Role of autophagy in fumonisin B1-induced toxicity in the mouse liver

Han, K.[1], Lee, S.[1], Chung, Y.[1], Song, S.[1], Lee, S.[1] and Oh, S.[2]

[1] Department of Anatomy, College of Medicine, Ewha Womans University, Republic of Korea, [2] Department of Molecular Medicine, College of Medicine, Ewha Womans University, Republic of Korea

Autophagy is a cellular degradative pathway and maintains homeostasis between cell death and survival. Fumonisin B1 (FB1) is a mycotoxin that causes liver toxicity by disrupting sphingolipid metabolism.
The purpose of this was to examine the role of autophagy in FB1-induced hepatotoxicity. C57BL/6 mice were intraperitoneally injected with FB1 at 0, 2.5, 5, 10 or 20 mg/kg/day for 5 days. Liver tissues were processed for immunoblot analysis, immunohistochemistry, transmission and electron microscopy and scanning electron microscopy.
In the groups administered with 10 and 20 mg/kg/day of FB1, serum liver enzymes (AST and ALT) were significantly increased. Also, liver tissues showed vacuolar change and focal necrosis. There was no statistical difference in the 2.5 and 5mg groups compared to the control. Expression of LC3 I/II, Atg3, Atg5, Atg16 and beclin-1 significantly increased in the 2.5 and 5 mg groups, but not in the 10 and 20 mg groups. In the 2.5 and 5 mg groups, LC3 immunoreactivity was localized to cytoplasmic vacuoles in hepatocytes. Transmission and scanning electron microscopy revealed that membrane-enclosed damaged organelles, sometimes fused with lysosomes, were predominantly observed in the 2.5 and 5 mg groups. Instead, in the 10 and 20 mg groups, typical features of necrotic cell death, such as swelling of organelles with membrane disruption, were observed.
These results suggest that autophagy may contribute to cell survival in response to low doses of FB1, and impairment response to higher doses of FB1 may cause necrotic cell damage.
This work was supported by funds from the National Research Foundation of Korea (NRF-2013R1A1A2058028 & 2017R1D1A1B03030573).