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Nedd4-1 is an exceptional prognostic biomarker for gastric cardia adenocarcinoma and functionally associated with metastasis

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Background: Gastric cardia adenocarcinoma (GCA) is the most aggressive subtype of gastric carcinoma. New molecular markers and therapeutic targets are needed for diagnosis, prognosis and treatment of GCA. This study is to establish the E3 ubiquitin ligase Nedd4-1 as a prognostic biomarker to predict the survival and guide the treatment of GCA patients.

Methods: Expression of Nedd4-1 in 214 GCA tumor samples was detected by immunohistochemistry staining (IHC) using tissue microarray assay (TMA). Association of Nedd4-1 with cumulative survival of the TNM stages I-III patients and clinicopathological characteristics was statistically analyzed. The role of Nedd4-1 in gastric cancer cell migration and invasion were determined by transwell and wound healing assays.

Results: Nedd4-1 is overexpressed in 83% of the GCA tumors. The 5-year survival rate in Nedd4-1 negative GCA patients is as high as 96%. Log-rank analysis indicated that overexpression of Nedd4-1 is inversely correlated with cumulative survival ($\chi^2 = 21.885$, $p < 0.001$). Multivariate logistic regression analysis showed that overexpression of Nedd4-1 is associated with an extremely low GCA survival rate with a hazard ratio (HR) = 0.068 ($p = 0.008$) in TNM stages I-III patients. Statistical analysis of association of Nedd4-1 overexpression with clinicopathological characteristics revealed that overexpression of Nedd4-1 is tightly associated with TNM stage ($p < 0.001$). Knockdown of Nedd4-1 in gastric cancer cell lines AGS and N87 dramatically inhibited the gastric cancer cell migration and invasion.

Conclusions: Our results indicate that Nedd4-1 is an exceptional prognostic biomarker for GCA and suggest that Nedd4-1 may play an essential role in GCA metastasis.

Biography

Wannian Yang completed his PhD in the North Carolina State University in 1993 and he has done with his Postdoctoral Training in St. Jude's Children's Research Hospital from 1993-1995. Currently he is a Staff Scientist at Geisinger clinic, USA.

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