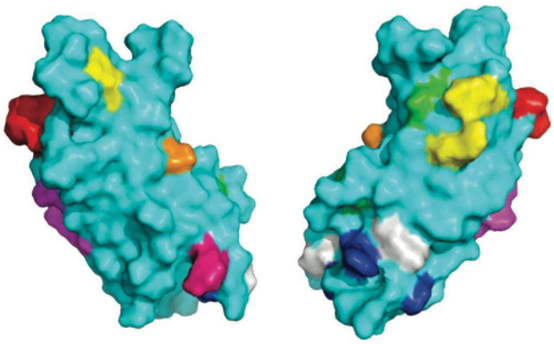
$cPLA_2$ inhibitors

Novel degradation-stable inhibitors of the $cPLA_2$

Invention

The cytosolic phospholipase A_2 ($cPLA_2$) is an enzyme that generates arachidonic acid by the cleavage of membrane phospholipids in response to stimuli like bacterial lipopolysaccharides. Arachidonic acid in turn is the precursor of the inflammatory mediator families of leukotrienes, prostaglandins and thromboxanes.



Basic residues of m-$cPLA_2$beta-C2 (taken from Ghomashchi et al, 2010)

Thus, the $cPLA_2$ is strongly involved in inflammatory reactions, and $cPLA_2$-deficient mice accordingly show reduced inflammatory, allergic and anaphylactic reactions as well as reduced infarction and neurologic deficits after experimental stroke.
Previously developed inhibitors of the $cPLA_2$ had the disadvantage of fast metabolic degradation, which only allowed topic application. The herewith offered group of substances is more degradation stable and thus displays a novel class of $cPLA_2$ inhibitors for systemic application in inflammatory and infectious diseases as well as other immunological disorders.

Commercial Opportunities

The $cPLA_2$ has been identified as target for the inhibition of inflammatory immune responses. The invented substances are of high interest for any pharma company with an immunological pipeline and may constitute the first-in-class $cPLA_2$ inhibitors for systemic application.

Current Status

The invented substances have been characterized with regard to the inhibition of the $cPLA_2$ (IC_{50} in the submicromolar range) and metabolic stability (tested in rat liver homogenates). The inventors are currently conducting such experiments with further, newly generated derivatives of the same inhibitor family. On behalf of the Westfalian Wilhelms-University of Muenster, PROvendis offers access to rights for commercial use as well as the opportunity for further co-development. In case of interest we will be pleased to inform you about the patent status.

Relevant Publications

Dennis EA, Cao J, Hsu YH, Magrioti V, Kokotos G. Phospholipase A_2 enzymes: Physical structure, biological function, disease implication, chemical inhibition and therapeutic invention. Chem. Rev. 2011; 111: 6130-85.
Ghomashchi F, et al. Interfacial kinetic and binding properties of mammalian group IVB phospholipase A_2 ($cPLA_2$) and comparison with other $cPLA_2$ isoforms. J. Biol. Chem. 2010; 285: 36100-11.

An invention of the Westfalian Wilhelms-University of Muenster.

Competitive Advantages

- **Degradation-stable $cPLA_2$ inhibitors**
- **Novel class of substances for systemic treatment of infectious and inflammatory disorders**

Contact:
Ref. No: 4441
Prof. Dr. Frank Entschladen

PROvendis GmbH
Schlossstr. 11-15
D-45468 Muelheim an der Ruhr
Germany
Phone: +49 (0)208 94 105 20
Fax: +49 (0)208 94 105 50
Email: fe@provendis.info
Web: www.provendis.info