

Glutathione transferase mu 2 protects glioblastoma cells against aminochrome toxicity by preventing autophagy and lysosome dysfunction

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U373MG cells constitutively express glutathione S-transferase mu 2 (GSTM2) and exhibit 3H-dopamine uptake, which is inhibited by 2 μ M of nomifensine and 15 μ M of estradiol. We generated a stable cell line (U373MGsiGST6) expressing an siRNA against GSTM2 that resulted in low GSTM2 expression (26% of wild-type U373MG cells). A significant increase in cell death was observed when U373MGsiGST6 cells were incubated with 50 μ M purified aminochrome (18-fold increase) compared with wild-type cells. The incubation of U373MGsiGST6 cells with 75 μ M aminochrome resulted in the formation of autophagic vacuoles containing undigested cellular components, as determined using transmission electron microscopy. A significant increase in autophagosomes was determined by measuring endogenous LC3-II, a significant decrease in cell death was observed in the presence of bafilomycin A1, and a significant increase in cell death was observed in the presence of trehalose. A significant increase in LAMP2 immunosta