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Recent advance in the studies of beta-glucans for cancer therapy

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Abstract
Mushroom has been used for thousand years in China and other Asian countries for health improvement and treatment of disease. A few decades ago, its main component beta-gluean was identified. Beta-glueans are now known to have beneficial effects for the prevention and treatment of many diseases including eanccr, infectious disease, hyperlipidemia, diabetes, atherosclerosis and obesity. The effects are mediated by the different properties of beta-glucans such as immune stimulation and bile acid trapping.

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EDITORIAL

Recent Advance in the Studies of Beta-glucans for Cancer Therapy

Mushroom has been used for thousand years in China and other Asian countries for health improvement and treatment of disease. A few decades ago, its main component beta-glucan was identified. Beta-glucans are now known to have beneficial effects for the prevention and treatment of many diseases including cancer, infectious disease, hyperlipidemia, diabetes, atherosclerosis and obesity [1-5]. The effects are mediated by the different properties of beta-glucans such as immune stimulation and bile acid trapping [I, 6]. In this special issue we have several experts to review the most recent advance in the field of the beta-glucan for cancer treatment.

Cancer is a severe disease with increasing accidence due to the aging population and western life style (obesity). Cancer caused death is only second to heart disease, accounting for 13% of all human deaths [7]. Cancer is caused by both genetic defects such as mutations of genes in survival signalling pathways and environmental factors such as obesity [8,9]. These factors result in activation of multiple signal pathways necessary for cancer initiation and maintenance [10]. At present chemotherapy and radiotherapy are usually applied to those cancers that cannot be removed by surgical procedure. However, the treatment outcomes are not satisfactory. Inhibition of intracellular signalling pathways, which is termed targeted therapy, is promising [11,12]. Multiple signalling pathways have been studied and many inhibitors have been developed to target these pathways such as *Src/PI3K1Akt/mTOR,* HGF/met, VEGF, EGFR, and MAPK [13-19]. Individualised targeted therapy may be needed as each patient may have different profile of altered signalling pathways [20]. Beta-glucans can be used for stimulating immune system. The immunotherapy via manipulation of immune system has also been applied for the treatment of cancer which facilitates the elimination of weaken cancer cells by chemotherapy or targeted therapy [21-25]. Different components of both innate and adaptive immune system may be manipulated such as antibody, T-cell, killer cells, dendritic cells and cytokines [26-29]. Beta-glucans can stimulate both innate and adaptive immune responses and could be used for immunotherapy for cancer treatment [I].

In this special issue Professor Van has introduced the effect of beta-glucan on dendritic cells (DCs), which are antigen-presenting cells. These cells bridge innate immunity and adaptive immunity. The molecular mechanisms for beta-glucan to stimulate DCs are well elucidated. Beta-glucans are recognised by pattern recognition receptors on DCs and activate these receptors to increase DC functions. Activation of DCs can result in adaptive immune responses such as CD8+ CTLs. Professor Van emphasises several receptors including CR3, LaeCer, SRs, Dectin-I in DCs and their downstream signals in the development of DCs and the secretion of cytokines. As various beta-glucans have different effects, it is proposed that a certain beta-glucan to be tested at a specific cancer to form personalized medicine.

After extensive studies of beta-glucans from mushroom in laboratory test and animal models, many clinical trials have been performed. Professor Aleem's article focuses on the use of beta-glucans on patients. After providing the interesting history of the medicinal implications of mushroom beta-glucans, she reviewed the clinical trials of several beta-glucans including letinan, Maitake D- and MD-fractions, extracts from *Agaricus sp.,* polysaccharide-K, and Schizophyllan. She also discussed combined consumption of mushroom with other phytochemicals. Interestingly several mechanisms other than immune stimulation effect such as direct effects of beta-glucans on cancer cells, on estrogen receptors, and P450 enzyme aromatase were also summarised.

Gastric cancer is the fourth and fifth most common cancer in men and women respectively and it is the third and fifth most common cause of cancer-related death in men and women according to most recent statistics [7]. Lentinan has been used clinically extensively for the treatment of gastric cancer. In his article, Professor Ina reviewed mechanisms for the treatment effect of letinan in gastric cancer and introduced how lentinan is used in combination with fluoropyrimidine to increase survival time of patients.

Metastasis is a major cause for cancer-related death [8, 30-33]. Professor Lee introduced the application ofbeta-glucans for the treatment of metastatic cancer. The effects of different beta-glucans including Grifolan, Lentinan, Agaricus Blazei, Schizophyllan, Sclerotiorum and yeast on metastatic models in animals are summarised. He also discussed the combinatorial therapies with irradiation, cytokines (INF-gamma and 11-2), chemotherapeutic agent fluropyridine in models of lung, liver and colon cancers. He pointed out that data from clinical trials are scarce and contradictory and further investigation is needed.

Most of research in beta-glucan has used mushroom extracts and purity ofbeta-glucans has been a major problem in the research of beta-glucans. Other components of mushroom may also have anti-cancer effect. This may interfere with the evaluation of beta-glucan anti-cancer effect. Professor Vetevicka discussed the application of synthesised oligo-saccharides for cancer treatment.

Beta-glucans are usually used in combination with other chemotherapeutic agents. Future work may further optimise the incorporation of beta-glucans in cancer treatment regimes. The studies of beta-glucans may be carried out in cancer stem cells as these cells are most related to cancer metastasis and drug resistance [34].

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