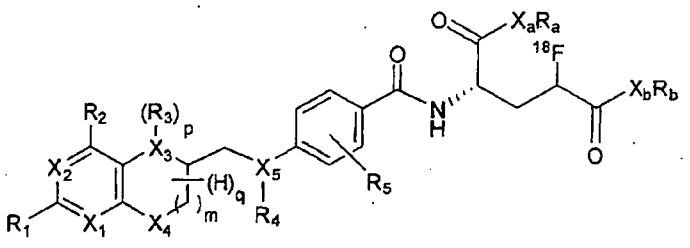
q has a value of 1 to 7

X_a, X_b are independently of each other C, N, O, S,

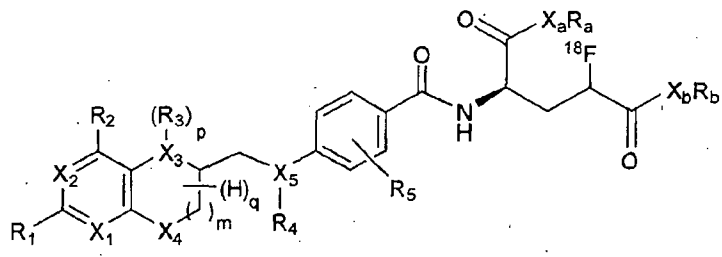
R_a, R_b are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl, C_5-C_{14} aryl or C_5-C_{14} heteroaryl, which independently of each other are unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -SO_2-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl; and

Z_1, Z_2 are independently of each other H or ^{18}F, with the proviso that one of Z_1 and Z_2 is ^{18}F.

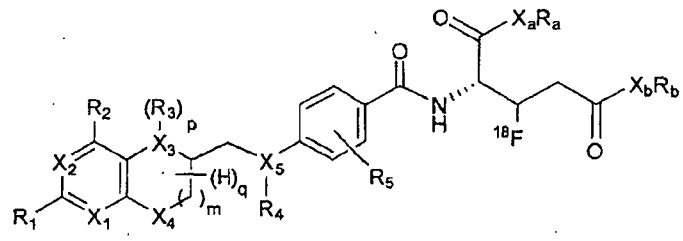
2. A compound according to claim 1 having formulae IIIa, IIIb, IVa, or IVb,



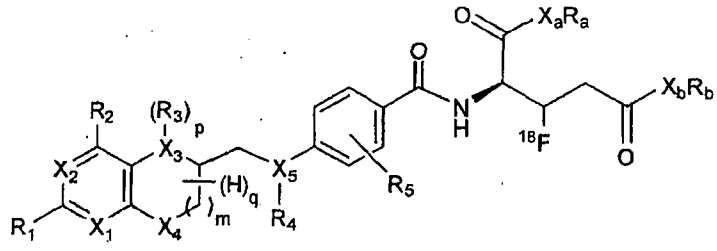
IIIa



IIIb



IVa



IVb

wherein

X_1 to X_5 are independently of each other C or N,

R_1 and R_2 are independently of each other H, Hal, -OR', -NR''R''', C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, and (C_1-C_{12} alkylamino)carbonyl, wherein R' is H or C_1-C_6 alkyl, and wherein R'' and R''' are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at

least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl,

R_3, R_4 are independently of each other H, formyl, trifluoroacetyl, iminomethyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl, or R_3 and R_4 form together a C_1 or C_2-bridge between X_3 and X_5,

R_5 is H, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl,

m is 0 or 1,

p is 0, 1 or 2,

q has a value of 1 to 7,

X_a, X_b are independently of each other C, N, O, S,

R_a, R_b are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl, C_5-C_{14} aryl or C_5-C_{14} heteroaryl, which independently of each other are unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR''-, -SO_2-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl.

3. A compound according to claims 1 or 2, wherein R_1 and R_2

are independently of each other H, alkyl, -OR', -NHR', wherein R' represents H or C_1-C_6 alkyl.

4. A compound according to any preceding claim, wherein R_3 is H, formyl, C1-C12 alkyl or C1-C12 alkanoyl.

5. A compound according to any preceding claim, wherein R_3 is H, formyl, or methyl.

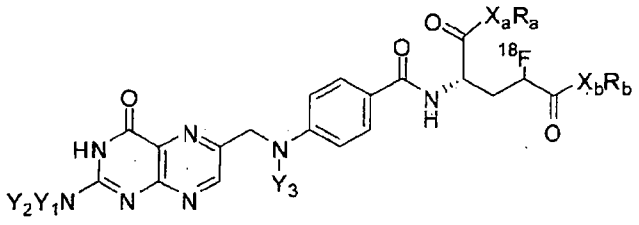
6. A compound according to any preceding claim, wherein R_4 is H, formyl, nitroso, C_1-C_6 alkyl, C_1-C_6 alkoxy, or C_1-C_6 alkanoyl.

7. A compound according to any preceding claim, wherein R_4 is H, formyl, or methyl.

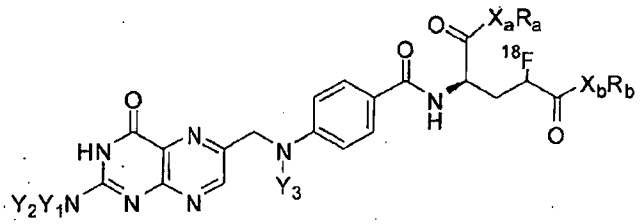
8. A compound according to any preceding claim, wherein R_5 is H, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl.

9. A compound according to any preceding claim, wherein R_5 is H.

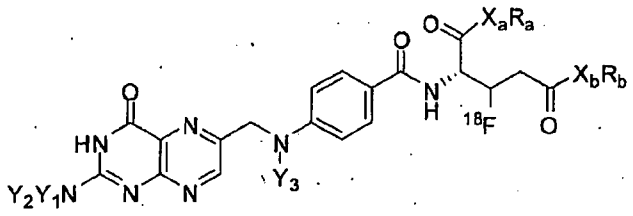
10. A compound according to claim 1 having formulae Va, Vb, VIa or VIb,



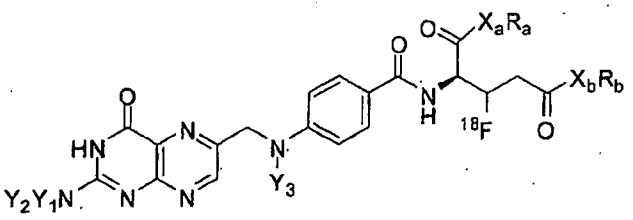
Va



Vb



VIa



VIb

wherein,

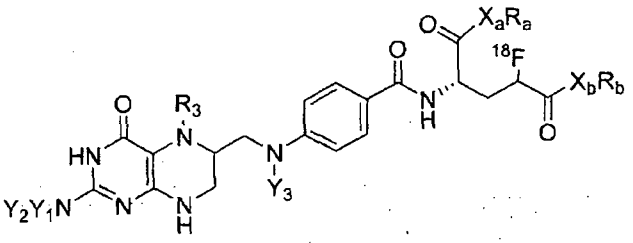
X_a, X_b are independently of each other C, N, O, S,

R_a, R_b are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl, C_5-C_{14} aryl or C_5-C_{14} heteroaryl, which independently of each other are unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, $-SO_2-$, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl;

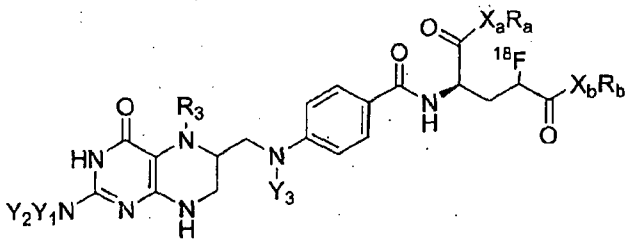
Y_1, Y_2 are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl,

Y_3 is selected from H, formyl, trifluoroacetyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl.

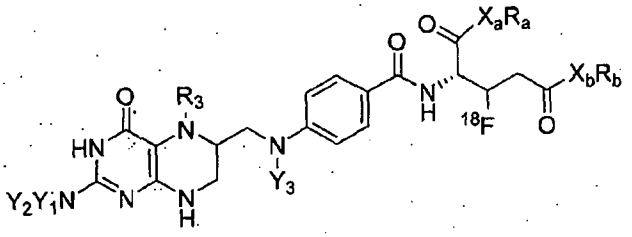
11. A compound according to claim 1 having formulae VIIa, VIIb, VIIIa or VIIIb,



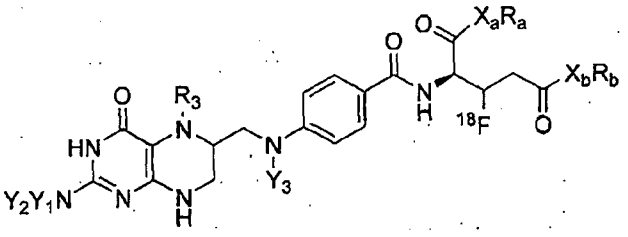
VIIa



VIIb



VIIIa



VIIIb

wherein,

X_a, X_b are independently of each other C, N, O, S,

R_a, R_b are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, C_3-C_6 cycloalkyl, C_5-C_{14} aryl or C_5-C_{14} heteroaryl, which independently of each other are unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, $-SO_2-$, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl;

Y_1, Y_2 are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl,

R_3 is H, formyl, iminomethyl, nitroso, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, halosubstituted C_1-C_{12} alkanoyl, and

Y_3 is selected from H, formyl, trifluoroacetyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, wherein R' is H or C_1-C_6 alkyl, or

R_3 and Y_3 form together a C_1 or C_2-bridge between the two N-atoms

to which they are attached to.

12. Pharmaceutical composition comprising a compound according to claims 1 to 11.

13. Compound according to claims 1 to 11 for use in diagnostic imaging of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

14. Compound according to claims 1 to 11 for use in diagnostic imaging of a cell or population of cells expressing a folate-receptor, said method comprising the steps of administering at least one compound according to claims 1 to 11 in a diagnostic imaging amount, and obtaining a diagnostic image of said cell or population of cells.

15. Compound according to claims 1 to 11 for use in diagnostic imaging or monitoring a subject comprising the steps of (i) administering at least one compound according to claims 1 to 11 in a diagnostic imaging amount, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound.

16. Compound according to claims 1 to 11 for use in monitoring therapy of cancer and inflammatory and autoimmune diseases in a subject comprising the steps of (i) administering to a subject in need thereof at least one compound according to claims 1 to 11 in a diagnostic imaging amount in combination with a therapeutically active, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound to

follow the course of therapy of cancer and inflammatory and autoimmune diseases.

17. Method for in vitro detection of a cell expressing the folate receptor in a tissue sample which includes contacting said tissue sample with a compound according to claims 1 to 11 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.