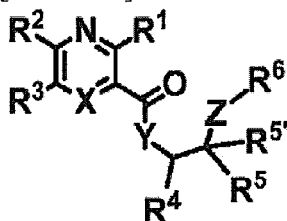


which compounds are useful for the prevention and/or the treatment of cancer and other immune-related diseases such as infection and sepsis.

Summary

[7a] In one aspect, there is provided a heterocyclic compound represented by the following Formula I, a stereoisomer thereof, an enantiomer thereof, or a pharmaceutically acceptable salt thereof:

[Formula I]



wherein:

X is CR⁷, or N;

Y is CHR⁸, NR⁸, or O;

Z is CH₂, CH₂O, C(=O), C(=O)O, C(=O)NH, NR⁸, NHC(=O), O or O(C=O);

R¹ is H, halogen, C₁₋₃ alkyl, NHR⁸ or OR⁸;

R² is H, halogen, C₁₋₄ alkyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂ alkylheterocyclyl or -L-aryl, which C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂ alkylheterocyclyl or -L-aryl may optionally be substituted with one or more R⁹;

R³ is H, halogen, CN, C₁₋₃ alkyl, cycloalkenyl, C₂₋₆ alkenyl, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, or C₁₋₂ alkylheterocyclyl which aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, or C₁₋₂ alkylheterocyclyl may optionally be substituted with one or more R⁹;

R⁴ and R⁵ each independently is H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₁₀ cycloalkyl, C(=O)R⁶, C₁₋₂ alkylaryl, aryl; or

R⁴ and R⁵ may be combined with each other to form a 3-7 membered cyclic ring or heterocyclic ring containing 1 or 2 of NR⁸, O or S, and the cyclic or heterocyclic ring may optionally be substituted with 1 or 2 halogen(s), C₁₋₄ alkyl or C₁₋₄ alkoxy;

R⁵ is H or R⁵ and R⁵ may be combined with each other to form carbonyl;

R⁶ is H, C₁₋₄ alkyl, C₁₋₆ alkoxy, -NR¹⁵R¹⁶, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂ alkylheterocyclyl, C₁₋₂ alkylbiaryl, -L-aryl or -L-biaryl, which C₁₋₄ alkyl, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂ alkylheterocyclyl, C₁₋₂ alkylbiaryl, -L-aryl or -L-biaryl, may optionally be substituted with one or more R⁹;

R⁷ is H, halogen or C₁₋₃ alkyl;

R⁸ is H, C₁₋₆ alkyl, C₁₋₄ fluoroalkyl, C₁₋₄ hydroxyalkyl, C₁₋₃ alkylaryl or

C(=O)R¹⁰ which C₁₋₆ alkyl or C₁₋₃ alkylaryl may optionally be substituted with one or more R⁹;

when Z is NR⁸, R⁸ and R⁶ may be combined with each other to form a 3-7 membered heterocyclic ring comprising 1 to 2 N or 0 to 2 O heteroatoms;

R⁹ is halogen, hydroxyl, -CN, -NO₂, -COOH, -(C=O)H, C₁₋₆alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₆ alkoxy, cycloalkenyl, aryl, heterocyclyl, heteroaryl, -NR¹⁵R¹⁶, -L-NR¹⁵R¹⁶, -L-COOR¹⁷, -L-alkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-heteroaryl, or -L-aryl which C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₁₋₄ hydroxyalkyl, C₁₋₆ alkoxy, cycloalkenyl, aryl, heterocyclyl, heteroaryl, -L-alkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-heteroaryl, or -L-aryl may be substituted with halogen, hydroxyl, -CN, -NR¹⁵R¹⁶, C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl, C₁₋₄ hydroxyalkyl, C₂₋₆ alkenyl, aryl, heterocyclyl, -L-heterocyclyl, or -(CH₂)_l-C(=O)-NR¹⁵R¹⁶; R¹⁰ is C₁₋₃ alkyl or C₁₋₃ alkylaryl; R¹⁵ and R¹⁶ each independently is H, C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl or SO₂R¹⁷; R¹⁷ is H, C₁₋₃ alkyl or C₁₋₃ alkylaryl; L is C₁₋₃ alkyl, C₁₋₃ alkylO, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, -(CH₂)_l-C(=O)-(CH₂)_m-, C(=O)O, -(CH₂)_l-C(=O)NH-(CH₂)_m-, -(CH₂)_l-NHC(=O)-(CH₂)_m-, -(CH₂)_l-NH-(CH₂)_m-, NR⁸, -NH-C(=O)-CR¹⁵R¹⁶-NH-C(=O)-, NHC(=O), O, O(C=O) S, S(=O), or SO₂; and l and m each independently is an integer of 0 to 2.

[7b] In another aspect, there is provided a pharmaceutical compositions comprising the heterocyclic compounds, the stereoisomer thereof, the enantiomer thereof, or the pharmaceutically acceptable salt thereof described herein together with pharmaceutically acceptable carriers.

[7c] In another aspect, there is provided use of compositions comprising, as active ingredients, the heterocyclic compounds, isomers thereof or pharmaceutically acceptable salts thereof described herein, in the manufacture of a medicament for treating or preventing immune-related diseases or cancer in a mammal including humans in need thereof.

[7d] In another aspect, there is provided use of compositions comprising, as active ingredients, the heterocyclic compounds, the stereoisomer thereof, the enantiomer thereof, or the pharmaceutically acceptable salt thereof described herein, in the manufacture of a medicament for preventing or treating cancer or immune-related diseases.

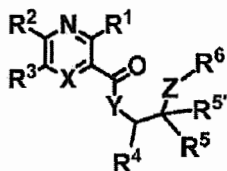
Solution to Problem

[8] Novel Mer kinase inhibitors

[9] The present invention relates to a heterocyclic compound represented by the following Formula I, a stereoisomer thereof, an enantiomer thereof, or a pharmaceutically acceptable salt thereof:

[10] [Formula I]

[11]



[12] wherein:

[13] X is CR⁷, or N;

[14] Y is CHR⁸, NR⁸, or O;

[15] Z is CH₂, CH₂O, C(=O), C(=O)O, C(=O)NH, NR⁸, NHC(=O), O or O(C=O);

[16] R¹ is H, halogen, C₁₋₃ alkyl, NHR⁸ or OR⁸;

[17] R² is H, halogen, C₁₋₄ alkyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂ alkylheterocyclyl or -L-aryl, which C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂alkylheterocyclyl or -L-aryl may optionally be substituted with one or more R⁹;

[18] R³ is H, halogen, CN, C₁₋₃ alkyl, cycloalkenyl, C₂₋₆ alkenyl, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, or C₁₋₂ alkylheterocyclyl which aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkyl-

heteroaryl, or C₁₋₂ alkylheterocyclyl may optionally be substituted with one or more R⁹;

[19] R⁴ and R⁵ each independently is H, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₁₀ cycloalkyl, C(=O) R⁶, C₁₋₂ alkylaryl, aryl; or

[20] R⁴ and R⁵ may be combined with each other to form a 3-7 membered cyclic ring or heterocyclic ring containing 1 or 2 of NR⁸, O or S, and the cyclic or heterocyclic ring may optionally be substituted with 1 or 2 halogen(s), C₁₋₄ alkyl or C₁₋₄ alkoxy;

[21] R⁵ is H or R⁵ and R⁵ may be combined with each other to form carbonyl;

[22] R⁶ is H, C₁₋₄ alkyl, C₁₋₆ alkoxy, -NR¹⁵R¹⁶, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂ alkylheteroaryl, C₁₋₂alkylheterocyclyl, C₁₋₂ alkylbiaryl, -L-aryl or -L-biaryl, which C₁₋₄ alkyl, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclyl, C₁₋₂ alkylaryl, C₁₋₂alkylheteroaryl, C₁₋₂ alkylheterocyclyl, C₁₋₂ alkylbiaryl, -L-aryl or -L-biaryl, may optionally be substituted with one or more R⁹;

[23] R⁷ is H, halogen or C₁₋₃ alkyl;

[24] R⁸ is H, C₁₋₆ alkyl, C₁₋₄ fluoroalkyl, C₁₋₄ hydroxyalkyl, C₁₋₃ alkylaryl or C(=O)R¹⁰

from the group consisting of: glioma, gliosarcoma, anaplastic astrocytoma, medulloblastoma, lung cancer, small cell lung carcinoma, cervical carcinoma, colon cancer, rectal cancer, chordoma, throat cancer, Kaposi's sarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, colorectal cancer, endometrium cancer, ovarian cancer, breast cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, hepatic carcinoma, bile duct carcinoma, choriocarcinoma, seminoma, testicular tumor, Wilms' tumor, Ewing's tumor, bladder carcinoma, angiosarcoma, endotheliosarcoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland sarcoma, papillary sarcoma, papillary adenocarcinoma, cystadenosarcoma, bronchogenic carcinoma, medullary carcinoma, mastocytoma, mesothelioma, synovium, melanoma, leiomyosarcoma, rhabdomyosarcoma, neuroblastoma, retinoblastoma, oligodendroglioma, acoustic neuroma, hemangioblastoma, meningioma, pinealoma, ependymoma, craniopharyngioma, epithelial carcinoma, embryonal carcinoma, squamous cell carcinoma, base cell carcinoma, fibrosarcoma, myxoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, leukemia and metastatic lesions secondary to these primary tumors.

[Claim 9]

The pharmaceutical compositions of claim 7, the immune-related diseases are selected from the group consisting of infection and sepsis.

[Claim 10]

Use of compositions comprising, as active ingredients, the heterocyclic compounds, isomers thereof or pharmaceutically acceptable salts thereof according to any one of claims 1 to 4, in the manufacture of a medicament for treating or preventing immune-related diseases or cancer in a mammal including humans in need thereof.

[Claim 11]

Use of compositions comprising, as active ingredients, the heterocyclic compounds, the stereoisomer thereof, the enantiomer thereof, or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 4, in the manufacture of a medicament for preventing or treating cancer or immune-related diseases.