

III. C-REACTIVE PROTEIN

a. Introduction

The protein complex known as C-reactive protein (CRP) finds use as a biomarker for diseases having an immune component. CRP is an “acute phase protein,” meaning that its levels in the blood increase dramatically, from under 0.003 mg/mL to about 1.0 mg/mL, within days of the start of inflammation. Interleukin-6 (IL-6) is the main inducer of CRP’s acute-phase response. CRP has several biological functions, such as its ability to bind to phosphatidylcholine, including the phosphatidylcholine of infecting bacteria as well as the phosphatidylcholine that is exposed on dying human cells that are apoptotic or necrotic (95). CRP increases during autoimmune diseases, cancer, atherosclerosis, and heart attacks, as outlined:

- CRP is elevated in patients with chronic, pathological inflammation in the gut, as in Crohn’s disease and ulcerative colitis. This inflammation increases the risk for colorectal cancer.
- Elevated CRP occurs in patients with colorectal cancer, nonsmall-cell lung cancer, prostate cancer, and breast cancer. CRP has been proposed to have prognostic value for

these cancers, that is, to be a biomarker that predicts outcome of the disease.

- Where CRP levels in the bloodstream are slightly elevated (not markedly elevated) on a chronic basis, CRP serves as a prognostic factor for atherosclerosis.
- Acute changes in plasma CRP reflect tissue damage resulting from a heart attack. Acute, markedly elevated levels of CRP occur during a heart attack, where the CRP may contribute to the mechanism of tissue damage.

b. Biochemistry of C-Reactive Protein

C-reactive protein is a pattern-recognition molecule that mediates innate immune response. Because of CRP’s role in innate immune response, CRP has a function analogous to other pattern-recognition molecules such as the toll-like receptors (TLRs) and nucleotide-binding oligomerization domain (NOD) proteins (96,97). Specifically, CRP binds to phosphocholine (PC) as a component of microbial capsular polysaccharide and mediates the innate immune response against microorganisms (98). Binding of CRP to the PC of bacteria promotes clearing of the bacteria from the bloodstream. CRP finds use in protecting against pneumococcal infections (99,100), *Salmonella*

⁹⁵Pegues MA, et al. C-reactive protein exacerbates renal ischemia-reperfusion injury. *Am. J. Physiol. Renal. Physiol.* 2013;304:F1358–65.

⁹⁶Lee MS, Kim YJ. Pattern-recognition receptor signaling initiated from extracellular, membrane, and cytoplasmic space. *Mol. Cells* 2007;23:1–10.

⁹⁷Hartvigsen K, Chou MY, Hansen LF, et al. The role of innate immunity in atherogenesis. *J. Lipid Res.* 2009;50 (Suppl.):S388–93.

⁹⁸Chang MK, Binder CJ, Torzewski M, Witztum JL. C-reactive protein binds to both oxidized LDL and apoptotic cells through recognition of a common ligand: phosphorylcholine of oxidized phospholipids. *Proc. Natl Acad. Sci. USA* 2002;99:13043–8.

⁹⁹Kim JO, Romero-Steiner S, Sørensen UB, et al. Relationship between cell surface carbohydrates and intrastain variation on opsonophagocytosis of *Streptococcus pneumoniae*. *Infect. Immun.* 1999;67:2327–33.

¹⁰⁰Briles DE, Forman C, Horowitz JC, et al. Antipneumococcal effects of C-reactive protein and monoclonal antibodies to pneumococcal cell wall and capsular antigens. *Infect. Immun.* 1989;57:1457–64.