biomarkers

**NESTIN PROMOTES PROLIFERATION AND APOPTOSIS AND CORRELATES WITH POOR PROGNOSIS IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA**

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**Aim:** Esophageal squamous cell carcinoma (ESCC) is a malignancy of the esophagus that is characterized by its high invasiveness and mortality. Nestin is a member of the class VI family of intermediate filament proteins and we previously demonstrated that the majority of tumor cells in non-small cell lung cancer samples are nestin-positive and showed that nestin expression was positively correlated with the subset of lung cancer patients displaying poor outcomes and high levels of proliferative markers. However, the precise mechanisms of nestin action in the proliferation and metastasis of ESCC require further elucidation.

**Methods:** A total of 93 ESCC samples were randomly selected from our tissue database and we explored the association of the nestin phenotype with malignant proliferation and apoptosis in esophageal squamous cancer cells. Nestin expression was determined in ESCC specimens and cell lines (Eca-109 and TE-1), and correlated with clinicopathological properties, including clinical prognosis and proliferative markers. The association of the nestin phenotype with apoptotic indicators was also analyzed.

**Results:** Nestin was expressed in ESCC specimens and cell lines (Eca-109 and TE-1). ESCC patients with nestin-positive tumors had significantly shorter median survival and progression-free survival times than those with nestin-negative tumors. Positive staining for the proliferation markers Ki67 and PCNA (proliferating cell nuclear antigen) was detected in 56.9% and 60.2% of ESCC specimens, respectively, and was strongly correlated with the nestin phenotype. Notably, expression of cyclin-dependent kinase-5 (CDK5) and P35 was detected in 53.8% and 48.4% of ESCC specimens, respectively, and was strongly associated with the nestin phenotype.

**Conclusions:** Our data demonstrate nestin expression in ESCC specimens and cell lines, and revealed a strong association of the nestin phenotype with poor prognosis in ESCC patients. Furthermore, we showed that nestin plays an important role in the malignant proliferation and supported the tentative conclusion that nestin likely promotes ESCC cell apoptosis. Targeted regulation of nestin may thus have therapeutic applications in the treatment of human esophageal cancer.

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