

## The Bidirectional Immunomodulatory Effects of *Trametes versicolor* Polysaccharopeptide (PSP) on Mouse Macrophage RAW264.7 Cells

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A large number of polysaccharides derived from mushrooms have been proved to possess immunomodulatory actions. These mushroom polysaccharides can boost host immunity which is thought to be of benefit to health. They can elevate functions of immune cells such as macrophages, T, B lymphocytes, NK and LAK cells etc. They can also activate reticuloendothelium system to produce cytokines like IL-1, IL-2, IFN and TNF and stimulate complement system. It is reported that neuro-endocrino-immunomodulation network could also be affected by some mushroom polysaccharides.

However, the immunity in organisms should be in a balance. Over activation of immunity also results diseases as that immuno-insufficiency does. For example, cytokines IL-1, IFN and TNF are not only regulators to activate immune cells and to kill cancer cells, they also mediate inflammation. It is known that inflammation is a causation related to numerous diseases such as rheumatoid arthritis, lupus erythematosus and atherosclerosis etc. Whether mushroom polysaccharides not only activate immune system but also act as an inflammatory trigger has not been well understood.

In this research, we first studied the regulation activity of *Trametes versicolor* Polysaccharopeptide (PSP) on mouse macrophage Raw 264.7 cells, by analyzing inflammatory mediators' production and related enzymes' expression. PSP provided by Shanghai Zhi-Herb Biotechnology Ltd is a polysaccharide-protein conjugate. It is derived from the deep-layer cultivated *T. versicolor* mycelia Cov-1 strain, and has been a national type II medicine in China applied for cancer patients to restore their immunity. Previous studies have shown that PSP can reduce dimethylbenzenexylene-induced mouse ear tumefaction, and antagonize phlogistic pain.

Our study revealed that while mouse macrophage Raw 264.7 cells incubated with PSP along, PSP stimulated nitric oxide (NO) and TNF- $\alpha$  production and increased inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression in a dose-dependent manner. It also significantly activated cell's phagocytosis as well. When mouse macrophage stimulated with lipopolysaccharide (LPS), an endotoxin from Gram-negative bacteria, NO, TNF- $\alpha$  production and iNOS, COX-2 expression were tremendously elevated, which could be over tens of folds higher comparing to PSP. Such high stimulation by LPS was reversely down-regulated by PSP. When co-incubating LPS with PSP, PSP could reduce about 10 to over 30% down of NO and TNF- $\alpha$  production and down-regulate iNOS and COX-2 expression as well. Further results revealed that PSP could retard NF- $\kappa$ B translocation into nucleus in LPS stimulated Raw 264.7 cells.

These results suggest that PSP can stimulate normal status mouse macrophage, but if the macrophage is highly boosted, PSP shows a reverse action. It plays as a biological response modifier that can regulate mouse macrophage immune reactions in a bi-directional way.

#### **Biography for Xiaotong Yang, Professor, Ph.D.**

Dr. Yang received a B.S. degree in Biology from Shanghai Normal University and a M.S. degree in Pharmacology from Su Zhou Medical College, China, and a Ph.D. degree in Cancer Biology and Biochemistry from The University of Hong Kong, Hong Kong SAR. Dr. Yang was also trained at BC Research Institute for Children's and Women's health of the University of British Columbia, Canada and New York Medical College as a visiting scientist.

Dr. Yang has worked in Shanghai Normal University since 1989, and was appointed as a professor in Department of Biology, Shanghai Normal University since 2007, and was appointed as a director of the Institute of Microbiology and Immunology, Shanghai Normal University since 2008.

Dr. Yang's primary research fields are (1) to identify bioactive components in medicinal mushrooms for the prevention and treatment of diseases, such as cancer; (2) to explore those components' mechanisms, especially in cancer inhibition and immunomodulation; and (3) to establish fermentation technology and (4) quality analysis and control methodology for those bioactive candidates.

His lab has established a series of cell-based in vitro bioassays for identification of active components, especially their synergistic combinations to target on cancer cell proliferation, apoptosis and invasion/metastasis, and to target on immuno cellular and humoral modulation. A series of clinically relevant animal models for cancer and immunomodulation are also used to systematically evaluate the efficacy of the candidate components and their synergistic combinations in prevention and treatment. Advanced techniques for cellular and molecular biology and biochemistry are also applied to purify and to produce the bioactive components, to elucidate the mechanisms of their actions, and to properly analyze the product's quality.

Dr. Yang's research contributions include the successful application of the Polysaccharopeptide of *Trametes versicolor* (PSP) as a Type II national medicine for cancer treatment in China. His research responsibilities include the identification of PSP bioactive fractions, study of immunomodulatory and anticancer mechanisms, and establishment of quality control methods. PSP has been the top one mushroom derived anticancer medicine in China market for many years and has become a worldwide well known mushroom health product. His other significant contributions include the development of a limulus G test assay for specifically detection of mushroom beta 1,3 glucan in crude polysaccharide extract mixture, and a polysaccharide characterization methods.

Dr. Yang has published 59 peer-reviewed original research papers, review papers and book chapters/editorials, and has applied 7 invention patents. Because of his significant accomplishment in medicinal mushroom research, Dr. Yang has earned national and international reputations. He was awarded a number of prizes including "Second prize of the National Education Committee Science and Technology Advancement Prize" and "Second prize of Shanghai Science and Technology Progressing". He has been elected as a council member of Chinese Mycological Society since 2008, and the vice director of Medicinal Mushroom Academic Group in this Society since 2008. He is now appointed as one of the International Scientific Committee and Publications Committee member of the 5<sup>th</sup> International Medicinal Mushroom Conference in 2009.