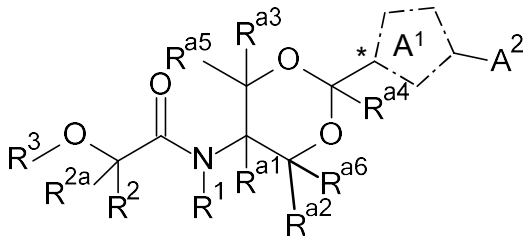
Patent Claims

1. A compound of formula (I)



(I)

or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein

R^{a1}, R^{a2}, R^{a3}, R^{a4}, R^{a5}, and R^{a6} are H;

A^1 is triazole or oxadiazole, provided that the ring atom of ring A^1 marked with an asterisk is a carbon atom, wherein A^1 is optionally substituted with one or more R^4, which are the same or different;

each R^4 is independently oxo (=O) where the ring is at least partially saturated, thiooxo (=S) where the ring is at least partially saturated, halogen, CN, OR^5, or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

R^5 is H or C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^2 is R^{6a} or A^{2a};

R^{6a} is OR^{6a1}, SR^{6a1}, $N(R^{6a1}R^{6a2})$, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen, OR^{6a3}, CN, and A^{2a}, wherein the substituents are the same or different;

R^{6a1} and R^{6a2} are independently selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and A^{2a}, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more substituents selected from the group consisting of halogen, CN, OR^{6a3}, A^{2a}, and OA^{2a}, wherein the substituents are the same or different;

R^{6a3} is H or C_{1-4} alkyl, wherein C_{1-4} alkyl is optionally substituted with one or more halogen, which are the same or different;

A^{2a} is phenyl, cyclobutyl, azetidinyl, or 5- to 6-membered aromatic heterocyclyl, wherein A^{2a} is optionally substituted with one or more R^6, which are the same or different;

each R^6 is independently R^{6b}, OH, OR^{6b}, halogen, or CN, wherein R^{6b} is cyclopropyl, C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein R^{6b} is optionally substituted with one or more halogen, which are the same or different; or
two R^6 are joined to form together with the atoms to which they are attached a ring A^{2b};

A^{2b} is phenyl, C_{3-7} cycloalkyl, or 3 to 7 membered heterocyclyl, wherein A^{2b} is optionally substituted with one or more R^7, which are the same or different;

each R^7 is independently C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are optionally substituted with one or more halogen, which are the same or different;

R^1 is H;

R^2 is H; and
R^3 is A^3

R^{2a} is H;

each A^3 is independently phenyl, pyridyl, pyrazinyl, pyrimidazyl, cyclopropyl, cyclobutyl, or cyclohexyl, , wherein A^3 is optionally substituted with one or more R^{10}, which are the same or different;

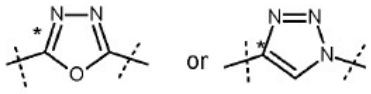
each R^{10} is independently F, Cl, Br, CHF_2, CF_3, OCF_3, CH=O, CH_2OH, or CH_3.

2. The compound of claim 1 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is unsubstituted or substituted with one or two R^4, which are the same or different, preferably A^1 is unsubstituted.

3. The compound of claims 1 or 2 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^4 is oxo, where the ring is at least partly saturated.

4. The compound of any one of claims 1 to 3 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^1 is

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5. The compound of any one of claims 1 to 4 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^2 is R^{6a}.

6. The compound of claim 5 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{6a} is OR^{6a1} and R^{6a1} is preferably A^{2a} or C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3};

or R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one A^{2a} and/or one OR^{6a3}.

7. The compound of claims 5 or 6 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein R^{6a} is OR^{6a1} and R^{6a1} is preferably C_{1-6} alkyl, optionally substituted with one or more F and/or one OR^{6a3}; or R^{6a} is C_{1-6} alkyl, optionally substituted with one or more halogen and/or one OR^{6a3}.

8. The compound of any one of claims 1 to 4 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^2 is A^{2a}.

9. The compound of any one of claims 1 to 6, and 8 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^{2a} is substituted with one or two R^6, which are the same or different.

10. The compound of any one of claims 1 to 6, and 8 to 9 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein each R^6 is independently F, Cl, CF_3, OCH_3, OCF_3, CH_3, CH_2CH_3, or cyclopropyl.

11. The compound of any one of claims 1 to 10 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein A^3 is substituted with one or two R^{10}, which are the same or different.

12. The compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein the compound is

2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1,3-dioxan-5-yl]acetamide;

2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-{5-[*cis*-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl}-1,3-dioxan-5-yl]acetamide;

2-(4-chloro-3-fluorophenoxy)-*N*-[*cis*-2-[1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl]-1,3-dioxan-5-yl]acetamide;

2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-[1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl]-1,3-dioxan-5-yl]acetamide;

2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-[5-(4,4,4-trifluorobutoxy)-1,3,4-oxadiazol-2-yl]-1,3-dioxan-5-yl]acetamide;

2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}-1,3-dioxan-5-yl]acetamide;

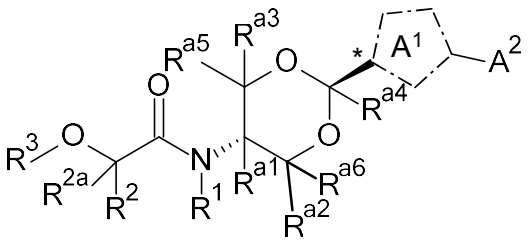
2-(4-chloro-3-fluorophenoxy)-*N*-[*trans*-2-{5-[3-(trifluoromethoxy)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}-1,3-dioxan-5-yl]acetamide;

2-[(6-chloro-5-fluoro-3-pyridyl)oxy]-*N*-[*trans*-2-[5-[*cis*-3-(trifluoromethoxy)cyclobutyl]-1,3,4-oxadiazol-2-yl]-1,3-dioxan-5-yl]acetamide;

2-[3-chloro-4-(difluoromethyl)phenoxy]-*N*-[*trans*-2-{5-[3-(trifluoromethoxy)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}-1,3-dioxan-5-yl]acetamide; or

2-(3,4-dichlorophenoxy)-*N*-[*trans*-2-{5-[2-(trifluoromethoxy)ethoxy]-1,3,4-oxadiazol-2-yl}-1,3-dioxan-5-yl]acetamide.

13. The compound of any one of claims 1 to 12 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof, wherein the compound is of formula (Ia)



(Ia).

14. A pharmaceutical composition comprising at least one compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof as defined in any one of claims 1 to 13 together with a pharmaceutically acceptable carrier, optionally in combination with one or more other bioactive compounds or pharmaceutical compositions.

15. A compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof of any one of claims 1 to 13 for use as a medicament.

16. Use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof of any one of claims 1 to 13 or a pharmaceutical composition of claim 14 in the manufacture of a medicament for treating or preventing of one or more diseases or disorders associated with integrated stress response.

17. Use of a compound or a pharmaceutically acceptable salt, solvate, hydrate, tautomer or stereoisomer thereof of any one of claims 1 to 13 or a pharmaceutical composition of claim 14 in the manufacture of a medicament for treating or preventing of one or more diseases or disorders selected from the group consisting of leukodystrophies, intellectual disability syndrome, neurodegenerative diseases and disorders, neoplastic diseases, infectious diseases, inflammatory diseases, musculoskeletal diseases, metabolic diseases, ocular diseases as well as diseases selected from the group consisting of organ fibrosis, chronic and acute diseases of the liver, chronic and acute diseases of the lung, chronic and acute diseases of the kidney, myocardial infarction, cardiovascular disease, arrhythmias, atherosclerosis, spinal cord injury, ischemic stroke, and neuropathic pain.