

## Applications of Copper Sensitive Fluorescent Dye to the Studies of the Role of Copper in Cisplatin Resistance in Human Cancer

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**Abstract :** Pt compounds have been among the most successful anticancer drugs in the last 40 years, but the development of resistance to them is an increasing problem. Cellular homeostasis of an essential metal, Cu, is known to be involved in Pt resistance, but mechanisms of this process are poorly understood. We used a novel ratiometric Cu(I)-sensitive fluorescent probe InCCu1 dye to detect Cu(I) in the mitochondria. Total Cu and labile Cu pool measured using AAS and InCCu1 dye in A2780 cells and their corresponding resistant cells A2780-cis.R cells treated with Cu and cisplatin. The main difference between both cell lines in the presence and absence of Cu(II) is that resistant cells have lower total Cu content but higher labile Cu levels than cisplatin-sensitive cells. This means that resistant cells can metabolize and export excess Cu more efficiently. Furthermore, InCCu1 has emerged not only as an indicator of labile cellular Cu levels in the mitochondria but as a potentially versatile multi-organelle probe.

**Keywords :** AAS and ICPMS, A2780 and its resistant cells, ratiometric fluorescent sensors, InCCu1, and total and labile Cu

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