学位論文の要旨

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主論文の題名

Heterogeneity of neuroblastoma cell lines in IGF-1 receptor/Akt pathway-mediated cell proliferative responses

主論文の要旨

31 NB cell lines, cultured in 3 different media, including Hybridoma-SFM medium (with insulin) and RPMI1640 with/without 10% FBS, showed Three growth patterns. In response to IGFs and insulin, cell proliferation and Akt phosphorylation were up-regulated in 13 cell lines, and suppressed by MK2206 (Akt inhibitor) and picropodophyllin (PPP, IGF-1R inhibitor). Interestingly, 3 of these 13 cell lines showed Akt self-phosphorylation and cell proliferation in RPMI1640; their proliferation was down-regulated by anti-IGF-1 or anti-IGF-2 neutralizing antibody, suggesting the existence of autocrine loop in the IGF-1R/Akt pathway. Eighteen NB cell lines did not proliferate in RPMI1640, even though Akt phosphorylation was up-regulated by IGFs and insulin. Based on the heterogeneous response of the IGF-1R/Akt pathway, the 31 NB cell lines could be classified into group 1 (autocrine IGFs-mediated), group 2 (exogenous IGFs-mediated) and group 3 (partially exogenous IGFs-mediated) NB cell lines. Additionally, group 3 NB cell lines were different from group 1 and 2, in terms of serum starvation-induced caspase 3 cleavage and PPP-induced G2/M arrest. These results indicate that the response of the IGF-1R/Akt pathway is an important determinant of the sensitivity to IGF-1R antagonists in NBs.