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Role of copper transporters in platinum resistance

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27 Abstract

Platinum (Pt)-based antitumor agents are effective in the treatment of many solid malignancies. However, their efficacy is limited by toxicity and drug resistance. Reduced intracellular Pt accumulation has been consistently shown to correlate with resistance in tumors. 15 proteins involved in copper homeostasis have been identified as Pt transporters. 19 In particular, CTR1, the major copper influx transporter, has been shown to play a significant role in Pt resistance. Clinical studies demonstrated that expression of CTR1 correlated with intratumoral Pt concentration and outcomes following Pt-based therapy. Other copper transporters such as CTR2, ATP7A and ATP7B, 64 may also play a role in Pt resistance. Recent clinical studies attempting to modulate CTR1 to overcome Pt resistance may provide novel strategies. This review discusses the role of 42 CTR1 as a potential predictive biomarker of Pt sensitivity and a therapeutic target for overcoming Pt resistance.

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