Background: Recent studies using mouse model of ovarian carcinoma have shown that chronic stress may influence tumor growth and angiogenesis by modulating the expression of matrix metalloproteinases (MMP) and vascular endothelial growth factor (VEGF) through the β-adrenergic receptor (β-AR)–cyclic AMP (cAMP)–protein kinase A (PKA) pathway. Our previous in vitro experiment data described that HIF-1α as regulatory hinge mediated β-AR signaling pathway. The purpose of this study was to test the hypothesis that chronic stress in a negative social and psychological state plays a critical role in pancreatic cancer development and progression.

Methods: We created a new stress model system to determine the effects of chronic stress on pancreatic cancer progression.

Results: Our study showed that chronic stress not only results in mice gaining depression behavior due to an elevated level of epinephrine, but also induces cancer progression. We further demonstrate that the pancreatic cancer development and progression induced by chronic stress was blocked by a β2-AR inhibitor ICI118 551 or a HIF-1α inhibitor 2-Methoxyestradiol and that the chronic stress up-regulates the expression of MMP-2, MMP-9, and VEGF via a HIF-1α-dependent β-AR signaling pathway. Our data suggest that β2-AR-HIF-1α axis regulates stress-induced pancreatic tumor growth and angiogenesis.

Conclusion: β2-AR-HIF-1α axis inhibitor may have a therapeutic or preventive potential for the patients with pancreatic cancer who are especially subject to psychosocial stress.