MOLECULAR MECHANISMS OF AFLATOXIN B1 (AFB1) INDUCED TOXICITY ON HUMAN LIVER CARCINOMA (HEPG2) CELLS

Philemon K. Kirui¹, Clement G. Yedjou¹, ², Paul B. Tchounwou¹, ², Barbara Graham¹, ², Kenneth Ndebele¹, ² and Raphael Isopehi³

¹Environmental Science Ph.D. Program; ²NIH-Center for Environmental Health, College of Science, Engineering and Technology, Jackson State University, 1400 Lynch Street, Box 18540, Jackson, Mississippi; ³Department of Biology, Bethune-Cookman University, Daytona Beach, Florida, USA

Abstract: Aflatoxin B1 are extremely toxic secondary metabolites, cancer causing chemical produced by a few species of fungus namely Aspergillus flavus and Aspergillus parasiticus. They are found almost everywhere in a wide range of agricultural products affecting about 25% of agronomic produce worldwide. Classified as group 1 carcinogen, aflatoxin B1 has been shown in epidemiological studies that it has a positive correlation between dietary aflatoxin and liver cancer. Our study objectives were (1) evaluate the cytotoxicity of aflatoxin B1 to HepG2 cells utilizing MTT assay, (2) determine whether oxidative stress plays a role in aflatoxin B1 induced toxicity to HepG2 cell utilizing lipid peroxidation assay, glutathione peroxidase assay and catalase assay and (3) determine whether aflatoxin B1 induces DNA damage in HepG2 cells utilizing comet assay. HepG2 cells were treated with different concentration of aflatoxin B1 for 48 hours prior to tests. Data generated from MTT assay indicate that at low concentrations, aflatoxin B1 had no effect on the viability of HepG2 cells, whereas a strong positive correlation was observed between higher concentration and cytotoxicity. Comet assay detected DNA damage in cells exposed to aflatoxin B1 compared to the controls. Our study finds that aflatoxin B1 induced toxicity on HepG2 cells through oxidation processes. Oxidation of Aflatoxin B1 leads to the formation of Aflatoxin B1-8, 9-epoxide, which is highly unstable. In the presence of biological nucleophils, it forms stable links to RNA and DNA inducing point mutations and DNA strand breaks, which was detected by Comet assay. This is the process that is highly correlated with carcinogenic effects in both animals and human cancer cases. In the presence of water molecules, Aflatoxin B1-8, 9-epoxide is hydrolyzed into aflatoxin B1-dihydrodiol, and becomes available to be linked with proteins such as lysin and albumin, explaining the toxicity of aflatoxin B1

Keywords: aflatoxins, hepatocellular carcinoma cells, liver cancer, DNA damage, toxicity

Acknowledgments: This research work was supported in part by the Mississippi INBRE, funded by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM103476, and in part supported by NIH-RCMI Grant # G1200MD007581 at Jackson State University.