Carvalho et al. BMC Proceedings 2010, 4(Suppl 2):P46
http://www.biomedcentral.com/1753-6561/4/S2/P46

BMC Proceedings

POSTER PRESENTATION Open Access

Recombinant trail: a synergistic effect in myeloid leukemias

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From 16th International Charles Heidelberger Symposium on Cancer Research
Coimbra, Portugal. 26–28 September 2010

The tumor necrosis factor (TNF)-related apoptosis inducing ligand (TRAIL/Apo-2L) is a member of the TNF superfamily that trigger and activate 2 death receptors, DR4 and DR5, and 2 decoy receptors, DcR1 and DcR2. Several studies demonstrated that TRAIL in monotherapy can induces cancer cell death cells, but few have been done in leukemias in combination with conventional drugs. The aim of this work is to analyse the potential synergist effect of a recombinant TRAIL (rhTRAIL) in myeloid leukemias.

For this, 2 myeloid leukemia cell lines, HL-60 (promyelocitic leukemia) and K-562 (Chronic Myeloid Leukemia) were treated with different concentrations of rhTRAIL as single agent and in combination with ATRA (all-transretinoic acid) and imatinib, respectively. The viability was measure using the trypan blue test and cell death by flow cytometry (FC) and Optical Microscopy. TRAIL and TRAIL-Rs were evaluated by FC.

Our results show that rhTRAIL induced a decrease in cell viability inducing cell death, in a time, dose and cell type dependent manner. We observe an IC_{50} in HL-60 treated for 48h of 250 ng/mL, although in K562 cells, rhTRAIL wasn't able to induce a significant effect. However, when we previously treated the cells with ATRA or IMATINIB a synergistic effect is observed, mainly in HL60 cells. These results may be correlated with the differential TRAIL receptors expression, namely the presence of the anti-apoptotic TRAIL receptors, in K562 cells. On the other hand, the higher percentage of pro-apoptotic TRAIL receptors may be related with the therapeutic efficacy of rhTRAIL in HL-60 cells. Our study suggests that rhTRAIL can be use as a new therapeutic aproach in APL, as single agent. However, it can potentiate the cytotoxic effect of conventional drugs.

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Published: 24 September 2010

doi:
Cite this article as: Carvalho *et al.*: Recombinant trail: a synergistic effect in myeloid leukemias. *BMC Proceedings* 2010 **4**(Suppl 2):P46.