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Dabrafenib rescue liver cells from the amatoxins-induced liver necroptosis through inhibit receptor-interacting protein 3

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Objective: To study the effect of receptor-interacting protein (RIP) 3 on amatoxins-induced liver necrosis.

Methods: 30 Kunming mice were randomly divided into five groups (n=6 per group): control group(C), α-amanita toxin group (AMA), AMA+necrostatin-1group (AMA+Nec), AMA+ dabrafenib group (AMA+Dab), AMA+Nec+Dab group(Mixed). The mice in AMA, AMA+Nec, AMA+Dab and Mixed groups were intraperitoneally injected with AMA 2ug/g. The mice in AMA+Nec and Mixed groups were intraperitoneally injected with Nec 6.25 ug/g before AMA injection. The mice of AMA+Dab and Mixed groups were treated by means of intragastric administration with dabrafenib 0.3 mg/g before AMA injection. All animals were treated for 24 hours. All the animals were euthanized and peripheral blood and liver tissues were collected for further experiments.

Results: Liver cells showed serious necrosis in AMA. Dabrafenib significantly reduced the necrosis of hepatocytes in α-amanita toxin poisoning.

Conclusions: Dabrafenib protects liver cells from the amatoxins-induced liver necrosis through inhibiting RIP 3. Dabrafenib treatment significantly attenuated liver necrosis in α-amanita toxin poisoning.