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Transcriptome profiling of human hepatocyte cell line HHL-16 in response to aflatoxin B1.

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Dietary exposure to aflatoxin (AFB1) can cause acute aflatoxicosis and liver cancer, and is associated with immune suppression and growth impairment. A non-neoplastic human hepatocyte cell line 16 (HHL-16) was used to understand the effects of AFB1 on the transcriptome and identify molecular pathways underlying toxicity and health effects.

HHL-16 cells were treated with different concentrations of AFB1 and the MTT assay was used to assess the cytotoxicity of AFB1. RNA samples were extracted for RNA-Sequencing and bioinformatic analysis (RNA-Seq) (Novogene Co. Ltd (Cambridge, UK)). RT-qPCR was used to validate gene expression of several differentially expressed genes.

A dose-dependent pattern of AFB1 toxicity was observed. RNA sequencing revealed 280 significantly up-regulated and 296 significantly down-regulated genes in HHL-16 cells after 20 µg/ml AFB1 treatment for 24 hours. In GO-term analysis of differentially expressed genes (DEGs), three main categories were identified: biological process, cellular component, and molecular function. KEGG pathway enrichment analysis indicated that DEGs were significantly enriched in the following pathways: cytokine-cytokine receptor interaction, NF-kappa B signalling pathway, TNF signalling pathway, IL-17 signalling pathway, Amoebiasis, MAPK signalling pathway, and lipid and atherosclerosis. In the most significant DEGs associated KEGG pathway, cytokine-cytokine receptor interaction pathway, 15 genes (IL24, IL11, IL6, LIF, CXCL8, BMP2, CXCL2, TNFSF15, NGFR, CXCL3, IL1RN, IL10RA, IL1RL1, TNFRSF9, CSF2) were up-regulated, and 4 genes (INHBB, IL17RE, TNFSF18, TNFSF4) were downregulated. Further, in the validation of the DEGs by RT-qPCR, dose-dependent increases of IL6, CCL20 and BMP2, and dose-dependent decrease of NDP gene expression were found in HHL-16 cells after 5, 10, and 20 µg/ml AFB1 treatments for 24 hours.

Conclusions: AFB1 modulates the expression of genes related to the pathways that play important roles in inflammatory response, growth, and cancers.