Selective Phospholipase A2 Inhibitors of Neurological Diseases

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BACKGROUND

The past two decades has resulted in a marked increase in our knowledge about phospholipase A2 (PLA2) enzymes. The PLA2 superfamily of enzymes has been divided into four main types: secreted sPLA2s, cytosolic cPLA2s, calcium-independent iPLA2s, and lipoprotein-associated/PAF acetyl hydrolase LpPLA2s.

The association of the different types of PLA2s with diverse indications has justified pharma’s interest in developing selective inhibitors to the specific types. Undeveloped indications exist in the central nervous system (CNS) and the ability to target those underserved indications would enable a new means for targeting the underlying inflammatory causes of numerous diseases.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego and their international collaborators have developed a portfolio of issued and pending patents disclosing composition of matter and methods of selectively inhibiting s, i, and cPLA2s. Compositions span three, distinct chemical classes (amides, oxoamides, and fluoroketones) and proprietary methods claim treatment of various neurological illnesses, including hyperalgesia, multiple sclerosis (MS), and spinal cord injury. More detailed, non-confidential information is available in the Detailed Description.

ADVANTAGES

Proof of concept and IP is available for compositions of matter, target enzymes, and disease applications for novel relatively unexplored targets for a variety of neurological diseases for which good treatment options do not exist.

STATE OF DEVELOPMENT

In vitro and in vivo experiments validate a suite of potent inhibitors of PLA2, with differential specificity for the sPLA2, cPLA2, and iPLA2. Specifically, sPLA2 inhibitors markedly improve functional recovery and enhance tissue protection and axon regeneration in the mouse spinal-cord contusion injury model, while cPLA2 and iPLA2 inhibitors reduce the severity of disease in a widely used animal model of MS (experimental autoimmune encephalomyelitis, or EAE) and iPLA2 inhibitors protect in rat models of hyperalgesia.

INTELLECTUAL PROPERTY INFO


Numerous foreign issued patents are available online and unpublished applications are available under confidentiality. See also WO/2010/011666, Amides as Inhibitors of Human Secreted Phospholipase A2.

RELATED MATERIALS

See related case SD1998-078 as described in U.S. patent number 7,294,496.

OTHER INFORMATION

See related case SD1998-078 as described in U.S. patent number 7,294,496.

CATEGORIZED AS

Medical

- Disease: Autoimmune and Inflammation
- Disease: Central Nervous System
- New Chemical Entities, Drug Leads

RELATED CASES