RETROVIROLOGY

MEETING ABSTRACT Open Access

A novel tetramethylnaphthalene derivative synergistically inhibits HTLV-1-infected cell proliferation in combination with cepharanthine

Masaaki Toyama[1*], Takayuki Hamasaki[1], Tomofumi Uto[1], Hiroshi Aoyama[2], Mika Okamoto[1], Yuichi Hashimoto[2], Masanori Baba[1]

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Background

We have previously found that the novel tetramethylnaphthalene derivative TMNAA selectively inhibits the proliferation of HTLV-1-infected T-cell lines but not HTLV-1-uninfected T-cell lines. Although its target molecule is still unknown, TMNAA did not affect NF-κB activity. Therefore, we further examined the antiproliferative activity of TMNAA against various T-cell lines in combination with cepharanthine (CEP), which is known to inhibit NF-κB.

Materials and methods

HTLV-1-infected and uninfected T-cell lines were cultured in the presence of various concentrations of TMNAA and CEP, and their proliferation and viability were determined by a tetrazolium dye method. The mode of cell death was also examined by flow cytometry and Western blot analysis.

Results

The 50% inhibitory concentrations (IC50s) of TMNAA and CEP for the ATL cell line (S1T) were 1.65 ± 0.03 and 1.97 ± 0.29 μM, respectively. On the other hand, the IC50 of TMNAA and CEP combination resulted in 0.93 ± 0.13 μM, indicating that the combination synergistically inhibited the proliferation of S1T cells. Such synergism was observed for another infected cell line (MT-2) but not for HTLV-1-uninfected cell lines. Moreover, TMNAA did not induce apoptosis of S1T cells, but CEP did. Interestingly, TMNAA significantly enhanced the CEP-induced apoptosis of S1T and MT-2 cells.

Conclusions

The combination of TMNAA and CEP selectively inhibits the proliferation of HTLV-1-infected cell lines through the induction of apoptosis. Therefore, TMNAA and CEP may have potential for chemotherapy of ATL.

Author details
[1]Center for Chronic Viral Diseases, Kagoshima University, Kagoshima 890-8544, Japan. [2]Institute of Molecular and Cellular Biosciences, The University of Tokyo, Tokyo 113-0032, Japan.

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* Correspondence: toyama@m2.kufm.kagoshima-u.ac.jp
[1]Center for Chronic Viral Diseases, Kagoshima University, Kagoshima 890-8544, Japan
Full list of author information is available at the end of the article