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Aldehyde Dehydrogenase 1A3 (ALDH1A3) is Regulated by Autophagy in Human Glioblastoma Cells

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Abstract:

Aldehyde dehydrogenase is a polymorphic enzyme, which responsible for the oxidation of aldehydes. It has been shown that ALDH1A3 is expressed in human glioblastomas and that its expression correlates with a worse prognosis. In our present study ALDH1A3 expression was associated with resistance against Temozolomide (TMZ) treatment and sensitivity could be re-established in ALDH1A3 knockout cells. TMZ treatment at high concentrations diminished ALDH1A3 protein and this downregulation made the tumor cells more sensitive to chemotherapy. ALDH1A3 was post-transcriptionally regulated since mRNA levels were not affected by TMZ treatment. With increasing concentrations of TMZ, autophagy was up-regulated, and we found evidence for a physical interaction between ALDH1A3 and p62, an important adaptor protein in autophagosomes indicating that ALDH1A3 protein was downregulated by autophagy. So far, the results of the exact role of autophagy in tumor development and tumor growth are inconsistent. Our data indicate that ALDH1A3, that is directly involved in therapy resistance of glioblastoma, is regulated by autophagy during chemotherapy.