

Abstract

The liver fluke, *Opisthorchis viverrini* causes opisthorchiasis *viverrini*, which is a major risk factor for cholangiocarcinoma (CCA). *O. viverrini* infection induces the disease through inflammation-mediated pathogenesis. Host-parasite interaction involves in the progression of the disease. For immune-mediate mechanisms, inflammatory response plays decisive roles in hepatobiliary disease including opisthorchiasis and carcinogenesis. During inflammation, the immune cells produce cytokines, chemokines, inflammation-related molecules and free radical. Leukocytes-derived proteins are associated with the pathogenesis of the disease. To investigate protein expression in peripheral blood mononuclear cells (PBMCs) against *O. viverrini* infection, proteomic approach using two dimensional-PAGE followed by LC-MS/MS was used to identify in human peripheral blood mononuclear cells (PBMCs) co-cultured with *O. viverrini* adult worms at different times (6, 12, and 24 h) *in vitro*. Comparative analysis of spot patterns on 2-DE showed 59 spots that were markedly changed in *O. viverrini*-stimulated PBMCs. Among of them, annexin A1 was found to be up-regulated at 12 and 24 h in *O. viverrini*-stimulated PBMCs, which is involved in anti-inflammatory, proliferation, differentiation, apoptosis, neutrophil migration. Western blot analysis was used to confirm proteomic data. The overexpression of annexin 1 was verified at transcriptional and translational levels in *O. viverrini*-infected hamsters and *O. viverrini*-induced CCA hamster. Animal studies revealed that the expression of annexin 1 was time-dependently increased in the liver tissues of the hamsters infected with *O. viverrini* and CCA, evaluated by Western blotting, realtime RT-PCR and immunohistochemistry. In hamster infection with *O. viverrini* and administration with curcumin, annexin 1 level increased expression compared to untreated group. Moreover, expression of an annexin 1 was investigated in human CCA microarray tissues by immunohistochemical analysis. The results showed that expression of annexin 1 was observed in cancer cells and epithelial bile duct. This study suggests that annexin 1 plays a role in inflammatory response to *O. viverrini* infection, and participates in parasite-induced CCA in humans which may serve as a novel molecule for diagnosis and chemoprevention.