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Identify specific gene associated with carcinogenesis by *Clonorchis sinensis* and N-nitroso-dimethylamine on host cell using transcriptome sequencing

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Clonorchis sinensis, the most prevalent parasite in Korea, has been reclassified as Group I bio-carcinogen for cholangiocarcinoma (CCA) in humans by IARC in 2009. *C. sinensis* associated cholangiocarcinoma (CCA) is still unknown. The aim of this study was to identify distinct gene expression associated with carcinogenesis of *C. sinensis*. In human cholangiocyte line, H69 cells were continuously exposed to N-nitroso dimethylamine (NDMA) and excretory-secretory product of *C. sinensis* (ESP) over one year. H69 cells that were continuously exposed to ESP of *C. sinensis* and NDMA showed cancer-like characteristics including cell proliferation was more than 5.7 times and the proportion of cells in the G2/M phase increased up to 42% compare to non-treated H69 cells. Moreover, the expression of the cell cycle protein E2F1 and the cell proliferation related proteins, ki67, and cytokeratin 19 were more than 30-fold increased when NDMA and ESP were added together. Based on these results, whole-transcriptome sequencing was performed to compare the genome-wide gene expression patterns of H69 stimulation with NDMA and/or *C. sinensis* ESP with non-treated H69. A total of 1301 differentially expressed genes (DEGs) were identified, 521 of which were up-regulated and 780 were down-regulated. Gene ontology and Kyoto Encyclopedia of Genes and Genomes enrichments revealed that numerous DEGs belong to cancer-relevant genes, involved in cell cycles, cell proliferation, and cell adherent-relevant pathways. Among them, we focused on the P53 K-ras signaling genes and found that two genes increased and eight genes decreased from a number of their genes. This result was also confirmed by real-time PCR. In conclusion, these data suggest that the P53 and K-ras signal plays a key role in regulation of cell proliferation, which may cause cholangiocarcinoma under stimulation by ESP of *C. sinensis* and NDMA.

Biography

Eun-Min Kim has completed his PhD from Seoul National University College of Medicine and had worked as a Research Professor in Busan National University College of Medicine. Currently, he is studying the mechanism of cholangiocarcinoma at Yonsei University in South Korea.

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