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COMMENTS TO AUTHORS

This review summarizes in a comprehensive fashion major aspects of sphingolipids in cisplatin mediated anticancer effects.

Minor: It would be helpful to explain uni- and bidirectional arrows in Fig.1. Furthermore 1-2 sentences (for explaining the figure) about the main pathway in the legend might be considered.

Response: Thanks for your good suggestions. We added the meaning of uni- and bidirectional arrows in the legend of Figure 1. Some sentences for explaining the main pathway are also added in the figure legend.

COMMENTS TO AUTHORS

1. Ceramide chain length in mammalian cells, ceramides are generally synthesized from sphingoid bases, and very long (C24) or long (C16) fatty acid chains are added by specific ceramide synthases. During cisplatin-induced apoptosis, although intracellular ceramide levels are not changed, long ceramides are specifically elevated (Sassa et al., BBA, 2012; Siskind et al., JBC, 2010). Ceramides containing different acyl chain lengths influence membrane composition and affect cisplatin-induced apoptosis (Sassa et al., BBA, 2012). Author should mention these findings. Sassa T, Suto S, Okayasu Y, Kihara A: A shift in sphingolipid composition from C24 to C16 increases susceptibility to apoptosis in HeLa cells. Biochim Biophys Acta., 2012, 1821: 1031-7.

Response: we are sorry not to mention these important reports in our previous version, and we added related information in the section 3.1.

2. aSMase-mediated CD95 redistribution Cisplatin-induced redistribution of CD95 had been reported in HT29 cells (Lacour et al., Cancer Res., 2004). In this report, some important data of the molecular mechanism of aSMase-mediated CD95 relocation into lipid microdomains was presented. You should summarize this report. Lacour S, Hammann A, Grazide S, Lagadic-Gossmann D, Athias A, Sergent O, Laurent G, Gambert P, Sokary E, Dimanche-Boitrel MT: Cisplatin-induced CD95 redistribution into membrane lipid rafts of HT29 human colon cancer cells. Cancer Research, 2004, 64: 3593-8

Response: Thanks for your good suggestions. We added related information into section

3.2 of this version.