肿瘤防治研究 2012, Vol. 39 Issue (2): 169-172 DOI: 10.3971/j.issn.1000-8578.2012.02.013
临床研究

运用MALDI-TOF MS方法建立食管癌患者血清蛋白指纹图谱诊断模型

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Serum Protein Fingerprint Diagnoic Patterns was Established by MALDI-TOF MS for Human Esophagial Carcinoma

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全文: PDF (2151 KB) HTML (0 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 目的

本研究利用基质辅助激光解析离子化飞行时间质谱（matrix-assisted laser desorption/ionization time-of-flight mass spectrometry，MALDI-TOF MS）技术检测食管癌患者血清蛋白指纹图谱，建立食管癌诊断模型，探讨其临床应用价值。方法采用弱阳离子蛋白芯片（WCX磁珠）对血清进行分析前处理，运用MALDI-TOF MS技术检测119例标本（75例食管癌和44例健康对照）血清蛋白质谱图，通过蛋白芯片数据分析系统进行数据处理，以遗传算法结合支持向量机运算建立食管癌与健康对照组、早期食管癌与中晚期食管癌组诊断模型，随机抽取79例建模标本（50例食管癌和29例健康对照）进行训练与交叉验证，并选择新病例（30例食管癌和23例健康对照）血清标本进行测试。结果采集食管癌患者和健康对照者的血清蛋白质纹图谱，经数据分析找到75个有显著性差异的质荷比峰（P<0.05）和71个有非常显著性差异的质荷比峰（P<0.01）；软件包运算后，建立两个诊断模型：模型1：区分食管癌与健康对照组，由11个蛋白质峰（2 087，2 210，3 258，3 973，4 283，4 645，4 092，4 210，1 985，2 818和2 046 Da）组成，该诊断模型检测食管癌的敏感度为92.4%，特异性为87.4%；模型2：区分早期食管癌与中晚期食管癌组，由8个蛋白质峰（4 195，4 074，4 268，2 106，4 905，5 965，2 863 和 3 953 Da）组成，该诊断模型检测食管癌的敏感度为87.5%，特异性为89.7%。结论运用MALDI-TOF MS技术结合磁珠分选的方法可检测食管癌血清质谱图，建立具有较高的敏感度和特异性食管癌诊断模型。

关键词： 食管癌 基质辅助激光解析离子化飞行时间质谱 血清蛋白质组学

Abstract: Objective

To find biomarkers and establish a serum protein fingerprint model for early diagnosis of ESCC through matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).MethodsSerum samples were collected from 75 patients with ESCC and 44 healthy individuals.Proteomic spectra of mass to charge ratio (m/z) was generated by weak cationic-exchanger magnetic beads (WCX-MB).Data were processed by protein microarray data analysis system.A diagnosis model to identify normal from early esophageal cancer or advanced esophageal cancer was established using support vector machines combined with genetic algorithms.79 specimens (50 cases of esophageal cancer and 29 cases of healthy controls) were randomly selected for training and cross-validation.At last, the new (30 patients with esophageal cancer and 23 healthy controls) serum specimens were detected as a testing cohort.ResultsTwo different patterns were established by MALDI-TOF MS.Pattern 1, using 11 protein peaks, were able to separate ESCC patients from the healthy individuals with a sensitivity of 92.4% and a specificity of 87.4%.Pattern 2, using 8 protein peaks, were able to separate ESCC of stage I and stage II from stage III and stage IV with a sensitivity of 97.5% and a specificity of 85.7%.ConclusionThese results suggested that MALDI-TOF MS combined with MB separation could generate a serum protein fingerprint model with high sensitivity and specificity for ESCC diagnosis.

Key words: Esophageal carcinoma Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry Serum proteomics

收稿日期: 2011-04-07;

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刘丽华,孟君,张璁等. 运用MALDI-TOF MS方法建立食管癌患者血清蛋白指纹图谱诊断模型[J]. 肿瘤防治研究, 2012, 39(2): 169-172.

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