AB034. P-02. Depletion of SRSF1 inhibits proliferation, promotes apoptosis and changes cellular proteome of cholangiocarcinoma cells

Pawee Tangwiriyarotkul[1], Phichamon Phetchahwang[1], Sucheewin Krobthong[2], Sittiruk Roytrakul[2], Sopit Wongkham[3], Worasak Kaewkong[1]

[1]Department of Biochemistry, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand; [2]National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Pathumthani, Thailand; [3]Department of Biochemistry, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Correspondence to: Pawee Tangwiriyarotkul. Department of Biochemistry, Faculty of Medical Science, Naresuan University, Phitsanulok, Thailand. Email: paweet57@email.nu.ac.th.

Background: Regarding to many reports demonstrates the aberrant splicing of various important genes in cholangiocarcinoma (CCA), but lack of information about the upstream splicing regulators. Therefore, this study aimed to characterize the expression of SR-protein family [12 serine-arginine rich splicing factors (SRSFs)] in CCA cell and investigate the functional involves in cancer proliferation, apoptosis and proteome changes using specific siRNA-silencing of candidate SRSF in CCA cells.

Methods: Expression of 12 SRSFs in cholangiocyte (MMNK1) and CCA cells (KKU-055, KKU-100, KKU-213 and KKU-214) was comparative analyzed by RT-PCR. Then, the candidate SRSF was subsequently depleted in KKU-055 and KKU-213 by specific siRNAs. The proliferation ability was determined by CCK-8 assay whereas the cell death and apoptosis were monitored by cell count, Annexin V/7-AAD staining coupled with flow cytometry and caspase 3/7 activity assay. In addition, the proteomics analysis of siRNA-mediated silencing of candidate SRSF was examined using LC-MS/MS mass spectrometry and analyzed by bioinformatics tools.

Results: SRSF1 was predominantly upregulated in CCA cells. Depletion of SRSF1 expression decreased cell proliferation and increased cell death via increasing of apoptotic cell number and activating caspase 3/7 activity. Proteomic analysis identified differentially expressed proteins mostly in protein class (nucleic acid binding) and molecular function (binding). There are 19 downregulated proteins and 3 upregulated proteins in SRSF1-depleted KKU-213 cells. Remarkably, downregulation of CLVS2, ZSCAN29 and EIF1B, and upregulation of SNAPC4 were significantly determined for prediction of molecular interaction with SRSF1 based on the STITCH database.

Conclusions: Our study identified the function of SRSF1 in CCA cell proliferation and evading from programmed cell death. In addition, its intracellular mediators potentially associated with cancer cell proliferation and apoptosis evading abilities were explored. This protein requires further molecular clarification for serving as the prognostic indicator or therapeutic target for CCA.

Keywords: Alternative splicing; cholangiocarcinoma; serine-arginine rich splicing factor 1 (SRSF1)

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