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Survivin HLA-A2+高亲和性CTL表位的预测及鉴定 点此下载全文

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摘要：

目的：采用生物信息方法预测和鉴定survivin抗原HLA A2 +限制性CTL表位，为探索基于survivin的肿瘤免疫治疗奠定基础。〖HT5W〗方法：〖HT5"SS〗采用超基序法和量化基序法对靶抗原survivin HLA A2 +限制性 CTL表位进行预测；选取得分>10的表位肽为候选对象，并进行人工合成。采用T2细胞，以HLA A2结合实验和流式细胞术（FITC染色）检测候选CTL表位肽的结合亲和力\[以荧光系数（fluorescence index,FI）表示\]；以HLA A2解离实验和流式细胞术检测其结合稳定性\[以复合物解离50%的时间DC 50 （dissociation complex 50%）表示\]。〖HT5W〗结果：〖HT5"SS〗预测到的候选survivin CTL表位肽分别是：20 STFKNWPFL 28 (SV 20 28)、 23 KNWPFLEGC 31 (SV 23 31)、 96 LTLGEFLKL 104 (SV 96 104)、6LPPAWQPFL 14 (SV 6 14)、 33 CTPERMAEA 41 (SV 33 41)、 46 CPTENEPDL 54 (SV 46 54)、 130 KVRRAIEQL 138 (SV 130 138)、 37 RMAEAGFIH 45 (SV 37 45)、 88 SVKKQFEEL 96 (SV 88 96)。亲和力分析显示： SV 20 28 、SV 96 104 、SV 130 138 、SV 23 31 的FI分别为8.61、6.88、5.89、3.81；SV 33 41 、SV 6 14 、SV 46 54 、SV 37 45 、SV 88 96 的FI分别为0.31、-0.29、 -0 4 、-0.16和-0.03；稳定性分析结果DC 50 为：SV 20 28 、SV 96 104 、SV 130 138 >8 h；SV 23 31 为4~6 h；SV 6 14 、SV 33 41 、SV 88 96 为2~4 h；SV 46 54 、SV 37 45 为0~2 h。结果提示,SV 20 28 、SV 96 104 、SV 130 138 为高亲和力表位肽，SV 23 31 为中等亲和力表位肽，SV 33 41 、SV 6 14 、SV 46 54 、SV 37 45 、SV 88 96 为低亲和力表位肽。〖HT5W〗结论：〖HT5"SS〗超基序法、量化基序法可快速有效地预测抗原表位，SV 20 28 、SV 96 104 、SV 130 138 有可能是survivin HLA A2 + CTL表位，可用于后续研究。

关键词：survivin CTL表位 T2细胞 生物信息方法

Prediction and identification of survivin specific HLA-A2+ CTL restricted high affinity epitope Download Fulltext

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Abstract:

Objective: To predict and identify survivin specific HLA A2 + CTL restricted epitopes by bio informatic methods, so as to provide a foundation for survivin based immunotherapy. Methods: Survivin specific HLA A2 + restricted CTL epotides were predicted by computer super motif algorithm combined with quantitative motif algorithm. Candidate epitopes were verified when their scores were higher than 10 and were then artificially synthesized. Affinity of candidate epitope was examined by HLA A2 binding assay combined with flow cytometry using T2 cells (shown as fluorescence index, FI). Stability of candidate epitope was evaluated by HLA A2 dissociation assay combined with flow cytometry (shown as 50% complex dissociation time, DC50). Results: Nine candidate epotides were obtained: 20 STFKNWPFL 28 (SV 20 28), 23 KNWPFLEGC 31 (SV 23 31), 96 LTLGEFLKL 104 (SV 96 104), 6LPPAWQPFL 14 (SV 6 14), 33 CTPERMAEA 41 (SV 33 41), 46 CPTENEPDL 54 (SV 46 54), 130 KVRRAIEQL 138 (SV 130 138), 37 RMAEAGFIH 45 (SV 37 45), and 88 SVKKQFEEL 96 (SV 88 96). HLA A2 binding assay showed that FI values of SV 20 28 , SV 96 104 , SV 130 138 and SV 23 31 epotides were 8.61, 6 88, 5.89 and 3.81, respectively; those of SV 33 41 , SV 6 14 , SV 46 54 , SV 37 45 and SV 88 96 epotides were 0.31, -0.29, -0 4 ,-0.16 and -0.03, respectively. HLA A2 dissociation assay showed that DC 50 values of SV 20 28 , SV 96 104 and SV 130 138 epotides were longer than 8 h; that of SV 23 31 epotide was 4 6 h; those of SV 6 14 , SV 33 41 and SV 88 96 epotides were all 2 4 h; those of SV 46 54 , SV 37 45 epotides were both 0 2 h. The above results demonstrated that SV 20 28 , SV 96 104 and SV 130 138 were high affinity epotides; SV 23 31 was intermediate affinity epotide; and SV 33 41 , SV 6 14 , SV 46 54 , SV 37 45 and SV 88 96 were low affinity epotides. Conclusion: Antigen epitope can be quickly and efficiently predicted by super motif algorithm combined with quantitative motif algorithm. SV 20 28 , SV 96 104 and SV 130 138 epitopes are survivin specific HLA A2 + restricted CTL epotides, which can be used for later research.

Keywords:survivin CTL epitope T2 cell bio informatic method