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Abstract　Kenta Saito

Pancreatic cancer is the main cause of cancer-related death. The death rates for patients with pancreatic cancer are increasing, so there is a need for the exploitation of new drugs with low toxicity. Xantohumol, a prenylated chalcone from hop (*Humulus lupulus* L.), has been shown to inhibit cell proliferation and NF-κB activation in various cancer cells. However, little is known for the effects of xanthohumol in pancreatic cancer. Also, we have previously reported that NF-κB activation is a key role for angiogenesis in pancreatic cancer. In this study, we investigated whether xanthohumol suppressed angiogenesis by blocking NF-κB activity in pancreatic cancer. Initially, we confirmed xanthohumol significantly inhibited the cell proliferation and NF-κB activation in pancreatic cancer. We next demonstrated the expression levels of VEGF and IL-8 mRNA and the secretion of VEGF and IL-8 were significantly inhibited with xanthohumol treatment in pancreatic cancer. We also revealed that the co-culture with BxPC-3 cells significantly enhanced the HUVECs tube formation and the enhancement was inhibited by treatment with xanthohumol. We finally demonstrated xanthohumol (10mg/kg, intraperitoneal injection weekly) inhibited tumor growth significantly in BxPC-3 subcutaneous xenograft tumors. Immunohistochemistry revealed that xanthohumol suppressed the expression of Ki-67, CD31-positive microvessel density, the expression of NF-κB p65, and the levels of VEGF and IL-8. These results showed that xanthohumol inhibited angiogenesis by suppressing NF-κB activation in pancreatic cancer. So, there is a possibility that xanthohumol may be a novel therapeutic agent for the treatment of pancreatic cancer.