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Impact of C-reactive protein on Band 3 protein function in human erythrocytes

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Abstract

C-reactive protein (CRP) has a functional role in the inflammatory process and its concentration increases in circulation during inflammatory events. Transcriptional induction of the *CRP* gene mainly occurs in hepatocytes in the liver in response to increased levels of inflammatory cytokines, especially interleukin-6 (IL-6), therefore CRP is used as a clinical marker of inflammation. Elevated serum CRP levels are related to different inflammatory diseases such as cholecystitis, cardiovascular disease, cancer, type 2 diabetes, appendicitis and pancreatitis. The present study addressed the impact of CRP on Band 3 protein (B3p) function in human erythrocytes. The activity of B3p, mediating Cl^-/HCO_3^- exchange through erythrocytes membrane, can be monitored by measuring the rate constant for $SO_4^=$ uptake. Blood was withdrawn from both patients with acute inflammation (13 ♀, 9 ♂, age range 28–75 years) and healthy volunteers (10 ♀, 10 ♂, age 28–70 years). CRP levels higher than 8 mg/L were considered as a strong predictor of inflammatory disease and the rate constant for $SO_4^=$ uptake was measured by a turbidimetric method. Elevated serum CRP levels induced a significant increase in both anion exchange capability through B3p and in $SO_4^=$ trapped by the cells with respect to control (healthy volunteers). Once serum CRP levels in patients with acute inflammation were brought back to control values, anion exchange capability through B3p was restored. The present findings show that: i) measurement of the rate constant for $SO_4^=$ uptake is a suitable tool to monitor the effect of elevated serum CRP levels on human erythrocytes due to acute inflammation; ii) high CRP levels seem to accelerate anion exchange capability through B3p; iii) inflammation remission seems to correspond to B3p function restoration. Future studies will evaluate whether this acceleration may depend on an altered Bp3 conformation possibly affecting B3p crosslink with Hb, or on altered oxidative and phosphorylative signaling on B3p function, in an attempt of better understanding the impact of inflammation processes on erythrocytes homeostasis.

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