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Introduction: Girdin, an actin-binding protein, is reportedly involved in the invasion and angiogenesis of various cancers. It has been suggested that the flavonoid Scutellarin (SCU) inhibits Girdin signaling. In this study, we investigated the function of Girdin in pancreatic cancer and its therapeutic application.

Methods & Results: Immunohistochemical staining of Girdin in resected pancreatic cancer specimens from our institution showed that high Girdin expression was correlated with poor overall survival (OS) and relapse-free survival (RFS), as well as with T factor, indicating invasion into the surrounding tissues. On the other hand, Girdin was highly expressed in almost all pancreatic cancer cell lines, and the migration ability of Girdin-knockdown cell lines was decreased even under epidermal growth factor (EGF) stimulation. In addition, SCU suppressed pancreatic cancer cell migration by inhibiting the phosphorylation of Girdin. The expression and production of vascular endothelial growth factor A (VEGF-A) were significantly decreased in Girdin-knockdown cell lines. Furthermore, in Matrigel tube formation assays performed using culture supernatant, the lumen-forming ability of vascular endothelial cells was also decreased in Girdin-knockdown cell lines. However, SCU treatment did not significantly alter the expression or production of VEGF-A.

Discussion: We suggest that Girdin is involved in EGF signaling-mediated migration of pancreatic cancer cells, that SCU inhibits pancreatic cancer invasion by suppressing Girdin activity, and that Girdin is also involved in angiogenesis via an activation pathway different from the action site of SCU.

Conclusion: Girdin may be a prognostic biomarker, and the development of a novel molecular-targeted drugs for Girdin may improve the prognosis of pancreatic cancer in the future.