Influence of Metallothioneins on Binding between Cisplatin and DNA in Cisplatin Resistant and Non-Resistant Neuroblastoma Cells

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Introduction

Cisplatin (CDDP) has been successfully used in the chemotherapy of multiple types of cancer. The cytotoxic effect of CDDP consists of DNA adducts formation and triggering apoptosis. However, CDDP can bind many potential platinum-binding molecules, such as metallothioneins (MT), which decrease its effective concentration. Aim of this study was to determine the binding capacity of DNA and MT isolated from neuroblastoma cells.

Materials/methods

CDDP resistant (UKF-NK-4^{CDDP}) and non-resistant (UKF-NK-4) neuroblastoma cells (4×10^6) were cultured with 0.1; 1.0; and 10 μM CDDP for 24 h. After trypsination and washing with

PBS and 10 mM EDTA cells were used for isolation of DNA and total protein. After denaturation of total protein (10 min, 90 ^{o}C) level of thermostable MT was analyzed. Finally, amount of bounded CDDP was analyzed in both, DNA and MT.

Results and conclusions

Since metalothioneins are intracellular metal-binding proteins we hypothesized that their expression may be involved in chemoresistance towards CDDP. Indeed, electrochemical measurements revealed higher expression (more than 4-fold) of metallothionein in UKF-NK-4^{CDDP} cells. Similarly to that we found that UKF-NK-4^{CDDP} cells accumulate higher amount of CDDP due to higher MT expression. Concurrently, UKF-NK-4 cells exhibited higher amount of CDDP in DNA. Taken together, our pilot study describes the possible chemoresistance phenomenon in neuroblastoma cells, based on interaction between CDDP and ubiquitous, intracellular MTs.

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