中国寄生虫学与寄生虫病杂志
CHINESE JOURNAL OF PARASITOLOGY AND PARASITIC DISEASES
ISSN 1000-7423
CN 31-1248/R
主管：中华人民共和国国家卫生和计划生育委员会
主办：中华预防医学会
中国疾病预防控制中心寄生虫预防控制所

中国寄生虫学与寄生虫病杂志 » 2013, Vol. 31 » Issue (6) :438-442 DOI:

细粒棘球蚴抗原B亚单位多表位重组抗原的血清学诊断评价

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Serodiagnosis of the Recombinant Multi-epitope Antigens from Antigen B Subunits of *Echinococcus granulosus*

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摘要 参考文献 相关文章

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摘要 目的 对6个细粒棘球蚴抗原B（AgB）亚单位多表位重组抗原和3个AgB亚单位抗原进行血清学平行比较分析，评价多表位抗原的诊断价值。 方法 在多表位重组抗原MEA-26中插入一段Linker序列，成为MEA-49抗原。用I-TASSER在线服务器模拟分析蛋白质三维结构，比较2个目标序列相同但三维结构不同的重组抗原（MEA-26和MEA-49）在样品检测中反应性的差异。用间接ELISA方法对6个多表位抗原（MEA-8、MEA-20、MEA-26、MEA-36、MEA-49和MEA-52）、3个亚单位抗原（AgB1、AgB2和AgB4）和2个对照抗原（Trx和Linker）平行检测232份血清样品（细粒棘球蚴病患者血清112份、多房棘球蚴病患者血清35份、囊尾蚴病患者血清43份和健康人血清42份），并用ROC曲线分析不同抗原对细粒棘球蚴病患者血清的诊断价值。 结果 三维模型预测结果显示，MEA-26的表位区域相互靠近，呈平行排列；MEA-49表位区域相互分离形成独立的结构域。用MEA-49抗原检测细粒棘球蚴病患者血清的反应性（2.88±2.02）、敏感性（92%）和诊断效率（89%）等均高于MEA-26抗原（2.54±2.02，78%，82%）。ELISA结果显示，MEA-20（2.24±1.31）、MEA-26（2.54±2.02）、MEA-36（2.44±1.51）、MEA-49（2.88±2.02）和MEA-52（2.50±1.37）等5个抗原检测细粒棘球蚴病患者血清的反应性均高于AgB1抗原（2.15±1.26）。多表位抗原检测多房棘球蚴病患者血清的反应性与AgB1抗原的比较，差异无统计学意义（P>0.05）。MEA-52抗原检测囊尾蚴病患者血清（1.27±0.70）的反应性显著高于AgB1抗原（0.95±0.13） （P<0.01）。6个多表位抗原检测健康人血清的反应性仅MEA-8抗原的反应性（1.04±0.15）与AgB1抗原（0.89±0.07）差异有统计学意义（P<0.01）。ROC曲线结果显示，3个亚单位抗原检测细粒棘球蚴病患者血清的敏感性以AgB1抗原最高，为77%；MEA-49（92%）、MEA-36（92%）、MEA-52（87%）和MEA-26（78%）等4个多表位抗原的检测敏感性均高于AgB1抗原。 结论 多表位抗原的总体反应性优于亚单位抗原，MEA-49抗原对不同患者血清的反应性均强于目标序列相同但三维结构不同的MEA-26抗原。

关键词： 细粒棘球蚴 AgB抗原亚单位 多表位重组抗原 血清学分析

Abstract: Objective To evaluate the diagnostic value of six recombinant multi-epitope antigens and three AgB subunit antigens from antigen B subunit of *Echinococcus granulosus*. Methods A linker sequence was inserted into the sequence of MEA-26 to make it an MEA-49. I-TASSER on-line server was used to analyze protein structure. The reactivity of two multi-epitope recombinant antigens with the same target sequence but in different tertiary structure was compared. The reactivity of six multi-epitope antigens (MEA-8, MEA-20, MEA-26, MEA-36, MEA-49, and MEA-52), 3 subunit antigens (AgB1, AgB2, and AgB4), and 2 control antigens (Trx and linker) was determined by indirect ELISA. The assays were performed on 232 serum samples separated as follows: 112 sera from patients with cystic echinococcosis, 35 sera from individuals with alveolar echinococcosis, 43 sera from patients with cysticercosis and 42 sera from healthy individuals. Their diagnostic performance was assessed by receiver operating characteristic (ROC) curve analysis. Results Tertiary structure prediction showed that the epitope regions of MEA-26 were closer to each other and aligned in parallel, while that in MEA-49 were farther apart from each other and formed two independent domains. Serological analysis revealed that the mean P/N value (2.88±2.02), sensitivity (92%) and diagnostic efficiency (89%) of MEA-49 were higher than that of MEA-26 (2.54±2.02, 78% and 82%). MEA-20 (2.24±1.31), MEA-26 (2.54±2.02), MEA-36 (2.44±1.51), MEA-49 (2.88±2.02) and MEA-52 (2.50±1.37) showed a high reactivity to the sera from patients with cystic echinococcosis, which was superior to that of AgB1 (2.15±1.26). There was no significant difference in the reactivity to sera from individuals with alveolar echinococcosis between multi-epitope antigens and AgB1 (*P*>0.05). MEA-52 showed a high diagnostic sensitivity in cysticercosis cases (1.27±0.70), superior to that of AgB1 (0.95±0.13) (*P*<0.01). The reactivity of MEA-8 (1.04±0.15) to sera from healthy individuals was significantly higher than that of AgB1 (0.89±0.07) (*P*<0.01). ROC analysis showed in the cases of cystic echinococcosis, the diagnostic sensitivity accomplished with AgB1, AgB2, and AgB4 was 77%, 55%, and 66%, respectively; the multi-epitope antigens of MEA-49 (92%), MEA-36 (92%), MEA-52 (87%), and MEA-26 (78%) revealed a higher sensitivity than

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AgB1. Conclusion The reactivity of multi-epitope antigens is superior to that of AgB subunit antigens. The reactivity of