Background

Focal Adhesion kinase (FAK) is a cytoplasmic tyrosine kinase important in adhesion-dependent cell growth, proliferation, survival and motility. Upon integrin mediated survival signaling, FAK co-localizes at sites of contact with extracellular matrix, becomes activated via phosphorylation and promotes cell cycle progression. As cancer progresses, malignant cells acquire the ability to survive in the absence of cell adhesion. Preinvasive, invasive and metastatic lesions show higher expression levels of FAK compared to normal epithelium. In vivo models demonstrate that FAK phosphorylation is crucial in conferring increased metastatic potential of certain human cancers. The role of FAK expression and phosphorylation in primary lung tumors and in their metastatic capability has not yet been studied.

Design

Immunohistochemical analysis of native FAK and its phosphorylated form (pFAK) was performed (BD Labs/Biosource antibodies) on tissue microarrays (TMA) containing normal controls, primary lung cancers and corresponding metastases to lymph node and/or brain tissue. Quantitation of staining intensity was obtained with the Automated Cellular Imaging System (ACIS/ Clarient). Average intensity of expression was calculated as a measure of integrated optical density (IOD). Statistical analysis was performed with SPSS program.

Results

FAK expression in lung cancer cells (primary or metastatic) is higher than in normal epithelium (p<0.001, t-test). There are significant differences of FAK expression among different histologic subtypes of lung cancer (p=0.004, ANOVA). Furthermore, carcinomas with high FAK expression demonstrate worse clinical prognosis in comparison to the low FAK expressing tumors (p 0.031, Kaplan-Meier).

Conclusions

As part of the integrin mediated survival signal, FAK overexpression contributes to adhesion independent growth, proliferation and survival of cancer cells. Our study demonstrates FAK overexpression in primary tumors of the lung and their metastasis. Histologic subsets show different FAK expression patterns and high FAK expression correlates with worse clinical prognosis within each histologic group. No statistically significant difference between metastatic and primary lesions was found within any of the histologic subsets. These data supports the notion that overexpression of FAK influences tumor behavior, promotes malignancy and represents a potential target for lung cancer therapy.

References


Endothelial matrix

Integrins

Cell membrane

FAK

Tyr 861

Crk/CAS

PI3K

Grb2, Ras

Cell motility

Survival

Proliferation

Akt

Erk

Cell Membrane

Integrins

Endothelial matrix

FAK

Tyr 861

Crk/CAS

PI3K

Grb2, Ras

Cell motility

Survival

Proliferation