Periostin Expression at Tumor Stromal Cells Might Be Associated with the Malignant Progression of Gastric Cancer

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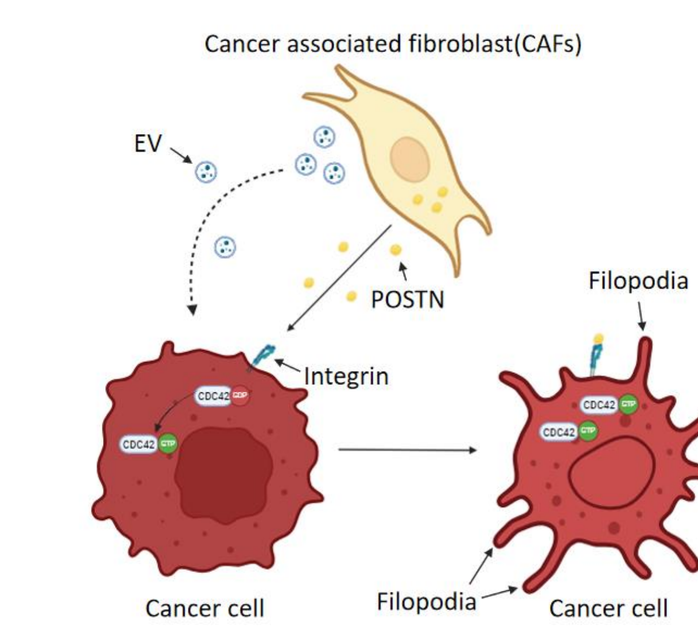
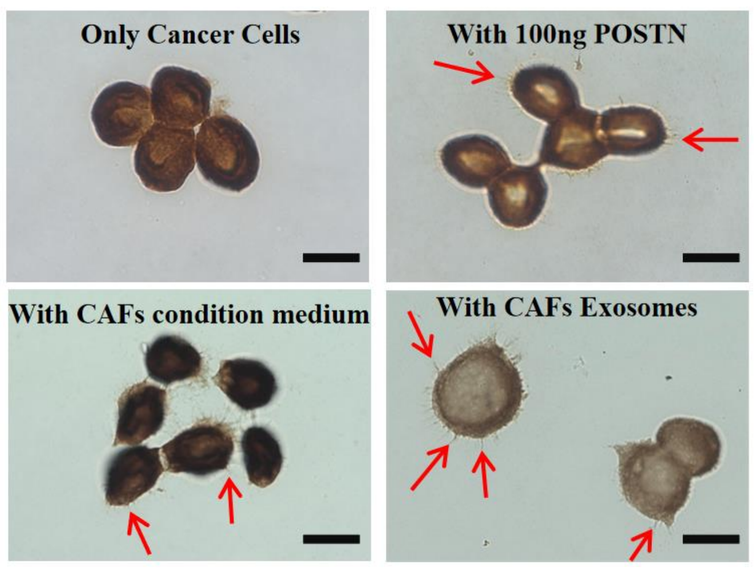
Abstract

Purpose: Tumor progression and metastasis are shaped by the tumor microenvironment. Cancer-associated fibroblasts (CAFs) and their extracellular matrix proteins contribute to gastric cancer progression. Periostin, a stromal matricellular protein, promotes cancer progression through integrin-mediated signaling. We investigated the clinicopathological significance of periostin expression in gastric cancer tissues and its effects on gastric cancer cell invasion and migration. Materials and Methods: A total of 1,286 gastric cancer tissue samples from patients who underwent gastrectomy at Osaka Metropolitan University Hospital were analyzed by immunohistochemical staining for periostin, and the results were correlated with clinicopathological factors and prognosis. Gastric cancer cell lines (OCUM-12, MKN-74, and MKN-45) were treated with 100 ng recombinant periostin. Transwell invasion and wound healing assays were performed. Results: High periostin expression in the tumor stroma was significantly associated with worse overall survival ($p < 0.001$, log-rank), diffuse-type histology ($p < 0.001$), deeper T invasion ($p < 0.001$), lymph node metastasis ($p < 0.001$), distant metastasis ($p < 0.001$), lymphatic invasion ($p < 0.001$), venous invasion ($p = 0.006$), tumor size ≥ 30 mm ($p < 0.001$), higher recurrence rates ($p < 0.001$), and more advanced stage ($p < 0.001$). Recombinant periostin significantly promoted the invasion and migration of gastric cancer cells.Conclusion: High stromal expression of periostin is associated with the malignant potential of gastric cancer. Periostin promotes invasion and migration, making the periostin–cancer cell interaction a promising therapeutic target.

Proposed Model of CAF–Cancer Cell Crosstalk



IHC staining of fascin1 in gastric cancer tissue samples

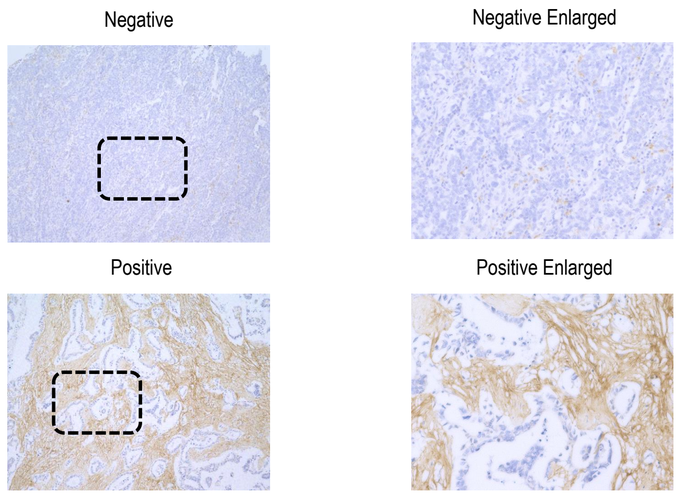


Introduction

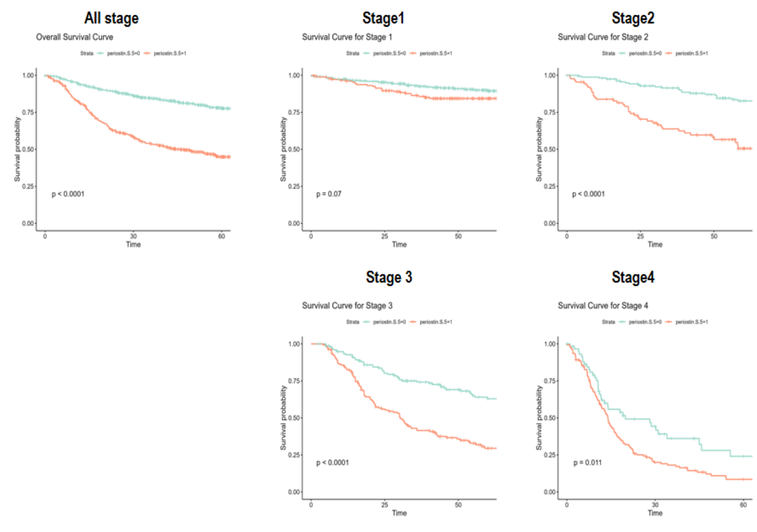
Cancer-associated fibroblasts (CAFs) have been reported to be closely associated with tumor progression in various types of cancer, including gastric cancer (GC). Periostin, a matricellular protein, is expressed in both cancer cells and surrounding tumor stromal cells such as CAFs, and regulates signaling pathways such as FAK through interaction with integrins on the surface of cancer cells, thereby stimulating their proliferation, invasion, and metastasis.

In this study, we performed immunohistochemical staining for periostin in 1,286 gastric cancer tissue samples and examined its association with clinicopathological factors and prognosis. In addition, we conducted in vitro assays using gastric cancer cell lines treated with recombinant periostin and obtained preliminary results showing that periostin enhances the invasion and migration abilities of gastric cancer cells.

IHC staining of Periostin in 1,296 gastric cancer tissue samples



Overall Survival of Patients with Gastric Cancer



Materials and methods

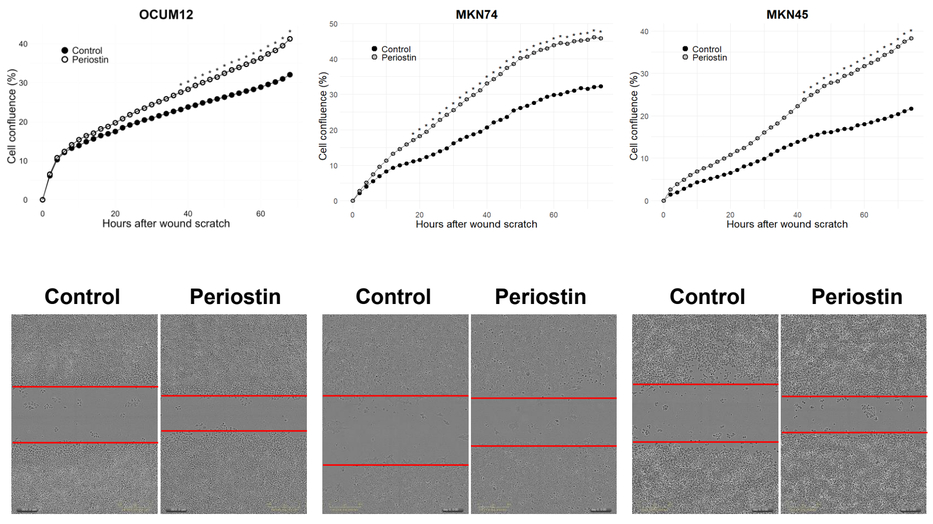
Materials

- **Tissue samples: A total of 1286 gastric cancer tissues**
- **Cell lines: 4 gastric cancer cell lines OCUM-12, NUGC3, MKN-74, MKN-45.**

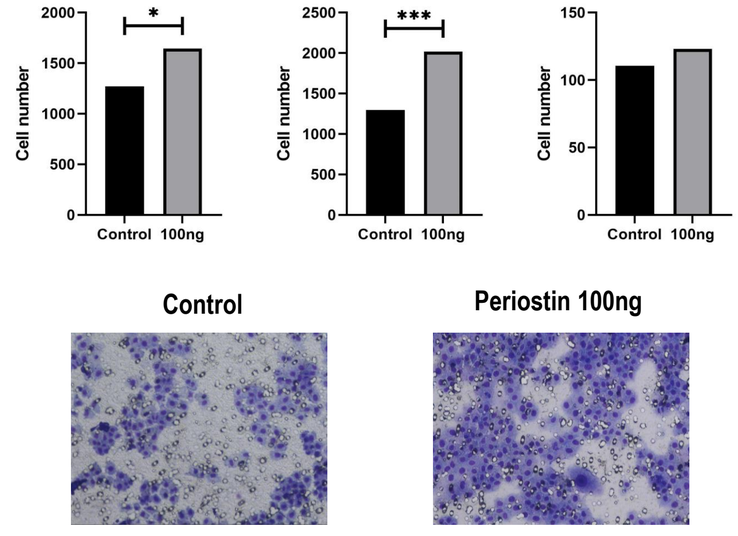
Methods

- **Immunohistochemistry**
- **Transwell Invasion Assays**
- **Wound healing**
- **Cell staining**

Wound healing assay



Transwell invasion assay



Conclusion

High stromal expression of periostin is linked to the malignancy of gastric cancer.

Periostin promotes invasion, suggesting that it may be a promising therapeutic target.