# Small molecular drugs

## Pyrazole compounds

Inventors: Kak-Shan Shia, Chun-Ping Chang, Yu-Sheng Chao

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Cannabinoid receptor 1 (CB1) is expressed in several peripheral tissues related to metabolic control in addition to its abundancy in the central nervous system. Activation of peripheral CB1 induces lipogenesis, gluconeogenesis and pancreatic β-cell death. In contrast, blockade of CB1 leads to inhibition of lipogenesis and increase of adiponectin expression, glucose uptake, and protection of β-cell survival. The present invention, pyrazole compounds as the peripheral CB1 receptor antagonists, can be a therapeutic strategy for treating anti-obesity, type 2 diabetes, anti-fatty liver disease, and metabolic syndromes.

The present series of compounds displayed much high affinity for the peripheral CB1 receptor (Ki = 0.53 nM). These compounds minimum penetration to the brain which can avoid the side effects caused by the CB1 receptor in the brain.

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## Heterocyclic compounds and use thereof

Inventors: Kak-Shan Shia, Jiing-Jyh Jan, Lun Kelvin Tsou, Chiung-Tong Chen, Yu-Sheng Chao

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Chemokines regulate the trafficking of various types of mononuclear cells. They are classified into four subfamilies of CC, CXC, CX3C, and C, based on positions of conserved cysteine residues in their N-termini. Stromal-derived factor-1 (SDF-1), a CXC chemokine, plays key roles in homing and mobilization of hematopoietic stem cells, endothelial progenitor cells, and hematopoietic progenitor cells. The physiological function of SDF-1 is mediated by the type 4 CXC chemokine receptor (CXCR4). The interaction between CXCR4 and SDF-1 contributes to multiple pathological conditions such as HIV, rheumatoid arthritis, asthma, and tumor metastases.

The present invention is based on an unexpected discovery that certain heterocyclic compounds effectively bind to CXCR4 and disrupt the interaction between CXCR4 and SDF-1. Another aspect of this invention is related to a method for mobilizing hematopoietic stem cells (HSC) and endothelial progenitor cells (EPC) into the peripheral circulation. It can be used for treating tissue injury, cancer, inflammatory disease, and autoimmune disease.

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## Aminothiazole compounds and use thereof

Inventors: Weir-Torn Jianng, Tsu Hsu

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Protein kinases are important in cellular signal pathways that regulate various cell functions, including differentiation, proliferation, migration, and apoptosis. Deregulation of protein kinases is implicated in cancer and a number of other diseases. Heterocyclic compounds have been extensively studied as potent protein kinase inhibitors. Among various classes of heterocyclic compounds, aminothiazoles appear as a recurring structural motif in many biologically active compounds.

The invention discloses a series of aminothiazole compoundsinhibit multiple protein kinases effectively, exerts high in vivo anti-cancer efficacy, and shows great safety. To practice the method of the present invention, a composition having one or more of the above-described aminothiazole compounds can be administered parenterally, orally, nasally, rectally, topically, or buccally.

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## Method and composition for decreasing the psychotomimetic side effect and addictive disorder of ketamine

Inventor: Hwei-Hsien Chen

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Ketamine has fast and sustained antidepressant effect. It shows promising for treatment-resistant major depressive disorder and depressed bipolar disorder in clinical trials. However, the adverse effects of ketamine including addiction, psychosis, and bladder toxicity become an obstacle to its application in the treatment of depression. The present invention indicates that dimethylglycine (DMG) and trimethylglycine (TMG) combined with ketamine, effectively reduce the side effects and enhance the antidepressant effect of ketamine, revealing the potential treatment of a combination medicine for refractory depression and suicidal ideation.

The research team discovered that DMG and TMG are the partial agonist of NMDA receptor glycine binding site. The present invention, a combination with DMG, TMG and ketamine for treatment of depression and related disorders, will reduce the side effects of Ketamine, enhance the safety and so will be able to apply for clinical trials soon.

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