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学位論文の題名	Xanthohumol inhibits angiogenesis by suppressing nuclear factor- $\kappa$ B activation in pancreatic cancer (キサントフモールは膵癌において nuclear factor- $\kappa$ B の活性化を抑制し、腫瘍血管新生を阻害する)  Cancer Science 2018; 109: 132-140
論文審査担当者	主査： 城 卓志 副査： 岡本 尚, 瀧口 修司

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. Xanthohumol, a prenylated chalcone from hop (*Humulus lupulus* L.), has been shown to inhibit cell proliferation and NF- $\kappa$ B activation in various cancer cells. However, little is known for the effects of xanthohumol in pancreatic cancer. Also, we have previously reported that NF- $\kappa$ B activation is a key role for angiogenesis in pancreatic cancer. In this study, we investigated whether xanthohumol suppressed angiogenesis by blocking NF- $\kappa$ B activity in pancreatic cancer. Initially, we confirmed xanthohumol significantly inhibited the cell proliferation and NF- $\kappa$ B 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- $\kappa$ B p65, and the levels of VEGF and IL-8. These results showed that xanthohumol inhibited angiogenesis by suppressing NF- $\kappa$ B activation in pancreatic cancer. So, there is a possibility that xanthohumol may be a novel therapeutic agent for the treatment of pancreatic cancer.