Septic shock

Most often due to gram negative sepsis.

Genetic deletions decreasing serum alpha-Klotho (alpha-KL) have been associated with rapid aging, multi-organ failure and increased mortality in experimental sepsis. Abdelmalik et al. hypothesized that lower Alpha klotho obtained at the onset of septic shock correlates with higher mortality.

Prospective cohort of 104 adult patients with septic shock. Alpha-KL was measured via ELISA on serum collected on the day of enrollment (within 72h from the onset of shock). Relationship between alpha-KL and clinical outcome measures was evaluated in uni- and multi-variable models.

Median (IQR) alpha-KL was 816 (1020.4) pg/mL and demonstrated a bimodal distribution with two distinct populations, Cohort A [n=97, median alpha-KL 789.3 (767.1)] and Cohort B [n=7, median alpha-KL 4365.1(1374.4), >1.5 IQR greater than Cohort A]. Within Cohort A, ICU non-survivors had significantly higher serum alpha-KL compared to survivors as well as significantly higher APACHE II and SOFA scores, rates of mechanical ventilation, and serum BUN, creatinine, calcium, phosphorus and lactate (all p≤0.05). Serum alpha-KL≥1005, the highest tertile, was an independent predictor of ICU mortality when controlling for co-variates (p=0.028, 95% CI 1.143-11.136).

Elevated serum alpha-KL in patients with septic shock is independently associated with higher mortality. Further studies are needed to corroborate these findings [1].

Liu et al. aimed to identify important genes associated with septic shock and then explore the possibly significant mechanisms of this disease. We downloaded GSE26440 expression data of samples from 98 children with septic shock and 32 normal controls from the Gene Expression Omnibus (GEO) database. Differentially expressed genes (DEGs) in samples from patients with septic shock were analyzed in comparison with those in samples from normal controls using a limma package. Functional enrichment analysis for DEGs was performed using DAVID, and a protein□protein interaction (PPI) network was constructed. Upstream transcription factors for DEGs were predicted using the CHIPBase database, and a transcriptional regulation network was constructed. A total of 383 significantly DEGs, including 141 downregulated and 242 upregulated genes, were obtained in the sepsis shock group compared with the normal group. The top five nodes in the PPI network were lysine (K)-specific demethylase 6B (KDM6B), histone deacetylase 2 (HDAC2), V-Myc avian myelocytomatosis viral oncogene homolog (MYC), heat-shock protein 90 kDa alpha (cytosolic), class B member 1 (HSP90AB1), and poly (A)-binding protein, cytoplasmic 1 (PABPC1). Nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB) was the transcription factor targeted by most genes, and it regulated the expression of KDM6B, HDAC2, MYC, HSP90AB1, and PABPC1. In conclusion, KDM6B, HDAC2, MYC, HSP90AB1, and PABPC1 may play important roles in the development of septic shock. Furthermore, NFκB may be involved in septic shock by regulating the expression of KDM6B, HDAC2, MYC, HSP90AB1, and PABPC1 [2].

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Abdelmalik PA, Stevens RD, Singh S, Skinner J, Carhuaopoma JR, Noel S, Johns R, Fuchs RJ. Anti-aging factor, serum alpha-Klotho, as a marker of acute physiological stress, and a predictor of ICU mortality, in patients with septic shock. J Crit Care. 2017 Nov 16;44:323-330. doi: 10.1016/j.jcrc.2017.11.023. [Epub ahead of print] PubMed PMID: 29268200.
2)

Liu SY, Zhang L, Zhang Y, Zhen Y, Wu YF. Bioinformatic analysis of pivotal genes associated with septic shock. J Biol Regul Homeost Agents. 2017 Oct-Dec;31(4):935-941. PubMed PMID: 29254296.