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Letter to the editors

Cisplatin induces modulation of transferrin receptor during cellular differentiation in vitro

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Sir,

cis-Diamminedichloroplatinum (II) (cisplatin) is a potent anticancer drug particularly useful in testicular cancer, bladder cancer, neuroblastoma, and other solid tumors [4]. Cisplatin is active as an alkylating agent, being a non-protein-bound platinum probably representing the biologically active molecule [6]. Very few data related to the drug-induced cellular differentiation and surface receptor modulation of neoplastic cells are available. Transferrin (Tf) receptor is a cell surface glycoprotein expressed by both normal and neoplastic mitotically active cells, and it is believed to be a reliable marker of cellular proliferation [2]. We evaluated the in vitro effect of cisplatin on the expression of Tf receptor in the human erythroleukemia cell line K562. K562 is a well-known cell line obtained from the pleural effusion of a CML patient [3]; these cells usually express high levels of Tf receptor evaluable with OKT9 monoclonal antibody [1]. Erythroid differentiation of such a line can be achieved by different inducers, e.g., hemin and butyrate [5]. We cultured K562 cells in the presence of 2.5 μg/ml (cytostatic dose) of cisplatin for a week in RPMI 1640 complete medium; $OKT9^+$ cells were checked daily by Ortho Spectrum III cytofluorimeter (see Table 1); hemoglobin synthesis was evaluated in parallel by spectrophotometric analysis (2.27 pg/cell at the 7th day versus 0.627 pg/cell when cells are untreated). Cisplatin induced characteristic morphological changes, cells becoming enlarged within 24 h while the Tf receptor decreased markedly after 72 h, erythroid differentiation being achieved contemporaneously with the production of a significant amount of hemoglobin.

Table 1. Percentage of $OKT9^+$ cells

Time (h)	Control	CDDP
0	92	91.7
24	89.6	78.5
48	93.5	79.4
72	90.1	59.9
96	91.8	53.5

Surface immunofluorescence, evaluated by OKT9 monoclonal antibody, was performed with Ortho-Spectrum III

These results appear to confirm that cisplatin modulates Tf receptor expression as well as inducing erythroid differentiation of K562 cells; the decrease in Tf receptor and the erythroid differentiation were paralleled by transition of the cells from the exponential to the quiescent phase of growth. We regard these results as preliminary evidence of pro-differentiative activity of cisplatin.

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