

Letters to the Editor

Function association of enhanced expressed genes between *Opisthorchis viverrini* and non *Opisthorchis viverrini*-related cholangiocarcinoma

Palabras clave: *Opisthorchis viverrini*. Cholangiocarcinoma.

Key words: *Opisthorchis viverrini*. Cholangiocarcinoma.

Dear Editor:

Cholangiocarcinoma is one of the serious malignancies. It is a type of primary hepatobiliary tumor, there is a wide spectrum of tumors of varying differentiation and malignancy grades (1,2). It is the second most common primary cancer in the liver, and its incidence is highest in the northeastern part of Thailand (3). The etiology of this cancer is very complex. One of the most widely mentioned underlying cause for cholangiocarcinoma is chronic *Opisthorchis viverrini* infection (4,5). However, a number of cholangiocarcinoma without chronic *Opisthorchis viverrini* infection can be seen (4,5). Although it has been determined for a long time, there is limited knowledge on the gene expression and biomarkers for this cancer (1,2). Systemic approach on the genomics and proteomics might provide useful information to better understand the gene expression and biomarker of cholangiocarcinoma. According to a recent study by Jinawath et al., the putative signature of *Opisthorchis viverrini*-related cholangiocarcinoma exhibited elevated expression of genes involved in xenobiotic metabolism (UGT2B11, UGT1A10, CHST4, SULT1C1), whereas that of non-*Opisthorchis viverrini*-related cholangiocarcinoma represented enhanced expression of genes related to growth factor signaling (TGFBI, PGF, IGFBP1, IGFBP3) (3). These data might serve as a starting point for the identification of novel diagnostic markers or therapeutic targets for the disease

(3). In this work, function association of enhanced expressed genes between *Opisthorchis viverrini* and non *Opisthorchis viverrini*-related cholangiocarcinoma was studied.

The author used gene ontology technique to perform this work. The functional association study was performed. The tool namely FuncAssociate was used. FuncAssociate is a web-based tool to help researchers use gene ontology attributes to characterize large sets of genes derived from experiment (6). The focused studied genes are UGT2B11, UGT1A10, CHST4, SULT1C1, TGFBI, PGF, IGFBP1, and IGFBP3 because these genes were reported to overexpress in cholangiocarcinoma (3). The condition was set for human cholangiocarcinoma. To test the functional association, the algorithm makes use of single hypothesis one-sided p-value of the association between attribute and query (based on Fisher's exact test) and p value was accepted as a statistical significant level at p value equal to or less than 0.05 (6). According to this work, there is neither overrepresented nor underrepresented attribution for single set of genes in separated *Opisthorchis viverrini* (UGT2B11, UGT1A10, CHST4, SULT1C1) and non *Opisthorchis viverrini*-related cholangiocarcinoma (TGFBI, PGF, IGFBP1, IGFBP3). Nevertheless, there is overrepresented attribution for the whole set of genes (UGT2B11, UGT1A10, CHST4, SULT1C1, TGFBI, PGF, IGFBP1, IGFBP3) for cholangiocarcinoma. The identified biological process for the whole set of genes is "cell growth and/or maintenance".

Until present, there is no success in finding of proper biomarker for classification of cholangiocarcinoma. There are several attempted to study the difference between *Opisthorchis viverrini* and non *Opisthorchis viverrini*-related cholangiocarcinoma by basic classical proteomics technique (7). However, the results are usually controversy and the main factor is the limitation of techniques and number of subjects. Recently, there is an interesting report on a possible of biomarkers that might be a useful tool for discriminate between *Opisthorchis viverrini* and non *Opisthorchis viverrini*-related cholangiocarcinoma (3). However, there is no verification. Here, the author used the gene ontology approach to study the functional association of candidate markers for discrimination of cholangiocarcinoma (3). According to this work, the simulation shows that there is no separated functional attribution for separated sets of genes but there is for

the whole set of genes. This implies that there is no actual separated set of gene that is functionalized and can be useful for discrimination. However, the whole set of candidates can be useful and can be served as biomarker for cholangiocarcinoma but not for discrimination between *Opisthorchis viverrini* and non *Opisthorchis viverrini*-related cholangiocarcinoma. Concerning the identified biological process, it can be clearly demonstrated that the whole set of seven genes has overexpression. Therefore, its biological process, cell growth can overexpress and this is strongly correlated to the tumorogenesis. Finally, it should be noted that the results obtained by this bioinformatics procedure should be confirmed using genetics or biological techniques (DNA microarrays, RT-PCR, etc.)

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