Genetic and Protein Alterations in ARID1A and their Clinical Significance in Cholangiocarcinoma

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ABSTRACT

Cholangiocarcinoma (CCA) is the second most common liver cancer that develops along the bile duct, with high incidence in Northeastern of Thailand. Recently, the mutational landscape of CCA has been characterized and identified recurrent mutations in ARID1A (17%). The mechanisms underlying the selection for loss of ARID1A function in cancer remain unknown and several therapeutic targets in ARID1A mutated cancers are in development. We analyzed the sequencing data of 489 CCA patients and found 14% (68/489) of CCA harbored ARID1A-truncating mutation. ARID1A mutation was significantly correlated with liver fluke-associated CCA (P=0.01) and significantly increased in stage IV CCA (P=0.04). Immunohistochemical staining in CCA tissues showed that low ARID1A expression was significantly correlated with metastasis (P=0.04). The results are considerable clinical relevance since loss of ARID1A expression may be predictive for a favorable treatment response to small molecule inhibitors which are currently under clinical investigation.

Keywords: Cholangiocarcinoma, AT-Interactive Domain-containing protein 1A (ARID1A), DNA mutation