Immunostimulatory Effect of Ginkgolides Enhances Resistance of Neutropenic Mice against Hematogenously Disseminated Candidiasis.

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We investigated immunostimulatory activity of ginkgolides (GLS), the primary active constituent of Ginkgo biloba leaves, against disseminated candidiasis due to Candida albicans. This fungus is a polymorphic opportunistic pathogen. BALB/c mice were induced neutropenia by intraperitoneal (i.p.) injection of cyclophosphamide (CP) 24 hours before an i.p. administration of GLS (2 mg/mouse) to the mice. Control mice received diluted (Dulbecco's phosphate saline solution; DPBS) instead of GLS. Four hours later, all of these mice were infected with live C. albicans yeast cells (2 x 10^3/mouse), intravenously. Prior to the experiments, an appropriate amount of CP that caused depletion of neutrophils in BALB/c mice was examined and found as 2 mg/mouse. In addition, antifungal activity of GLS were determined by susceptibility test. The GLS analyzed in our other study were used. Results from measurement of survivability showed that GLS-treated mice had a mean survival time of 36 days, compared with 14 days for DPBS-given control mice. Three mice of the five GLS-treated animals survived the 52-day observation period. The antifungal susceptibility test resulted in no killing of the yeast at a concentration of 50 mg GLS, showing that the GLS had no antifungal activity. Our studies show that the ginkgolides exhibit immunostimulatory effect.

Dendritic Cell as an effective cancer immuno-cell therapy module II. : Anti-tumor effect of cultured DCs in murine melanoma metastasis model

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Dendritic cells (DCs) are known to professional antigen presenting cell (APC). Due to the role as an effective activator of cytotoxic T lymphocytes by expressing MHC, adhesion and co-stimulatory molecules, DCs are now widely recognized to play an important role in the immune responses to tumors. We investigated the effect of cultured DCs in murine melanoma pulmonary metastasis model. To follow the metastasis protocol, syngenic melanoma cells were inoculated intra-venously into the mouse (B16F10 into the C57BL/6) 8 days prior to the first DC injection (1x10^6 DCs/mouse, i.p.) and the autologous tumor cell lysate pulsed-DCs were injected as a therapeutic module twice in two weeks. Myeloid lineage cells were selected by antibody panning from mouse bone marrow cells. And ex vivo culture was done with GM-CSF and IL-4 (1,000 U/ml each) for 7 days in media. On the 6th day, DCs were pulsed with autologous tumor cell lysate for 18 hr (p-DC). One week after the final injection, mice were sacrificed for the systemic immune monitoring. Ex vivo cultured myeloid-DCs produced IL-12 more than IL-10 indicating the possibility of stimulating TH1-related immunity. In the auto-MLR assay, T cell proliferations (divisions) significantly increased by the DC stimulation. In the p-DC treated mice, increased antigen-specific IFN-γ production and the T cell proliferations were observed with the inhibition of pulmonary tumor nodule formation. These data indicating the effectiveness of cultured DCs to treat the pulmonary metastasized melanoma in mice.

Isolation of Ginkgolides and the Effect of These Components on Inflammation in Mice Induced by Complete Freund's Adjuvant.

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