SUBCELLULAR LOCALIZATION OF PROHIBITIN IN CISPLATIN-TREATED HUMAN MELANOMA CELLS

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Melanoma incidence is increasing worldwide and represents a clinical challenge, as their treatment outcome is still poor (less than 30% in the more advanced cases). The molecular bases for chemoresistance are poorly understood. In a previous study, we had observed an increase in the amounts of prohibitin in cisplatin-treated melanoma cells. There is evidence that prohibitin may be either anti- or proapoptotic depending on its subcellular localization. Here we used two distinct antibodies to follow prohibitin accumulation and subcellular compartmentalization upon treatment of different melanoma cell lines with cisplatin. The two antibodies recognize either a nuclear isoform or a mitochondria-associated isoform of prohibitin. LB373 melanoma cells, and their cisplatin-resistant counterpart, LBR01 accumulated cisplatin both in the nucleus and in the cytoplasm upon cisplatin treatment. Nuclear staining was not homogeneous, but rather compartimentalized in structures resembling nuclear speckles, as observed in LBR01. Cytoplasmic prohibitin was found mainly in mitochondria, as observed in colocalization studies. Other melanoma cell lines tested rendered similar results, suggesting that prohibitin accumulation and subcellular redistribution is part of the response to cisplatin-induced cellular stress, which may result either in cell death or selection of resistant cells. Dissection of the molecular pathways involved in compartmentalization of this bifunctional molecule may lead to novel strategies for improving tumor cell chemosensitivity.
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