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Abstract

The purposes of this study were to determine whether organic cation transporters (OCTs) can mediate platinum uptake, and whether OCT down-regulation confers resistance against cisplatin (CDDP) in cancer cells. Two lung cancer cell lines, PC-6 and PC-14, and their CDDP-resistant derivatives, PC-6/CDDP and PC-14/CDDP, were analyzed. OCT expression levels were assayed using quantitative RT-PCR and Western blotting. Both gene and protein expression of OCT6 were decreased in both CDDP-resistant cell lines compared with their expression in their respective parental cells. Additionally, the effect of OCT6 overexpression, induced by transfection of the OCT6 gene SLC22A16 using a forced expression vector, on intracellular platinum accumulation and on cellular sensitivity to CDDP was measured using PC-14/CDDP cells. Intracellular accumulation of platinum was decreased in PC-14/CDDP cells compared with the parental cells after CDDP treatment. Furthermore, OCT6 overexpression induced by transfection of the OCT6 gene (SLC22A16) forced expression vector-sensitized PC-14/CDDP cells to CDDP and oxaliplatin (L-OHP) concomitant with increased intracellular concentration of platinum. These results indicate that OCT6 is a mediator of CDDP uptake and that the down-regulation of OCT6 directly confers to resistance against CDDP via decreasing the intracellular platinum concentration.