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Peptidoglycan Vaccine-On-Chip against a Lipopolysaccharide-Induced Experimental Sepsis Model

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Abstract : Lipopolysaccharide (LPS) is commonly used in murine sepsis models, which are largely associated with immunosuppression (incretion of MDSCs cells and Tregs, imbalance of inflammatory/anti-inflammatory cytokines) and collapse of the immune system. After adapting the LPS treatment to the needs of locally bred BALB/c mice, the present study explored the protective role of Micrococcus luteus peptidoglycan (PG) pre-activated vaccine-on chip in endotoxemia. The established protocol consisted of five daily intraperitoneal injections of 0.2mg/g LPS. Such protocol allowed longer survival, necessary in the prospect of the therapeutic treatment application. The so-called vaccine-on-chip consists of a 3-dimensional laser micro-texture Si-scaffold loaded with BALB/c mouse macrophages and activated in vitro with 1μg/ml PG, which exert its action upon subcutaneous implantation. The LPS treatment significantly decreased CD4+, CD8+, CD3z+, and CD19+ cells, while increasing myeloid-derived suppressor cells (MDSCs), CD25+, and Foxp3+ cells. These results were accompanied by increased arginase-1 activity in spleen cell lysates and production of IL-6, TNF-a, and IL-18 while acquiring severe sepsis phenotype as defined by the murine sepsis scoring. The in vivo application of PG pre-activated vaccine-on chip significantly decreased the percent of CD11b+, Gr1+, CD25+, Foxp3+ cells, and arginase-1 activity in the spleen of LPS-treated animals, while decreasing IL-6 and TNF-a in the serum, allowing survival to all animals tested and rescuing the severity of sepsis phenotype. In conclusion, these results reveal a promising mode of action of PG pre-activated vaccine-on chip in LPS endotoxemia, strengthening; thus, the use of treatment is septic patients.

Keywords : myeloid-derived suppressor cells, peptidoglycan, sepsis, Si-scaffolds
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