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Racial disparities in hexokinase 2 (HK2) expression in hepatocellular carcinoma (HCC)

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Background: The mitochondrial high affinity HK2 that catalyzes the first committed step in glycolysis is highly expressed in HCC. Normal hepatocytes exhibit only low affinity hexokinase (glucokinase [GK]) but during tumorigenesis, there is a switch from GK to HK2 expression. Therefore in HCC there is a high level of HK2 and GK is silenced, and the highly glycolytic HCC cells are dependent on HK2. In a previous study, we reported that HK2 expression is higher in diabetes, in biologically aggressive HCCs, and is progressively higher in lesional progression from cirrhosis to dysplasia and ultimately HCC. The incidence and mortality rates for HCC are 2-3 times higher in African Americans than Caucasians, and diabetes and viral hepatitis are more common among African Americans than Caucasians with HCCs for reasons that are not completely understood. Our aims were to determine immunohistochemical (IHC) levels of HK2 in human HCCs, and to study associations between HK2 and clinical parameters such as ethnicity.

Design: We analyzed a liver tissue array from 159 subjects with cirrhosis (45 with HCC + 108 without) and 6 with normal liver for HK2 expression by IHC. HK2 immunoexpression was quantified by image analysis in normal, cirrhosis, dysplasia, and HCC tissues. Relationships between HK2 expression and clinical parameters were analyzed using non-parametric tests (Kruskal-Wallis and Mann-Whitney U-tests) in SPSS Statistics 17.0.

Results: Overall, the HK2 mean level in normal controls was 36.67 (15.20; n=6), cirrhosis 44.18 (32.71; n=106), dysplasia 59.94 (39.86; n=143), and HCC 64.42 (34.89; n=45). In the cirrhotic tissues of subjects with HCC, HK2 expression was significantly higher ($p = .008$) in subjects of African American race (68.80) in comparison to other ethnicities (30.09). Further, HK2 levels in AA race versus Caucasians, Hispanics, or other, when assessed in cirrhotic tissues in the HCC group approach significance ($p=0.052$).

Conclusion: A racial disparity of HK2 levels in HCC may contribute to biological differences of HCC outcomes among the different ethnicities. Verifying the findings in this pilot study using a larger cohort is necessary to determine whether higher HK2 levels of HCCs among African Americans impacts upon the poor prognosis of the disease in this group.

Biography

Grace Guzman, MD is an Associate Professor of Pathology at the University of Illinois Hospital and Health Sciences System where she teaches gastrointestinal and liver pathology and serves as the Medical Director of Liver Pathology Services there. She completed her pathology residency at Cedars-Sinai Medical Center in Los Angeles, California, and liver pathology fellowship at the University of Pittsburgh Health and Sciences Center. She has published over 60 peer reviewed manuscripts. Dr. Guzman focuses on the translational study of hepatocellular carcinoma by developing human progression tissue arrays and characterizing biomarkers. GG/GG 05292012

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