Transcriptome meta-analysis reveals altered metabolic pathways in leukocytes from septic patients.

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Background: Immune cells function is modulated during sepsis. Metabolic regulation is strictly related with the immune response. Here we analyzed three sepsis microarray databases searching for metabolic alterations in leukocytes from septic patients.

Methods: Three microarray databases of whole blood or leukocytes from septic patients were selected from GEO (Expression Omnibus Gene Expression) and ArrayExpress: E-MTAB-5273 (46 patients/10 controls), GSE65682 (468 patients/42 controls) and E-MTAB-1548 (82 patients/15 controls). Analyses were performed with LIMMA package from R software. Sepsis differentially expressed genes (DEGs) were those with Log2 fold change > 1 and p value < 0.05. DEGs found in at least two datasets and with similar modulation, e.g. up- or down-regulated, were analyzed with Ingenuity Pathway Analysis (IPA) and with hallmark gene sets in Molecular Signatures Database v6.2. Signatures were significant when FDR < 0.05.

Results: We identified 1451 DEGs modulated in the same direction in at least two datasets; most of them (853) were negatively regulated compared to controls. Functional analysis with IPA showed impaired effector functions of immune cells but pointed to preserved phagocytosis. Different molecular signatures related to metabolic pathways, such as hypoxia, glycolysis, mTORC1 signaling fatty acid metabolism and oxidative phosphorylation were top scored in septic patients. Genes related to glycolysis and electron transport chain were mostly upregulated in septic patients, while genes related to PI3k/Akt/mTOR were predominantly downregulated. Genes related to fatty acid metabolism were also disturbed.

Conclusion: Metabolic pathways appears as important altered functions in septic patients. Our results corroborate the importance of metabolic alterations in immune regulation during sepsis.