Background: Pancreatic cancer is a leading cause of cancer-related death in the world. With a feature of aggressive behaviours, pancreatic cancer showed early metastasis and quick recurrence from surgery. Arginine deiminase (ADI) has been shown that it can inhibit the growth of some tumor cells deficient in argininosuccinate synthetase by arginine deprivation. However, whether the agent can inhibit pancreatic cancer cell invasion is not clear.

Methods: Human pancreatic cancer cells BxPc-3 and PANC-1 were cultured. Scratch test and Transwell chamber invasion assay were used to examine the migration and invasion of BxPc-3 and PANC-1 cells treated with ADI. Also, the levels of molecular changes in ADI-treated pancreatic cancer cell were measured by Western blotting and real-time quantitative polymerase chain reaction (qPCR).

Results: Treatment with ADI decreased the migration and invasion of PANC-1 cells deficient in argininosuccinate synthetase (ASS) in a dose- and time-dependent manner (from 0.5 mU to 5 mU), but not BxPC-3 pancreatic cancer cell expressed high level of ASS. In mRNA analysis, ADI (1 mU) down-regulated the levels of MMP-2, MMP-9, and uPA in PANC-1 cell, while up-regulated TIMP-2 and E-Cadherin level. Further protein expression analysis showed that ADI (1 mU) modulated the expression of MMP2, uPA, and E-Cadherin similar to mRNA detection. For getting the molecular mechanism of PANC-1 cells invasion inhibition by ADI treatment, we analyzed PI3KCA expression, and phosphorylation levels of p65, AKT and ERK1/2 in PANC-1 cells treated by ADI (1 mU) in combination with or without PI3K inhibitor LY294002 (20 µM), and the findings showed ADI reduced the expression levels of p-p65 (Ser536) and p-AKT (Thr308), which can be enhanced by addition of LY294002. However, ADI (1 mU) did not downregulate ERK1/2 phosphorylation at Thr202/Tyr204, as compared with control.

Conclusion: Our results suggest that arginine deprivation by ADI can inhibit argininosuccinate synthetase-deficient PANC-1 cell invasion via suppression of PI3K/AKT/NF-κB signal.