Human Tissue Kallikreins As New Serological Biomarkers For Lung Cancer

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ABSTRACT

Tissue kallikreins are a family of 15 genes (KLK1-KLK15) co-localized in tandem to chromosome 19q13.4, encoding serine protease enzymes. Previous reports indicate that dysregulated KLKs expression is associated with multiple diseases, primarily cancer. As a consequence, many kallikreins, in addition to KLK3/PSA, used in clinical medicine for the screening, diagnosis and monitoring of prostate cancer, have been identified as promising diagnostic and/or prognostic biomarkers for several hormone related cancers. The aim of the present study was to investigate the expression of several members of the kallikrein family to determine whether any of them have value as serological biomarkers for lung cancer. Sera samples collected by the UCLA Lung Cancer SPORE program from 101 subjects (51 cases and 50 controls) were analyzed blindly, using ELISA assays developed in-house. We identified statistically significant differences in the KLK5, KLK7, KLK10-14 protein expression between cases and controls (p<0.05), but not for KLK1, PSA, KLK4 and KLK6. In this series of lung carcinoma samples, KLK7, 8, 10 and 12 were generally under-expressed in cancerous sera samples than in controls, while KLK11 and KLK13 were over-expressed in 34% and 26% of the tumour samples at 95% specificity. In total, approximately 67% of patients with lung carcinoma had elevations in at least one of the kallikreins studied. We could not find any correlation between KLK alterations and cancer histotype. However, most elevations in KLKs were seen in patients with stage IV tumours. In conclusion, these preliminary results indicate that many members of the kallikrein family are dysregulated in lung carcinoma and that KLK11 and KLK13, or panels of members may constitute novel markers for lung cancer, but likely only for late stage disease.

INTRODUCTION

Despite the development of therapeutic strategies and advances in surgical treatment, lung cancer is the major cancer-related mortality worldwide in both men and women. This cancer is classified into two main histological groups: small cell carcinoma (SCC) and non-small cell carcinoma (NSCLC). NSCLC accounts for approximately 80% of all cases and comprises of 3 major histological subtypes: adenocarcinoma, squamous carcinoma and large cell carcinoma.

Serum tumor markers are non-invasive diagnostic tools for malignant tumors and they are commonly used for the screening of cancer and as an indicator of the treatment effect. A number of serum tumor antigens have been evaluated as biomarkers for NSCLC, including squamous cell carcinoma antigen (SCC), carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), cytokeratin 19 fragment (CYFRA 21-1), cancer antigen 125 (CA125) and tissue polypeptide antigen (TPA). However, expression of these antigens does not appear to be sufficiently sensitive and specific enough to be reliable for the diagnosis of the majority of lung malignancies. Therefore, there is a urgent and critical need to discover novel biomarkers for this major cancer.

Human Tissue Kallikreins are a family of 15 structurally similar serine protease genes that co-localize in tandem to chromosome 19q13.4.

OBJECTIVES

In addition to KLK3/PSA, many other members of the kallikrein family, dysregulated in cancer, have been identified as promising diagnostic and/or prognostic biomarkers for several cancer types, including ovarian, breast, prostate, and testicular cancers.1,2


REFERENCES

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