mCRP as Therapeutic Target in Affective Disorder

An anti-inflammatory treatment for the treatment of psychiatric disorders such as depression

Reference: mCRP as Therapeutic Target

IP Status

Patent application submitted

Seeking

Development partner, Seeking investment

About LMU Munich

Ludwig-Maximilians-Universität München is the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. The LMU Munich community is engaged in generating new knowledge for the benefit of society at large.
Background

The project is related to the use of monomeric C-reactive protein (mCRP) as a therapeutic target in affective disorders. CRP is a widespread marker of inflammation, it exists in two isoforms, the 'normal' pentameric CRP (pCRP) and its dissociation product, the monomeric CRP (mCRP). pCRP has pro- and anti-inflammatory effects, while mCRP plays the key role in promoting inflammation especially in the central nervous system by activation of the pro-inflammatory cascade and enhancing the transmigration through the blood-brain-barrier. Preliminary results of animal experiments and patients-studies show that mCRP levels may serve as a diagnostic marker and that mCRP-triggered anxious and depressed behaviour can be reversed by antibodies against mCRP. The project aims to develop a mCRP antibody as an antidepressant.

Treatment resistance in affective disorders - e.g. to standard antidepressant therapy - occurs in ca. 30% of patients. The successful treatment of these patients is an unmet need in psychiatry. Moreover, 'closer' to the pathological process of affective disorders than drugs influencing neurotransmitters (serotonin, noradrenalin, dopamine) are specific therapies acting on the inflammatory cascade. Biomarker, genetic-, neuroimaging-, and therapeutic studies underline that low-grade inflammation plays an important role in the pathophysiology of affective disorders. Anti-inflammatory drugs show therapeutic effects in affective disorders. A key player in inflammation is C-reactive protein (CRP), CRP levels are enhanced in monopolar and bipolar depression and in anxiety disorder. CRP levels predict the antidepressant effect of an anti-TNF antibody in treatment-resistant depression. Preliminary results of LMU Munich’s own studies showed significantly higher serum levels of mCRP in depressed patients compared to controls. In a first series of animal experiments, it could be shown that the i.v. injection of mCRP raised inflammation in the central nervous system. In animal models of depression and anxiety, the application of mCRP increased anxious and depressed behaviour, while mCRP antibodies antagonized this effect. Moreover, impaired cognition (concentration, attention, memory) is a typical syndrome in affective disorders. A further series of LMU Munich experiments showed that cognition was impaired after application of mCRP and the application of mCRP antibodies reversed that impairment.

Tech Overview

Antidepressants are the most widely used drugs in affective disorders. Current antidepressants – a market of ca. 15 billions € per year - target the serotonergic, noradrenergic, dopaminergic, melatonergic neurotransmission, mostly by reuptake inhibition. The tremendous amount of failed antidepressant studies during the last years show that this approach is exhausted. A new promising approach is anti-inflammatory treatment, which has been described to be effective in affective disorders. General anti-inflammation, e.g. using cyclo-oxygenase (COX) inhibition seems not to be specific and target-oriented enough. mCRP is a promising candidate molecule for specific treatment of affective disorders, the effects of mCRP antibodies in animal experiments underline this view. The author was one of the first researchers who described the role of the immune system and inflammation in psychiatric disorders and the first one who showed the benefit of COX-2 inhibition in affective disorders,
specifically in depression. The confirmation of the therapeutic effect of an mCRP antibody in further animal experiments, a dose-response study, and planning a phase 1 study in humans are the next steps.

Further Details


Stage of Development

The project represents a very early stage of drug development. mCRP as a molecule of own pro-inflammatory action different from CRP was only recently described. It is discussed for therapeutic use also in certain heart diseases, macula degeneration, and Alzheimer’s disease. Preliminary results in humans show increased levels of mCRP in depression. In mice, pro-inflammatory effects of mCRP in the CNS were found (increase of IL-8 analogue) and in behavioral experiments of anxiety, depression and cognition, the anxiety and depression-inducing effect of mCRP, as well as the cognitive disturbance after application of mCRP, was shown. Two different antibodies against mCRP antagonized these effects. mCRP and antibodies are provided by cooperation partners in Manchester, GB.

Benefits

- Closer to the pathogenesis of affective disorders
- Therefore not only treatment of symptoms but sustainable cure of the disorder
- More target-oriented and specific treatment
- Effective in treatment resistance to standard antidepressants

Applications

Potential treatment of:

- Anxiety Disorder
- Depression (Market of antidepressants: worldwide estimation 15 billions € per year in 2015)
- Bipolar Disorder
Opportunity

LMU Munich is looking for partners for the next steps: the confirmation of the therapeutic effect of an mCRP antibody in further animal experiments including a dose-response study, and planning a phase 1 study in humans. Partners with know-how in animal studies, possibly in the development of antibodies and in planning a phase 1 study are warranted.
For further information, please contact us.

Ludwig-Maximilians-Universität München (LMU Munich)
Office for Research and Technology Transfer
- Corporate Partnerships -

Dr. Barbara Blaurock
+49(0)89 2180-722 13

corporatepartnerships@lmu.de
www.lmu.de/researchservices/corporatepartnerships/

Dr. Laura Gerwin
+49(0)89 2180-722 12