ORIGINAL ARTICLE

Serum Human Epididymis Secretory Protein 4 (HE4) is a Potential Prognostic Biomarker in Non-Small Cell Lung Cancer

Dongping Mo [1] and Fang He [2]

[1] Department of Clinical Laboratory, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China
[2] Department of Clinical Laboratory, Nanjing Integrated Traditional Chinese and Western Medicine Hospital Affiliated with Nanjing University of Chinese Medicine, Jiangsu, China

SUMMARY

Background: Human epididymis secretory protein 4 (HE4) is a secreted glycosylated protein belonging to the WFDC family, which is an ideal biomarker in ovarian cancer. However, the role of HE4 in lung cancer is still unclear. The study aimed to evaluate serum levels of HE4 as a prognostic biomarker in patients with non-small cell lung cancer (NSCLC).
Methods: The subjects consisted of 217 NSCLC patients, which were compared to a control group of 80 patients with benign lung disease and 110 healthy controls. Serum levels of HE4 were measured with electrochemiluminescence assays in a Roche E601 Immunoassay Analyzer.
Results: Serum levels of HE4 in NSCLC patients were significantly higher than in benign lung disease and healthy controls ($p < 0.001$). Using the cutoff value of 78.84 pmol/L, HE4 levels differentiated NSCLC from healthy controls with a sensitivity of 84.2% and a specificity of 78.3%. In the NSCLC subgroups, HE4 was a better discriminator of lung adenocarcinoma (cutoff value, 72.70 pmol/L, area under curve, 0.909; 95% confidence interval, 0.871 - 0.947). Higher serum HE4 levels were significantly correlated with histological type, high TNM stage, and positive lymph node metastasis ($p = 0.019, 0.018, 0.002$, respectively). Kaplan-Meier analysis demonstrated that high HE4 levels predicted poor survival (log-rank test: $p = 0.007$), especially in the adenocarcinoma group (log-rank test: $p = 0.001$). In the Cox model, serum HE4 level was an independent prognostic factor for NSCLC.
Conclusions: Higher serum levels of HE4 predict poor prognosis in NSCLC patients, especially in patients with adenocarcinoma.
(Clin. Lab. 2018;64:xx-xx. DOI: 10.7754/Clin.Lab.2018.180222)

Correspondence:
Dr. Dongping Mo
Department of Clinical Laboratory
Jiangsu Cancer Hospital & Jiangsu Institute of
Cancer Research & The Affiliated Cancer Hospital of
Nanjing Medical University
Baizi Ting No. 42
210009 Nanjing
Jiangsu
China
Phone: +86-25-83286400
Email: modongping1223@163.com

Supplementary Table and Figure

Table S1. General characteristics of these 203 cases with complete follow-up data.

Characteristics	Number of patients	%
Age (years)		
≤ 60	94	46.31
> 60	109	53.69
Gender		
Male	118	58.13
Female	85	41.87
Smoking		
Ever	126	62.07
Never	77	37.93
Histology		
Adenocarcinoma	110	54.19
Squamous carcinoma	76	37.44
Large cell carcinoma	17	8.37
Tumor stage		
I	36	17.73
II	43	21.18
III a	24	11.82
III b	42	20.69
IV	58	28.58
Lymph node metastasis		
No	86	42.36
Yes	117	57.63

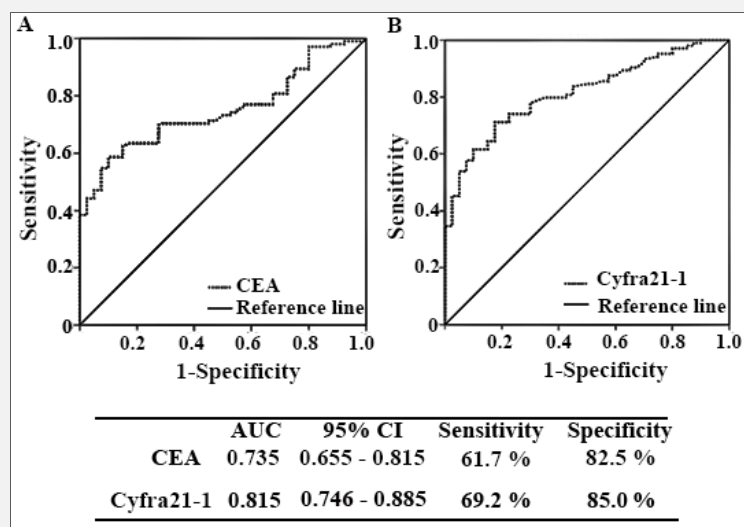|	AUC	95% CI	Sensitivity	Specificity
CEA	0.735	0.655 - 0.815	61.7 %	82.5 %
Cyfra21-1	0.815	0.746 - 0.885	69.2 %	85.0 %

Figure S1. ROC curve analysis of serum CEA (A) and Cyfra21-1 (B).