

Answer 1:

Bibliographic Information

Levamisole plus 5-fluorouracil inhibits the growth of human colorectal xenografts in nude mice. Van Ginckel, Robert; Distelmans, Wim; De Bradander, Marc; Callens, Myriam; Janssens, Boudewijn; Jagers, Els; Wouters, Luc; De Coster, Roland; Janssen, Paul A. J. Janssen Res. Found., Beerse, Belg. Eur. J. Cancer, Part A (1992), 28A(6-7), 1137-9. CODEN: EJCTEA Journal written in English. CAN 117:184434 AN 1992:584434 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Fragments of human colorectal adenocarcinomas were inserted under the renal capsule of nude mice. The growth of these tumor grafts was inhibited by the combination of 5-fluorouracil (5-FU) and levamisole. An alternating regimen of 2.5 kg levamisole/kg and 20 mg 5-FU/kg decreased the size of tumor implants by 33-59% and/or increased the no. of macroscopically disappeared fragments in the combined treatment group compared with ineffective monotherapy with saline, levamisole, or 5-FU. This model could be valuable for investigating the mechanism of action of levamisole and for evaluating the effects of this adjuvant therapy in other oncol. settings.

Answer 2:

Bibliographic Information

Experimental modulation of IL-1 production and cell surface molecule expression by levamisole. Kimball E S Oncology and Endocrinology Research, Janssen Research Foundation, Spring House, Pennsylvania 19477-0776 Annals of the New York Academy of Sciences (1993), 685 259-68. Journal code: 7506858. ISSN:0077-8923. Journal; Article; (JOURNAL ARTICLE); General Review; (REVIEW) written in English. PubMed ID 8103313 AN 93370859 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Data from a variety of sources suggest that one target cell for levamisole might be the macrophage. Current results reveal that oral levamisole pre-treatment provides elicited peritoneal macrophages with the ability to respond better to ex vivo LPS stimulation, and that levamisole can directly act on LPS-stimulated macrophages in vitro, resulting in enhanced production of IL-1, a key mediator of the immune response. These data offer further biological and immunologic evidence that IL-1 production is indeed enhanced by levamisole. Finally, these phenomena were not confined to macrophages taken from mice given levamisole. Increased IL-1 expression was found to occur for cells treated in vitro with levamisole, demonstrating that there were direct effects by levamisole on LPS-stimulated macrophage cytokine production. IL-1 has been reported to have a number of direct and indirect anti-tumor effects which might be sufficient to provide localized protection against tumor invasion or growth in the adjuvant setting. The findings described above are therefore consistent with suggestions of an increased host response in certain types of cancer due to levamisole treatment, and are also consistent with reports of levamisole's providing a beneficial effect in other cases of immunodeficiency disease. Recent clinical data provided by Janik et al. demonstrate that levamisole administration caused increases in circulating levels of neopterin and soluble IL-2 receptor (sIL-2R). This in vivo result is consistent with in vitro data showing augmented IL-1 induction after levamisole treatment, since neopterin is a marker for macrophage activation and sIL-2R release correlates with IL-2 production and binding after IL-1 activation of T-cells. These data are therefore consistent with the hypothesis that levamisole can induce a macrophage-derived cytokine cascade which may have beneficial effects in host responses to human cancer.

It is attractive to speculate that there may be increased cytokine expression in vivo (yet to be confirmed) which might contribute to the added clinical benefit when 5-FU is combined with levamisole. Data from nude mice bearing human tumor xenografts demonstrate improved antitumor responses to 5-FU in combination with levamisole, and it will be interesting to determine whether increased interferon, TNF, or other cytokines can be observed in this model. In addition, the ability of levamisole to increase ICAM-1 expression on certain tumor cell lines may be a mechanism by which similar cells are rendered more sensitive to host effector mechanisms in vivo (ABSTRACT TRUNCATED AT 400 WORDS)