Adipose Tissue Role in Neonatal Sepsis.

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Background: The role of adipose tissue (AT) in the course of infectious diseases such as sepsis remains underappreciated. However, AT role has emerged as an important source of endocrine and immunologically active cell populations with multiple effects on homeostasis regulation. Alterations in the systemic and tissue environment can be recognized by adipocytes, leading them to respond to bacterial, fungal, or viral components and promoting altered immune cell responsiveness, metabolic pathways, and inflammatory vigor. Thus, our goal was to investigate the role of the white (WAT) and brown adipose tissue (BAT) depots and physiological outcomes during neonatal sepsis.

Methods: Postnatal day 5 (PD5) CD1 mice were I.P. treated either with saline (Control), LPS, or Pam3CSK4, weight and temperature were accessed, and pups were euthanized after 3 hours. Subcutaneous WAT and BAT depots were dissected out and snap-frozen in N2. Total RNA was extracted with TRIzol Plus PureLink™ RNA Purification Kit. Clariom™ S Assay mouse and the Affymetrix GeneChip Mouse Gene ST 2.0 arrays were performed for transcriptome analysis. Differential gene expression was analyzed using a cutoff of 2-fold change and P-value of 0.01 and t-test in comparison to the control.

Results: Systemic inflammation promoted either by Gram-positive or Gram-negative infection resulted in significant weight loss gain. The cutaneous temperature remained without significant changes in the control, whereas LPS induced a major variation of -1.5°C, and -0.5°C followed by Pam3CSK4. Within the decreasing body temperature and mass, we set out the hypothesis the AT is contributing to these alterations. To this end, a total of 103 genes were upregulated by LPS exposure, and 238 genes following Pam3CSK4 in BAT, while 85 and 249 genes were downregulated, respectively. The enriched terms network showed 3 clusters in the LPS group, in which, Collagen-containing extracellular matrix, Hippocampus development, Inflammatory response were the tops GO enriched in BAT. Pam3CSK4 promoted GO enrichment of Blood coagulation, mRNA metabolic process, Condensed chromosome, and Chromocenter showing 5 networks clusters. In WAT, 153 and 204 genes were upregulated by LPS and Pam3CSK4, respectively, while 299 and 402 were downregulated. GSEA followed by LPS revealed Chemokines Receptors, Action Potential, and C1q Complex Response highly enriched. In the network GSEA following Pam3CSK4, solely 2 clusters were observed. Cluster 1 presented a strong network among Lipid Catabolic process, Lipase activity, phenol-containing compound metabolic process and temperature homeostasis.

Conclusions: Collectively, these findings highlight the heterogeneity of AT depots in response to the systemic inflammatory insult along with dysregulated temperature and decreased bodyweight control. Thus, in the course of neonatal sepsis, AT involvement can lead to important physiological outcomes for the newborn.