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Invasiveness and anchorage independent growth ability augmented by PTEN inactivation through the PI3K/AKT/NFkB pathway in lung cancer cells

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Invasiveness and anchorage independent growth ability augmented by PTEN inactivation through the PI3K/AKT/NFkB pathway in lung cancer cells
Previous ArticleRegulation of VEGF-expression by patupilone and ionizing radiation in lung adenocarcinoma cells
Next ArticleEUS-FNA for the detection of left adrenal metastasis in patients with lung cancer

Abstract

PTEN is inactivated in a subset of lung cancer; therefore, we investigated the involvement of PTEN inactivation in invasiveness of lung cancer cells. AKT at Ser473 was phosphorylated in several lung cancer cell lines with loss of PTEN expression. Therefore, we created a tetracycline inducible expression system of wild-type PTEN (PTEN-WT) as well as catalytically (PTEN-G129R) and lipid phosphatase (PTEN-G129E) inactive PTEN mutants using the PC14, PC9 and PC3 lung adenocarcinoma cell lines, in which endogenous PTEN expression was not detected and AKT at Ser473 was phosphorylated by Western blot analysis. Induction of PTEN-WT reduced phosphorylation of AKT and inhibited the transcriptional activity of NFkB, whereas PTEN mutants did not, suggesting that PTEN inactivation results in the activation of the AKT/NFkB pathway in PC14, PC9 and PC3 cells. Furthermore, overexpression of PTEN-WT suppressed anchorage independent growth in soft agar and reduced invasiveness in a trans-well chamber assay of PC14 cells. Neither PTEN-G129R nor PTEN-G129E had suppressive effects on anchorage independent growth and invasiveness. Augmentation of invasiveness by constitutively active AKT was also shown in mouse NIH3T3 cells. Therefore, it was strongly indicated that activation of the PI3K/AKT/NFkB pathway by PTEN inactivation results in augmented invasiveness in lung cancer cells and lipid phosphatase activity of PTEN plays a key role in this process.

Keywords

- PTEN
- AKT
- NFkB
- Invasion
- Lung cancer
- Gene cloning

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