

论著

内毒素休克小鼠肝脏血管内皮细胞特异性结合肽的体内筛选及初步鉴定

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摘要 目的: 利用体内噬菌体展示技术筛选能与内毒素休克小鼠肝脏血管特异性结合的短肽。
方法: 尾静脉注射噬菌体环七肽库至内毒素休克小鼠体内, 循环10 min后, 回收肝脏中的噬菌体。将回收的噬菌体扩增、纯化, 并以此为起始物进行下一轮筛选。经过4轮筛选后, 将所得文库与正常小鼠做一次差减筛选。随机挑取噬菌体单克隆进行测序, 序列分析后, 进行噬菌体的体内回输实验及免疫组化分析, 验证所筛得噬菌体克隆的导向情况。

结果: 经过4轮体内筛选, 肝脏中噬菌体回收率逐步提高, 证明噬菌体文库在肝脏血管中得到有效富集。DNA测序后发现, 10条序列中有5条为LTTWAPA, 体内回输实验和免疫组化实验均证实表达该序列的噬菌体能有效地靶向于休克小鼠肝脏血管内皮细胞。

结论: 筛选到的短肽LTTWAPA能特异性结合于内毒素休克小鼠肝脏血管内皮细胞, 有可能对内毒素休克的治疗具有重要意义。

关键词 [噬菌体展示](#); [休克](#); [脓毒性](#); [肝](#); [内皮细胞](#); [特异性结合肽](#)

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In vivo screening and characterization of peptides specifically binding to vasculature endothelial cells of liver in mice with septic shock

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Abstract

AIM: To screen peptides specifically binding to vasculature of liver in mice with septic shock.
METHODS: Peptide display libraries were injected into septic shock mice by tail vein injection. After circulating for 10 min, the phages from mouse livers were recovered, amplified and purified following a routine protocol, and then re-injected for the next round screening. After screening for 4 rounds in vivo, the phage libraries were injected into normal mice by tail vein injection and the phages were recovered by serum collection to subtract the peptides binding with endothelial cells of normal mice. Then the phage clones were sequenced and further analyzed by bioinformatics. The interested phage clones were reinfused to the mice with septic shock, and appraised by titering the phage distribution in vivo and immunohistochemical staining of the mouse liver.

RESULTS: After 4 rounds of biopanning, the phage recovery rates increased step by step, indicating that the phage library was successfully enriched in the livers of mice with septic shock. Fifty percent (5/10) of the analyzed sequences were identical, and with a sequence of LTTWAPA. In vivo titering and immunohistochemical staining displayed that this sequence selectively targets liver of mice with septic shock.
CONCLUSION: The peptide of LTTWAPA specifically binds to vascular endothelial cells of liver in septic shock mice, which may have important significance for the therapy of septic shock.

Key words [Phage display](#) [Shock](#) [septic](#) [Liver](#) [Endothelial cells](#) [Specific binding peptide](#)

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