

Fibronectin promotes tyrosine phosphorylation of paxillin and cell invasiveness in the gastric cancer cell line AGS

Dan Li¹, Jian Ding², Xiaozhong Wang¹, Chengdang Wang², and Ting Wu²

¹Digestive Department, the First Affiliated Hospital of Fujian Medical University;

²Digestive Department, the Union Hospital of Fujian Medical University, Fuzhou, Fujian, China.

Dan Li and Jian Ding contributed equally to this research

ABSTRACT

Aims and background. Paxillin is a central protein within the focal adhesion and serves as a critical transducer of signals from fibronectin. Although abnormal expression of fibronectin and paxillin is often observed during the development of human malignancies, the relationship between paxillin and cell invasion in gastric cancer is still unclear. The current study was designed to investigate the potential role and mechanisms of fibronectin in tyrosine phosphorylation of paxillin and in the invasiveness of gastric cancer cells.

Methods. Expression of paxillin in human gastric cancer samples was examined by immunohistochemical staining. A gastric cancer cell line, AGS, was stimulated by fibronectin with gradient concentrations, and expression of paxillin and phosphorylation of paxillin tyrosine 118 (tyr118) was detected by immunoprecipitation and Western blotting. The invasiveness of AGS cells was measured by the modified Boyden chamber assay. Small interfering RNA (siRNA) targeting paxillin was used to establish the role of paxillin(tyr118) in the process of cell invasion enhanced by fibronectin. siRNA targeting focal adhesion kinase (FAK) was used to verify the effect of FAK tyrosine 397 (tyr397) on phosphorylation of paxillin(tyr118).

Results. Positivity for paxillin staining in human gastric cancer was associated with tumor stage. AGS cell showed dose dependence on fibronectin for invasiveness and phosphorylation of paxillin (tyr118). Invasiveness and phosphorylation of paxillin(tyr118) in AGS cells reached their peak when the concentration of fibronectin reached 100 nmol/L. siRNA targeting paxillin decreased the phosphorylation of paxillin(tyr118) and the invasiveness of AGS cells significantly as compared with controls. Blockage of FAK(tyr397) can inhibit phosphorylation of paxillin(tyr118) stimulated by fibronectin.

Conclusions. Fibronectin promotes paxillin(tyr118) phosphorylation and invasiveness of AGS cells. Paxillin silencing by RNA interference inhibits the cell invasiveness stimulated by fibronectin. Paxillin is a key factor in the fibronectin-stimulated invasiveness of AGS cells.

Key words: fibronectin, paxillin, focal adhesion kinase, invasiveness, gastric cancer.

Acknowledgments: Grant sponsor: Grants-in-Aid for Youth in Scientific Research from the Health Bureau of Fujian Province, China (Grant number: 2006-1-10); Grants-in-Aid for Youth in Scientific Creation Research from the Sci-Tech Bureau of Fujian Province, China (Grant number: 2006F3050).

Correspondence to: Dr Jian Ding, Digestive Department, The First Affiliated Hospital of Fujian Medical University, Chating Street, 350002, Fuzhou, Fujian, China.

Tel +86-0591-88808826;
e-mail docdingjian@yahoo.com.cn

Received February 26, 2008;
accepted October 28, 2008.