AZT CYTOTOXICITY, CELLULAR DRUG RESISTANCE AND DNA METHYLATION IN *IN VITRO* CELL SYSTEMS.
REP. # 2 – EFFETTO DELL'AZT SULLA FUNZIONALITÀ DEL RECETTORE DELLA TRASNFERRINA IN CELLULE ERITROLEUCEMICHE.

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During the previous project (30A.0.66 – proposal 358/1997) we had shown, using an *in vitro* cellular erythroleukemia model, that AZT causes, besides a significant reduction of proliferation and differentiation capabilities of these cells, an increase in the number of membrane receptors for transferrin, while the affinity of these receptors for their ligand remains unchanged. By studying the kinetics of biosynthesis and of internalization of the transferrin receptors, we could show that there is essentially a slowing down of receptor turnover, which leads to a paradoxical decreased iron uptake. The hypothesis of an iron-chelating role of phosphorylated AZT metabolites was verified and discarded. It was shown instead that, in the presence of AZT, there is a consistent decrease of the α-2,8 sialylated isoform of the transferrin receptor, due to a specific inhibition of the α-2,8 sialyltransferase activity, while the α-2,3 e α-2,6 sialyltransferase activities are not affected. AZT appears instead unable to perturb, under several conditions, either the differentiation or the apoptosis of K562 cells.

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