Differential expression of Apo2L receptors is a possible mechanism of tumor selective-cytotoxicity by Apo2L

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Background Apo2L is a member of tumor necrosis factor cytokine family that triggers apoptosis in many types of cancer cells, but not in most normal cells. Although the exact mechanism of tumor-selective cytotoxicity of Apo2L is unknown, one possible mechanism is differential expression of death-inducing receptors (DR4 and DR5) and antagonising or decoy (DcR1 and DcR2) receptors. We attempted to study the expression of Apo2L and its receptors on cells from two hematologic and one non-hematologic cell lines and the amount of Apo2L-induced apoptosis in each cell lines.

Methods We investigated surface expression of Apo2L and its receptors (DR4, DR5, DcR1, and DcR2) on Colo205, Jurkat, and KG1 cell lines by flow cytometry using developed monoclonal antibodies against human Apo2L and its receptors. To determine the effects of human Apo2L on apoptosis in these cell lines, fresh cells from each cell lines were propagated in short-term cultures in the presence or absence of human Apo2L (0~3,000 ng/mL). The amount of apoptosis was measured by flow cytometry utilizing FITC-conjugated Annexin V.

Results In cells from three cell lines, the expression of Apo2L was minimal (1.7% in Colo205, 0.5% in Jurkat, 0.7% in KG1). In contrast, Apo2L receptors were constitutively expressed on three cell lines with unique patterns: DR4 82.8%, DR5 98.6%, DcR1 1.2%, and DcR2 2.1% in Colo205; 21.0%, 82.4%, 0.1%, and 1.8% in Jurkat; 18.9%, 5.1%, 7.9%, and 0.8% in KG1. A maximal increase in apoptosis was observed in cell lines after exposure to human Apo2L above 300 ng/mL (67.4% in Colo205; 88.5% in Jurkat; 16.9% in KG1).

Conclusion There are distinct differences in expression of Apo2L receptors in each cell lines. The results of apoptosis analysis show that cytotoxic effect was increased following Apo2L exposure in cell lines which has greater expression of agonistic receptors and lesser expression of antagonistic receptors with dose dependent manners. These results suggest that a different level of apoptosis in certain cell lines depends upon pattern of expression of Apo2L receptors. Thus, the differential expression of Apo2L receptors might be a possible mechanism to explain tumor-selective cytotoxicity by Apo2L.