Ribotoxic stress by mycotoxins

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More than 10% of the world's annual harvests are destroyed by mold (Normile 2010). Many fungi produce mycotoxins that accumulate in human tissues and induce toxic effects (Muñoz et al. 2009; Degen et al. 1997; Magdalan et al. 2009; Degen and Hengstler 2008; Klarić et al. 2008; Huang et al. 2009). The best known mycotoxin is aflatoxin B₁, which is one of the strongest human liver carcinogens (Hengstler et al. 1999; Hewitt et al. 2007). Aflatoxin B₁ is particularly critical for humans as they lack efficient detoxification of aflatoxin B₁ epoxide which is generated in the liver (Degen and Neumann 1978, 1981). In contrast, many mouse strains express specific isoforms of glutathione-S-transferase which detoxify aflatoxin B₁ metabolite and—in contrast to humans—render mice resistant to aflatoxin B₁ toxicity.

Besides aflatoxin, mycotoxins have not obtained the widespread attention and publicity that they deserve. Relatively, little is known about the outbreaks of severe gastroenteritis in China, the largest affecting 130,000 people, which were caused by rain-damaged wheat products (Pestka 2010, this issue). Mycotoxins in food are certainly having a major input on life spans in developing countries (Normile 2010).

The editors are happy that Professor James J. Pestka from Michigan State University accepted our invitation and has contributed a review about the mechanisms of action, human exposure and toxicological relevance of trichothec-

enes and specifically the most relevant deoxynivalenol (DON) (Pestka 2010, this issue). DON is the most commonly detected trichothecene in cereal grains and was responsible for numerous large outbreaks of human gastroenteritis. DON acts by interference with both translation and activation of protein kinases, representing toxic mechanisms that are cutting-edge topics of our journal (Muguruma et al. 2008; Glahn et al. 2008; Hengstler and Bolt 2008a, b; Decker et al. 2009; Periyakaruppan et al. 2009; Ito et al. 2009).

Of particular interest is DON's action as a “ribotoxin”, where protein kinases are mobilized to the ribosome and subsequently phosphorylated. This review is a must-read for everyone interested in mycotoxins and toxicity mediated via compromised ribosomes.

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