Mitochondrial remodeling involved in cisplatin resistance

C. Vianello [1], D. Catanzaro [1], V. Cocetta [1], E. Ragazzi [1], M. Montopoli [1]
[1] Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Largo E. Meneghetti 2, 35131 Padova, Italy.

Although cisplatin is used to treat a multitude of cancers including lung, ovarian and testicular cancer[1], unfortunately, the resistance is a common limit to its clinical effectiveness and the molecular mechanisms are not completely understood.
Classically, cisplatin is studied as a DNA-damaging chemotherapy agent, but more recent studies showed that only 5-10% of intracellular platinum is bound to nuclear DNA, while the great majority of the intracellular drug can interact with a variety of cellular component including phospholipids, cytosolic, cytoskeletal and membrane proteins, RNA and mitochondrial protein and mtDNA[2].
The aim of this study was to investigate the mitochondrial remodeling in cisplatin-resistant cells to reveal targets for overcoming this important form of resistance.
Previously we have demonstrated that cisplatin-resistant ovarian cancer cells (C13) are characterized by a reduced respiratory chain activity and lower mitochondrial mass when compared to the cisplatin-sensitive counterpart (2008) as well as a different susceptibility to various metabolic stresses, in particular the exposure of glucose-free/galactose medium or rotenone, inhibitor of mitochondrial respiratory chain[3].
In this scenario we analyzed others cisplatin-resistant and sensitive cancer cells, in particular cervix squamous human carcinoma (A431 and A431-Pt), osteosarcoma (U2OS and U2OS-Pt) and ovarian carcinoma (SKOV3 sensitive and SKOV3 CDDP3) cell lines.
Previous results show no significant differences in mitochondrial membrane potential ($\Delta\Psi$) and mitochondrial mass between CDDP-resistant and sensitive cells; but we can see a different mitochondrial phenotype, in particular a fragmented mitochondrial network in all resistant clones. Mitochondria are highly dynamic organelles that are constantly dividing and elongating to form a network. Thus, our purpose will be to investigate the mitochondrial dynamics that may in part be involved in the patho-physiology of CDDP resistance.
The study of the processes that influence mitochondria impairment of cancer cells can be useful to develop more effective treatments to target specific cancer cells based on their mitochondrial profile to sensitize to anticancer treatments.

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