Two types of humoral response in acute myocardial infraction

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Background: Atherothrombosis and myocardial infarction are accompanied by the development of an inflammatory reaction. The severity of the immune reaction and its role in the acute myocardial infarction (AMI) remain contradictory to date.

Purpose: The objective of this study was to analyze 39 cytokines and chemokines in the serum of patients hospitalized with AMI compared to the healthy volunteers.

Methods: All patients included in the study were COVID-19 negative. Patients' blood was collected within 1–2 days after hospitalization in the cardiology department. Cytokine and chemokine detection in the serum of patients (n=20) and donors (n=20) was performed using a 39-plex set of cytometric beads.

Results: Among all factors analyzed TGFa, IL-17A, IL-1b, 3, 5, 9 were not detected both in patient and donor sera. Three groups of factors were identified in the normal serum: housekeeping chemokines and vascular factors (F1) ranged from 1000 to 22000 pg/mL (Fig. a); sentinel innate immunity factors F2 (Fig. b), 30–200 pg/mL; and acute phase factors F3 (Fig. c, d), 0–30 pg/mL, detected only in 0–30% of donors but in all AMI patients. Severe imbalance was found in AMI sera at all three levels including chemokine, growth factors, and cytokines. Among AMI patients 65% (Gr1) demonstrated 2–4 times increased level (Fig. a, grey brackets) while 35% (Gr2) had a decreased level of F1 factors in a comparison with donor sera. There was not significant difference between clinical features of the patients in Gr1 and Gr2. GRO, PDGF-AA, and sCD40L levels decreased 35, 15, and 10 times accordingly. Gr1 and Gr2 also differed in F2 and some F3 concentrations: Gr1 had 3–5 times increased level of multiple factors (Fig, b), among them – IL-6, IL-8, and IL-10 were increased 5, 6, and 14 times. At the same time Gr2 had a normal level of these factors (Fig, b, blue brackets). Finally, multiple cytokines and growth factors F3 were significantly increased in both AMI groups (Fig, b, d, red brackets). Of note, IL-12, IFN-g, IL-15, GM-CSF, FLT-3T were increased 8, 6, 5, 5, 5 times accordingly in pooled Gr1+Gr2. There were no correlations found between cytokine profiles in Gr1 and Gr2 and their clinical parameters.

Conclusions: Two types of humoral response in AMI patients were identified which differed in the levels of GRO, PDGF-AA, and sCD40L. IL-6 as well as TNF-a can not serve as master cytokines because their levels were increased only in Gr1 patients. These data show that Th1 cytokine increase is specific for AMI. Further studies are needed to identify groups of patients who may be exposed to new therapeutic targets.

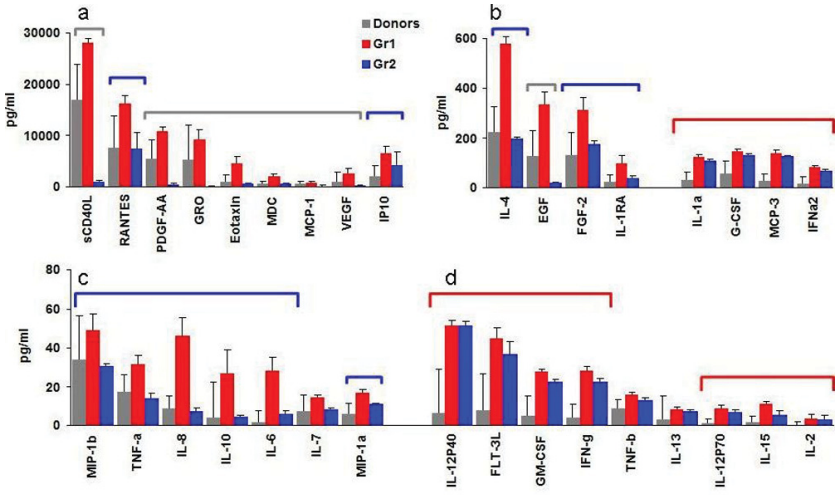

Figure. Concentration of humoral factors in blood sera of healthy donors (grey) and patients with acute myocardial infarction characterized by high (Gr1, red) and low (Gr2, blue) level of major house-keeping factors sCD40L, PDGF-AA, and GRO (a). Concentration of innate immunity factors (b) and acute phase ones (c, d). Significant difference between Gr1, Gr2 data from donors is shown with grey and red brackets; between Gr1 and donors – by blue brackets