Ceramide synthase inhibition by fumonisins—a "perfect storm" of perturbed sphingolipid metabolism, signaling and disease

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Supplement C. Additional information on CerS2 KO mice

CerS2 knockout mice (1) have altered renal architecture (2), develop hepatocarcinomas (2, 3), have increased susceptibility to diethylnitrosamine-induced liver tumorigenesis (4) and develop pheochromocytoma (5). Biophysical effects of CerS2 knockout (6) include changes in membrane fluidity, phase separation, curvature and morphology, and hepatic plasma membrane functions such as receptor internalization (7), clathrin-mediated endocytosis (8), TNFα secretion (9) and gap junction activity (10). ROS generation from mitochondria is elevated due to impaired complex IV activity, and although levels of anti-oxidant enzymes are elevated, lipid peroxidation, protein nitrosylation, and ROS increase (8, 11). CerS6 knockout also induces apoptosis via activation ATF-6, a transcription activator that initiates the unfolded protein response (UPR) during endoplasmic reticulum stress (12).

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