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LS-11-P-2186 Fumonisin B1 alters the expression of cyclin-dependent kinases (CDK) and CDK inhibitors in mouse liver

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Fumonisin B1 (FB1), the most prevalent member of a family of toxins produced by fusarium verticillioides, induces cell proliferation in the liver. Cell proliferation requires a coordinated interaction of cyclin-dependent kinases (CDK) and CDK inhibitors. The purpose of this study was to examine the expression of CDKs and CDK inhibitors in FB1 treated liver. C57BL/6 mice were divided into 3 groups and received FB1 (0, 5, and 20mg/kg/day, i.p) for 5 days. Liver tissues were processed for immunohistochemistry and immunoblot analysis. Low-dose FB1 (5 mg/kg) did not affect AST levels. However, high-dose FB1 (20 mg/kg) significantly increased AST serum levels and caused extensive necrosis. Both low-dose and high-dose FB1 significantly induced cell proliferation. Immunohistochemical detection of PCNA and quantification revealed that cell proliferation increased by 4.69-fold (5 mg group) and 4.86-fold (20 mg group), respectively. Expression of CDK2, CDK4, and CDK6 significantly increased in both low-dose and high-dose FB1 groups. Also, expression of CDK associated cyclins (D1 and D3) increased in both FB1 groups. Confocal microscopy showed that expression CDK2 was co-localized with PCNA in the nucleus of many hepatocytes. In contrast, expression of P18INK4C and P27KIP1 significantly decreased in both low-dose and high-dose FB1 groups. Interestingly, localization of P27KIP1 shifted from the nucleus to the cytoplasm in both FB1 groups. These results suggest that expression and intracellular redistribution of CDKs and CDK inhibitors may play an important role in FB1-induced cell proliferation in the liver.

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