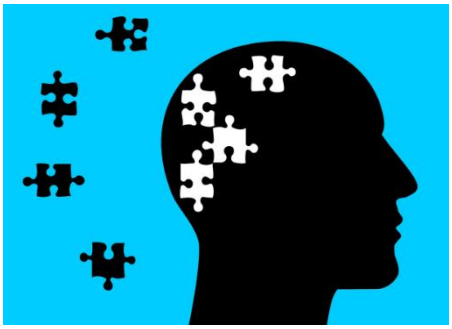
BioLab Assays

Monomeric CRP

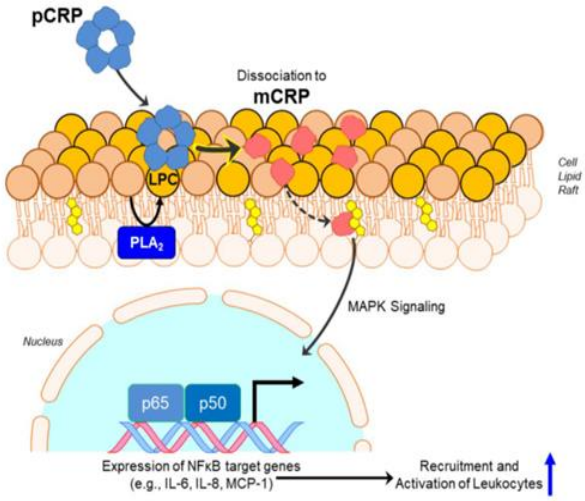


A KEY MOLECULE DRIVING DEVELOPMENT OF ALZHEIMER'S DISEASE?

BACKGROUND

C-reactive protein (CRP) is a multipotent protein that undergoes conformational changes between circulating native pentameric CRP (pCRP), pentameric symmetrical forms (pCRP*) and monomeric CRP (mCRP) forms. mCRP exhibits strong pro-inflammatory activity and activates platelets, leukocytes, and endothelial cells. Abundant deposition of mCRP in inflamed tissues plays a role in several disease conditions, such as ischemia/reperfusion injury, Alzheimer's disease, and cardiovascular disease.

Conversion of pCRP to mCRP induces inflammatory signalling, monoacyl phosphatidylcholine generated by PLA_2, or by oxidation lipid acyl chains, promotes binding and dissociation of pCRP to mCRP. mCRP gains functionally active neoepitopes that carry out highly pro-inflammatory and pro-thrombotic features, thus mCRP can bind cholesterol and enter plasmatic membrane and activate pro-inflammatory responses.

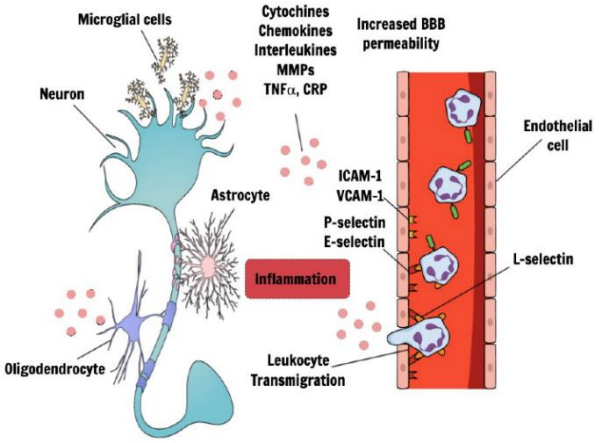


Reference: Rajab, Ibraheem & Hart, Peter & Potempa, L.A.: How C-Reactive Protein Structural Isoforms With Distinctive Bioactivities Affect Disease Progression. Frontiers in Immunology; 11. 2126 (2020)

Deposition of mCRP, which has a much lower aqueous solubility than pCRP, has been shown in the brain in infarcted areas of Alzheimer diseases patients and in regions with amyloid burden, in atherosclerotic plaques in vascular disease and in other foci of inflammatory tissue injuries.

Reference: Garcia-Lara E, Aguirre S, Clotet N, Sawkulycz X, Bartra C, Almenara-Fuentes L, et al. Antibody Protection Against Long-Term Memory Loss Induced by Monomeric C-Reactive Protein in a Kouse Model of Dementia. Biomedicines 9(7):828 (2021)

PRESENCE OF CRP IN THE BRAIN



Reference: Cipollini V et al.: Emerging Biomarkers in Vascular Cognitive Impairment and Dementia: From Pathophysiological Pathways to Clinical Application. Int J Mol Sci. 8;20(11):2812 (2019)

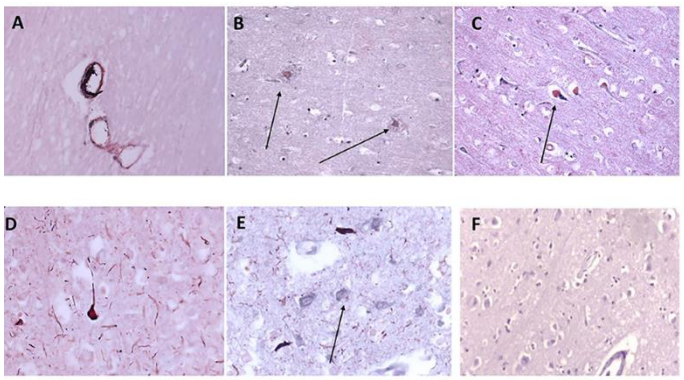
CRP is primarily produced by the liver in response to macrophage secreted IL-6. CRP expression, however, may be upregulated in glutamate neurons during specific disease states, such as Alzheimer's dementia. Human and animal studies show that mCRP co-localizes with α-amyloid plaques and with phosphorylated-tau protein in hippocampus. Other studies indicate that CRP is produced in the CNS, either in neurons, glia, and/or microvessel endothelial cells, during immune and homeostatic challenges with some indications that CRP may be neurotoxic. Furthermore, CRP contributes to increasing blood-brain barrier permeability through the endothelial modifications (e.g. after trauma) and thus allowing other inflammatory signaling factors to enter the CNS.

MONOMERIC CRP AND DEMENTIA

Inflammatory damage spreading from small blood vessels and linked dysregulation of amyloid β metabolism in the neurons have been implicated in the origin of Alzheimer disease. It is known that mCRP accumulates in brain micro-vessels after ischemic stroke, where it promotes aberrant angiogenesis, accumulation of amyloid β and probably de novo synthesis of amyloid β. Therefore, mCRP may cause both vascular and neuronal degeneration and underlie the processes leading to poststroke dementia. Specific targeting of mCRP can be a therapeutic approach in areas in which rapid increases in its local generation are expected, such as stroke-affected brain areas, in order to halt subsequent neurodegeneration and dementia. The prevalence of dementia in stroke survivors is about 30%, and a high proportion of these patients suffer from Alzheimer disease in addition to those with either vascular or mixed Alzheimer disease together with vascular dementia.

Al-Baradie described mCRP localized in the cerebral tissue of damaged vascular brain regions associated with neuroinflammation and neurodegeneration in an immunohistochemical study. They described co-localization of mCRP with β-amyloid or p-Tau in IHC samples from individuals with eurodegenerative disease.

Co-localization of mCRP with β-amyloid (A–C, microvessels, plaques and neurons, respectively) and co-localization of mCRP with p-Tau in neurons/fibrils (D,E) was shown. Control sample (F) shows a cortical region unaffected (no evidence of neurodegeneration).



Reference: Al-Baradie RS et al.: Monomeric C-Reactive Protein Localized in the Cerebral Tissue of Damaged Vascular Brain Regions Is Associated With Neuro-Inflammation and Neurodegeneration-An Immunohistochemical study. Front Immunol.; 12:644213 (2021)

BioLab Assays

IMPACT OF CIRCULATING MONOMERIC CRP ON ALZHEIMER DISEASE

Mouse model: Zhang et al. published a study with mice treated with mCRP, and showed that peripheral mCRP causes cerebrovascular inflammation and damages in ApoE4, but not in ApoE2 or ApoE3, mice via decreasing CD31 and increasing phosphorylated CD31. Garcia-Lara et al. found that anti mCRP antibody was able to completely block mCRP-induced chronic memory loss in a murine model of dementia where mCRP was injected into the hippocampus resulting in symptoms of neurodegeneration.

References:

Zhang Z et al.: Monomeric C-reactive protein via endothelial CD31 for neurovascular inflammation in an ApoE genotype-dependent pattern: A risk factor for Alzheimer's disease? Aging Cell; 20(11) (2021)

Garcia-Lara E, Aguirre S, Clotet N, Sawkulycz X, Bartra C, Almenara-Fuentes L, et al. Antibody Protection Against Long-Term Memory Loss Induced by Monomeric C-Reactive Protein in a Kouse Model of Dementia. Biomedicines 9(7):828 (2021)

Human studies: Need to be performed.

Human Monomeric CRP ELISA

BioLab Assays

Cat.No. BA1026

Sandwich ELISA: capture MAb specific to mCRP

Size: 96 wells

Measuring range: 1 - 50ng/ml

Sample type: serum

Regulatory status: RUO

Manufactured by **BioLab Assays s.r.o.**

Křižíkova 2697/70, 613 00 Brno, Czech Republic
www.biolabassays.eu info@biolabassays.eu

国内代理店：

株式会社　東京未来スタイル
Tel: 029-851-9222
Email: info@tokyofuturestyle.com