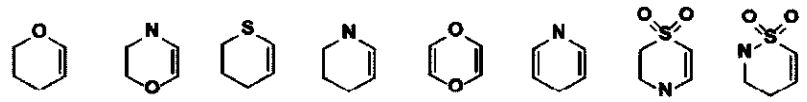
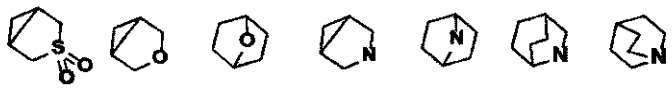
with a partially unsaturated bond include, but are not limited to, those with a structure shown below and the like.
[Chemical Formula 44]



[0044]

Specific examples of "6-membered non-aryl heterocycle" with a partially crosslinked structure include, but are not limited to, those with a structure shown below and the like.
[Chemical Formula 45]



[0045]

"C_{1-6} alkoxy" or "C_{1-6} alkoxy group" refers to "C_{1-6} alkyloxy", and the "C_{1-6} alkyl" moiety is defined the same as the "C_{1-6} alkyl" described above. "C_{1-6} alkoxy" is preferably "C_{1-4} alkoxy" or "C_{2-6} alkoxy", and more preferably "C_{1-3} alkoxy". Specific examples of "C_{1-3} alkoxy" include methoxy, ethoxy, propoxy, 1-methylethoxy, and the like. Specific examples of "C_{1-4} alkoxy" include, in addition to the specific examples specified for the "C_{1-3} alkoxy~~alkyl~~" described above, butoxy, 1,1-dimethylethoxy, 1-methylpropoxy, 2-methylpropoxy, and the like. Specific examples of "C_{2-6} alkoxy" include ethoxy, propoxy, 1-methylethoxy, butoxy, 1,1-dimethylethoxy, 1-methylpropoxy, 2-methylpropoxy, pentyloxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 1-methylbutoxy, 2-methylbutoxy, 4-methylpentyloxy, 3-methylpentyloxy, 2-methylpentyloxy, 1-methylpentyloxy, hexyloxy, and the like. Specific examples of "C_{1-6} alkoxy" include, in addition to the specific examples specified for the "C_{1-4} alkoxy~~alkyl~~" described above, pentyloxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 1-

non-aryl heterocyclyl oxy group". Specific examples of "4- to 10-membered non-aryl heterocyclyl oxy group" include, but are not limited to, a tetrahydrofuranyloxy group, tetrahydropyranyloxy group, azetidinyloxy group, pyrrolidinyloxy group, piperidinyloxy group, and the like.

[0050]

The C_{1-6} alkyl moiety of "C_{1-6} alkylthio group" is defined the same as the C_{1-6} alkyl described above. "C_{1-6} alkylthio group" is preferably a "C_{1-4} alkylthio group", and more preferably a "C_{1-3} alkylthio group". Specific examples of "C_{1-6} alkylthio group" include, but are not limited to, a methylthio group, ethylthio group, propylthio group, butylthio group, isopropylthio group, isobutylthio group, tert-butylthio group, sec-butylthio group, isopentylthio group, neopentylthio group, tert-pentylthio group, 1,2-dimethylpropylthio group, and the like.

[0051]

"C_{3-10} alicyclic thio" or "C_{3-10} alicyclic thio group" refers to a (C_{3-10} alicyclic group)-S-group, and the C_{3-10} alicyclic moiety is defined the same as the C_{3-10} alicyclic group described above. "C_{3-10} alicyclic thio group" is preferably a "C_{3-6} alicyclic thio group". Specific examples of "C_{3-6} alicyclic thio group" include, but are not limited to, a cyclopropylthio group, cyclobutylthio group, cyclopentylthio group, cyclohexylthio group, and the like.

[0052]

The C_{6-10} aryl moiety of "C_{6-10} arylthio" or "C_{6-10} arylthio group" is defined the same as the C_{6-10} aryl described above. "C_{6-10} arylthio group" is preferably a "C_6 or C_{10} arylthio group". Specific examples of "C_{6-10} arylthio~~oxy~~ group" include, but are not limited to, a phenylthio group, 1-naphthylthio group, 2-naphthylthio group, and the like.

[0053]

The 5- or 6-membered heteroaryl moiety of "5- or 6-membered heteroarylthio" or "5- or 6-membered

(Corning, Cat# 353962) coated with poly-L-lysine (Sigma-Aldrich, cat# P4707) and iMatrix-511 silk (Matrixome, cat# 892021). Half of the culture solution was exchanged once every 3 to 4 days.

[0197]

(2) Fluorescent calcium probe treatment, addition of compound, and evaluation of intracellular calcium concentration

Half of the culture solution was removed on day 60 from induction of differentiation or thereafter. A medium for measurement comprising a fluorescent calcium probe (Molecular Device, product name: FLIPR Calcium 6 Assay Bulk Kit, cat# R8191) was added at an amount equal to the remaining medium. The culture was left standing for 30 minutes and subjected to measurement. As the medium for measurement, 20 mM Hepes (Thermo Fisher Scientific, cat# 15630-080) and 0.1% bovine serum albumin (Sigma-Aldrich, cat# A9576)-containing Hank's buffer (Thermo Fisher Scientific, cat# 14065-056) was used.

[0198]

The test compounds were serially diluted with a dimethyl sulfoxide (DMSO) solution so that the final concentration would be 0.1 to 100 μM to prepare a concentrate with a concentration that is 6-fold of the final concentration.

[0199]

The intensity of fluorescence of a calcium probe was measured over time with FDSS7000EX (Hamamatsu Photonics) to evaluate the change in intracellular calcium concentrations. First, the intensity of fluorescence was measured for 2

minutes. The compound solutions were then added using FDSS7000EX for an additional 8 minute measurement of fluorescence intensity. The amplitude of spontaneous calcium oscillation was quantified as an indicator of nerve excitation. With the amplitude for 2 minutes before the addition of the compound solutions as 100%, the ratio of amplitudes for the last 2 minutes after addition of the compound solutions was calculated. The inhibitory activity (%) at each serial dilution concentration was determined, and the 50% inhibitory concentration (IC50) or the inhibition ratio (%) at a certain concentration (the concentration described after @ in Tables 2-1 and 2-2) was determined for each test compound. Tables 2-1 and 2-2 show inhibitory activity data for representative compounds.