Diabetogenic Glucose Enhances Aggressive Activities of Cholangiocarcinoma Cell Lines

Charupong Saengboonmee[1,3], Wunchana Seubwai[2,3], Sopit Wongkham[1,3*]
[1]Department of Biochemistry, [2]Department of Forensic Medicine, [3]Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Background and Objective: The epidemiology studies indicate hyperglycemia and Diabetes Mellitus (DM) as risk and promoting factors in many cancers including cholangiocarcinoma (CCA). As DM and CCA are highly prevalent in the Northeast of Thailand, we hypothesized that high glucose condition can promote the aggressiveness of CCA.

Methods: The human CCA cell lines; KKU-M055, KKU-M213, KKU-M214, and highly metastatic KKU-M214L5 were cultured in Dulbecco's Modified Eagle Medium (DMEM) with normal glucose (NG: 5.6 mM) or high glucose (HG: 25 mM) conditions. The phenotypes related to metastasis, i.e., proliferation, migration and invasion were compared between cells cultured in the normal vs. high glucose conditions. The molecular mechanisms underlined these aggressive phenotypes were explored.

Results: All CCA cell lines cultured in HG medium had significantly higher proliferation rates, and migration abilities than those cultured in NG medium. The high glucose condition also enhanced invasion ability of KKU-M213, KKU-M214 and KKU-M214L5; but not KKU-M055. Reducing glucose concentration in the medium to NG could decrease the proliferation rate of all CCA cell lines. suggesting that CCA growth can be reduced if the glucose concentration is controlled.

Conclusion: High glucose condition plays significant role in promoting aggressive phenotypes of CCA cell lines. Adjusting glucose concentration to normal condition could decrease proliferation rate of CCA. These results suggest that the progression of CCA may be controlled via controlling blood glucose level in CCA patients with DM.

Oral