

# 1*R*,2*R*-シクロヘキサンジアミンを配位子にもつ 四価および二価白金錯体の細胞毒性

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## Cytotoxicity of Platinum(IV) and Platinum(II) complexes Containing 1*R*,2*R*-Cyclohexanediamine as a Ligand

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**ABSTRACT** Several Pt(IV) and Pt(II) complexes containing 1*R*, 2*R*-cyclohexanediamine (1*R*,2*R*-dach) as a carrier ligand were synthesized. The cytotoxicities and the uptake of the platinum complexes by leukemia L1210 cells were compared in order to study the correlation between their structures and cytotoxicities.

[Pt(II)Cl<sub>2</sub>(1*R*, 2*R*-dach)], [Pt(II)(oxalato)(1*R*, 2*R*-dach)], and [Pt(II)(malonato)(1*R*,2*R*-dach)], which have excellent anticancer properties, exhibited very high cytotoxicities and were easily taken up by leukemia L1210 cells. [Pt(IV)Cl<sub>2</sub>(1*R*, 2*R*-dach)], *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>(oxalato)(1*R*,2*R*-dach)], and *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>(malonato)(1*R*,2*R*-dach)] also had high cytotoxicities. After a short incubation time, the uptake of [Pt(II)Cl<sub>2</sub>(1*R*,2*R*-dach)], [Pt(II)(oxalato)(1*R*, 2*R*-dach)], and [Pt(II)(malonato)(1*R*,2*R*-dach)] by leukemia L1210 cells were respectively very similar to those of [Pt(IV)Cl<sub>4</sub>(1*R*,2*R*-dach)], *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>(oxalato)(1*R*,2*R*-dach)], and *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>(malonato)(1*R*,2*R*-dach)].

In addition, *trans*(OH)-[Pt(IV)(OH)<sub>2</sub>Y<sub>2</sub>(1*R*,2*R*-dach)] (Y<sub>2</sub>: oxalato or malonato) did not exhibit cytotoxicity towards leukemia L1210 cells, whereas *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>Y<sub>2</sub>(1*R*,2*R*-dach)] (Y<sub>2</sub>: oxalato or malonato) were highly cytotoxic. The accumulation of *trans*(OH)-[Pt(IV)(OH)<sub>2</sub>Y<sub>2</sub>(1*R*,2*R*-dach)] in leukemia L1210 cells was much lower than that of *trans*(Cl)-[Pt(IV)Cl<sub>2</sub>Y<sub>2</sub>(1*R*,2*R*-dach)]. Platinum(IV)

complexes, in which leaving groups are replaced by hydroxide groups, have decreased cytotoxic activity, because the hydroxide groups of the platinum(IV) complex reduce the uptake of platinum by the cells. *trans*(OH)<sub>2</sub>,*cis*(Cl<sub>2</sub>)-[Pt(IV)(OH)<sub>2</sub>Cl<sub>2</sub>(1*R*,2*R*-dach)], which has hydroxide and chloride groups, was easily incorporated into the cells and exhibited the high cytotoxic activity. This behavior indicates that the chloride group apparently overcomes the ameliorating effect of the hydroxide group.

抄録 1*R*,2*R*-シクロヘキサンジアミンをキャリアーリガンドとする四価および二価白金錯体10種を合成した。白血病L1210細胞に対するこれら錯体の細胞毒性と細胞への取り込みを比較検討し、錯体の化学構造と抗腫瘍活性の相関性を明らかにした。

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