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Author Hsuan-Kai Tseng
Author's Email Address No Public.
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Abstract
The Phellinus linteus (Hymenochaetaceae), found on mulberry trees growing on wild mulberry trees, is a well-known fungus which belonged to one of perennial mushrooms. In South Korea and Japan, it have been served as a pharmaceuticals and health food for preventing cancer. Recent studies also have shown that Phellinus linteus has the effects of anti-tumor and immunomodulation without any side-effect. However, the wild Phellinus linteus is growing slowly and show serious productive limit, thus we try to develope a proprietary production technology based on submerged fermentation in this study to evaluate the molecular mechanism of adjuvant action of polysaccharide extract of Phellinus linteus (PLPE) and/or combined with anticancer drugs (eg. cisplatin and etoposide) in original and metastatic tumors by the models of xenografted tumor histoculture and metastatic animal.
First, the cytotoxity of PLPE in several cancer cells, lung cancer cell (LL2, A549) and melanoma cell (B16F10) was estimated in vitro. Continuously, the lung cancer cells and melanoma cells were implanted onto the ICR nude mice, then they were taken off the tumors, while the proliferating solid mass grew up to be exceed 1 cm around the tumor. In the presence of macrophages, the tissue samples were treated with the PLPE in the co-culture system of xenografted tissues and macrophages, to explore the anti-proliferation and the potential benefits of adjuvant chemotherapy via the activation of immune response. Finally, we evaluate the synergistic effects of PLPE with chemotherapies for the inhibition of tumor proliferation and the improvement of animal survival in metastatic animal model using the direct-Injection model of melanoma cell by tail vein.
The phenol-sulfuric acid method and antioxidant test showed that PLPE from the use of hot-water extraction and alcohol precipitation had better antioxidant activity than others. It was found that PLPE was significantly synergistic with anti-cancer drugs (cisplatin, etoposide) in the cytoxicity of cancer cells and cell migration assay in vitro. In the cocultured histoculture system containing macrophage cells (RAW 264.7), PLPE also inhibited the growth of LL2, not B16F10, however, the combination of PLPE and anti-cancer drugs had a remarked growth inhibition of B16F10, through

decreasing the expression of p-AKT. Using the ELISA assay, the stimulation of PLPE resulted in the elevated TNF- level and M-CSF level decreased in the medium 24h later. We also found that PLPE can diminish the tumor weight in body weight ratio, reduce incidences of tumor nodules and elevate the survival of BALB/c mice with increasing the numbers of white blood cells and platelets in metastasis studies. Taken together, we believed that PLPE itself could alleviate the invasive tumor growth and PLPE also potentiate the effectiveness of chemotherapies treatment by a better side-effect profile in metastastic animal model.
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