Dr. Lance D. Dworkin Department of Medicine Research Symposium

Characterization of Human Liver Tissue for Harmful Algal Bloom Exposure in Cancer and Non-Cancer Patients

John Najjar[1*], Anish Sharma[1], Sara Kazmi[1], Bella Khatib-Shahidi[1], Caitlin Murphy[1], Humza Bashir[1], Julissa Vargas[1], Bivek Timalsina[1], Apurva Lad[1], David Kennedy[2], Steve Haller[2]

[1]College of Medicine and Life Sciences, The University of Toledo, Toledo, OH

43614

[2]Division of Cardiology, Department of Medicine, The University of Toledo, Toledo,

OH 43614

*Corresponding author: jnajjar@rockets.utoledo.edu

Published: 14 December 2023

Introduction: Harmful algal blooms (HABs) are occurring more frequently not only in the Great Lakes region but also globally. HABs release cyanotoxins, which present public health concerns and significant health risks including associations with hepatocellular carcinoma. Cyanotoxins may enter humans through water ingestion, aerosol inhalation, or direct skin contact. We have previously demonstrated that cyanotoxins exacerbate pre-existing liver and inflammatory bowel disease in mice. However, the effects of cyanotoxin producing cyanobacteria in humans with liver cancer is unknown.

Objectives: We sought to identify the presence of cyanobacteria in Formalin-Fixed Paraffin Embedded (FFPE) liver tissue obtained from patients residing in the Great Lakes region. We hypothesized that the levels of cyanobacteria correlate with markers of tumor severity in hepatocellular carcinoma (HCC).

Methods: DNA and RNA were extracted using an optimized extraction/purification protocol designed for Formalin-fixed paraffin-embedded (FFPE) liver tissues from HCC (n=4) and age and sex matched non-HCC controls (n=4). Presence of cyanobacteria and markers of tumor severity were determined using quantitative PCR analysis.

Results: Cyanobacteria levels were elevated in liver cancer tissues compared to non-cancer (1.0 ± 0.23 vs 2.8 ± 1.0, p=0.06) although this was not statistically significant. Interestingly, while markers of tissue remodeling were not significantly correlated with cyanobacterial load overall in both cancer and non-cancer samples, within the HCC samples, cyanobacterial load was positively correlated with tissue inhibitor of metalloproteinases isoform 1 (TIMP-1, r=0.9103, p=0.0008).

Conclusion: Our results suggest that cyanobacteria may be increased in the setting of hepatocellular carcinoma and may impact the expression of key tissue remodeling genes within these tumors. This data is in agreement with clinical and experimental evidence suggesting an association between cyanobacteria and cancer progression in other settings and supports the need to investigate the potential

role of cyanobacteria in liver cancer progression. Analysis of additional samples is ongoing to establish this relationship in an expanded cohort.