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Title: Autophagy induction by low dose cisplatin; the role of p53 in autophagy

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Body: Cisplatin has been mainly used for lung-cancer,. However, cisplatin has many side effects, so the usage of cisplatin has a limitation. Recently, autophagy has become an important mechanism of cell death. The purpose of this study was to determine whether low dose cisplatin treated lung cancer cell induce autophagy and the autophagy inhibition resulted in apoptosis or necrosis. H460 cells were treated with 5 μM or 20 μM cisplatin for 12, 24, or 48 h. To detect the cisplatin-induced autophagy, we examined the autophagic vacuoles, and LC3 localization. To confirm the low-dose of cisplatin could induce autophagy, we detectd acidic vesicle using autophagy specific inhibitors(3-MA). To confirm the result of autophagy inhibition, we had done Annexin-V/PI and cell cycle assay. To find out the cisplatin mediated autophagic mechanisms, we examined the apoptotic regulator, p53. We used p53-/- null cancer cell line, H1299, to prove the role of p53 during autophagy. Low dose of cisplatin(5 μM) induced the autophagy after 24 h treatment in H460. Also low dose of cisplatin showed autophagic vacuoles and cytoplasmic LC3 formation in H460. The induction of autophagy by low dose cisplatin was inhibited by 3-MA, which was proven by reduced acidic vesicles. When the autohpagy inhibited, Annexin-V+/PI- and subG1 was an increased. The inhibition of autophagy resulted in decrease of LC3B-II band. Also cleaved caspase-3 and PARP were increased. Taken together, low dose cisplatin induced autophagy and the inhibition of autophagy resulted in the apoptosis.