Identification of Potential Biomarkers of Hepatocellular Carcinoma in Type 2 Diabetic Patients through the Investigation of the Biological Impact of Glycated Albumin on Cancer Cell Lines

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Abstract

Type 2 diabetes (T2D) is the most common form and a long-term chronic metabolic disorder characterized by hyperglycaemia due to untreated insulin resistance, generating glycated albumin. There is an increased risk of liver cancer in T2D patients, particularly hepatocellular carcinoma (HCC). Therefore, for early diagnosis and therapeutic strategy, we aimed to identify potential biomarkers of liver cancer in T2D patients by investigating the biological impact of glycated albumin on HCC cell lines HepG2 and HuH7. After treatment with various concentrations (25-200 μg/mL) of glycated albumin (GA), cell viability, migration and invasion were assessed using Crystal violet staining, scratch assay, and Boyden chamber. Expression of signaling and oncology-related proteins was monitored using Western blot and protein array. GA significantly modulated cell viability, migration, and oncogenic phospho-extracellular signal-related kinase (p-ERK) in a bell-shaped curve, compared to untreated cells, the control. At 50-100 μg/mL, GA significantly stimulated cell invasion and upregulated EpCAM and Galectin-3 in HuH7 cells, and to a lesser extent in HepG2 cells. Increased Galectin-3 and metabolic signaling phospho-pS6 was observed by immunohistochemistry in HCC tissues from T2D patients compared to their non-diabetic counterparts. A larger cohort will be needed to confirm these potential protein biomarkers of HCC in T2D patients.

Keywords

Hepatocellular carcinoma, Type 2 diabetes, Biomarkers, Liver tissue.