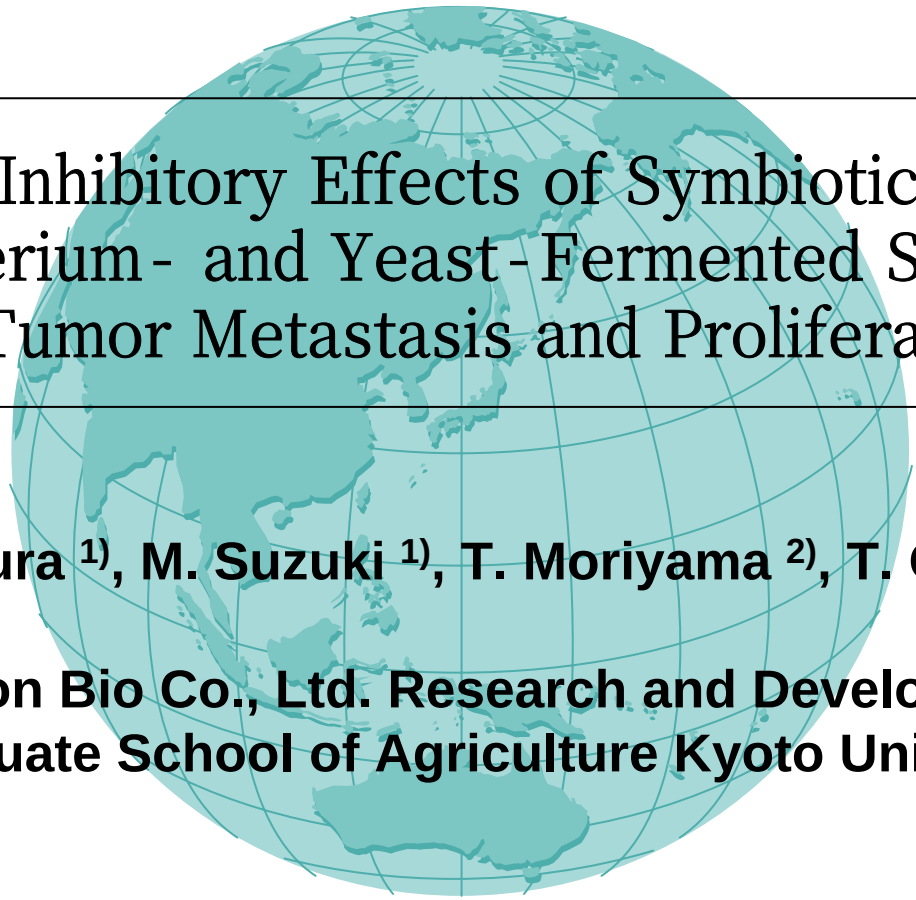
Inhibitory Effects of Symbiotic Lactobacterium- and Yeast-Fermented Soy Extract on Tumor Metastasis and Proliferation



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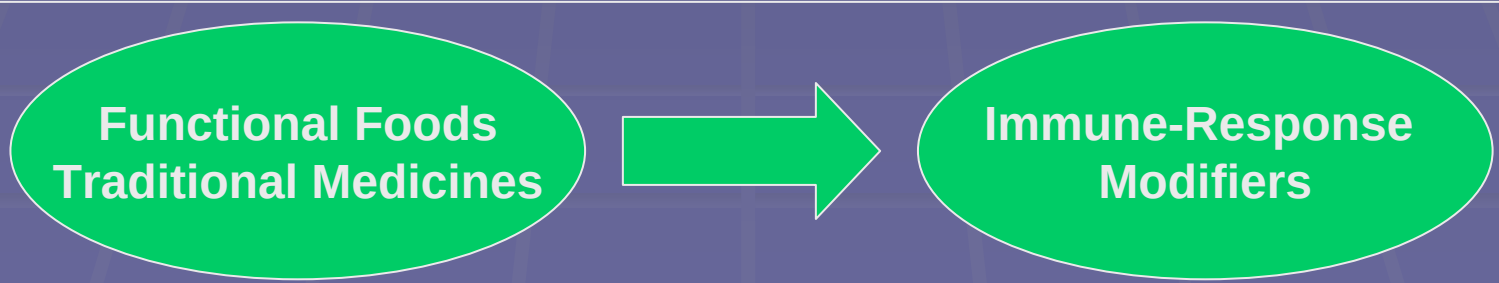
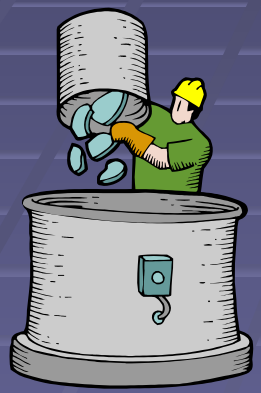
Introduction

- Recently, all over the world face to serious health problem. Patients of neoplasm, allergy, and virus infection involved in immune systems are increasing continuously, since our immune systems are getting worse with daily life, food and endocrine disrupting chemicals. In the course of our studies for developing immune-response modifiers from functional foods including fermented materials and traditional medicine, we found that symbiotic Lacto bacterium- and Yeast-fermented soy extract (LYS) inhibited tumor metastasis and proliferation by the stimulation of immune systems.



Symbiotic Lacto bacterium- and Yeast-fermented Soy Extract (LYS)

Soy (No genetic recombination)



1) Water, *r.t.*, 24 h
2) Homogenize
3) 100℃, 1h
4) Filtration

Soy Extract

Symbiotic Fermentation

1) Enzyme Reaction (Cellase, Amylase, Protease)

2) Fermentation
Lacto Bacterium; E. faecalis, L. helveticus, L. casei, L. sp
Yeast; Saccharomyces cereviciae

1) 30℃, 4 d
2) 100℃, 1h
3) Freeze dry

Symbiotic Lacto bacterium- and Yeast-fermented Soy Extract (LYS)

Apply for various Assays

View
Activities of LYS

- Gastro protection (Inhibition of gastric lesions, ~1g/kg rat or mouse)
- Antiflatuents (Regulation of intestinal function)
- Anti-diabetes (①Suppression of high blood glucose level,② Inhibition of aldose redactase: improvements of complication)
- Control of immune systems (anti-allergy, immune-response activator)

Effect of LYS on Macrophages Activation ①

Male ddY mouse (30 g)

Wash with PBS

Selection (Preculture)

Mouse peritoneal macrophage

LYS (~300 μg/ml)
or
LPS (10 μg/ml, positive control)

37℃, 20 h

Measurement of Nitric oxide (NO)
in the culture medium by Griess reagent

①Collected from mouse peritoneal macrophage

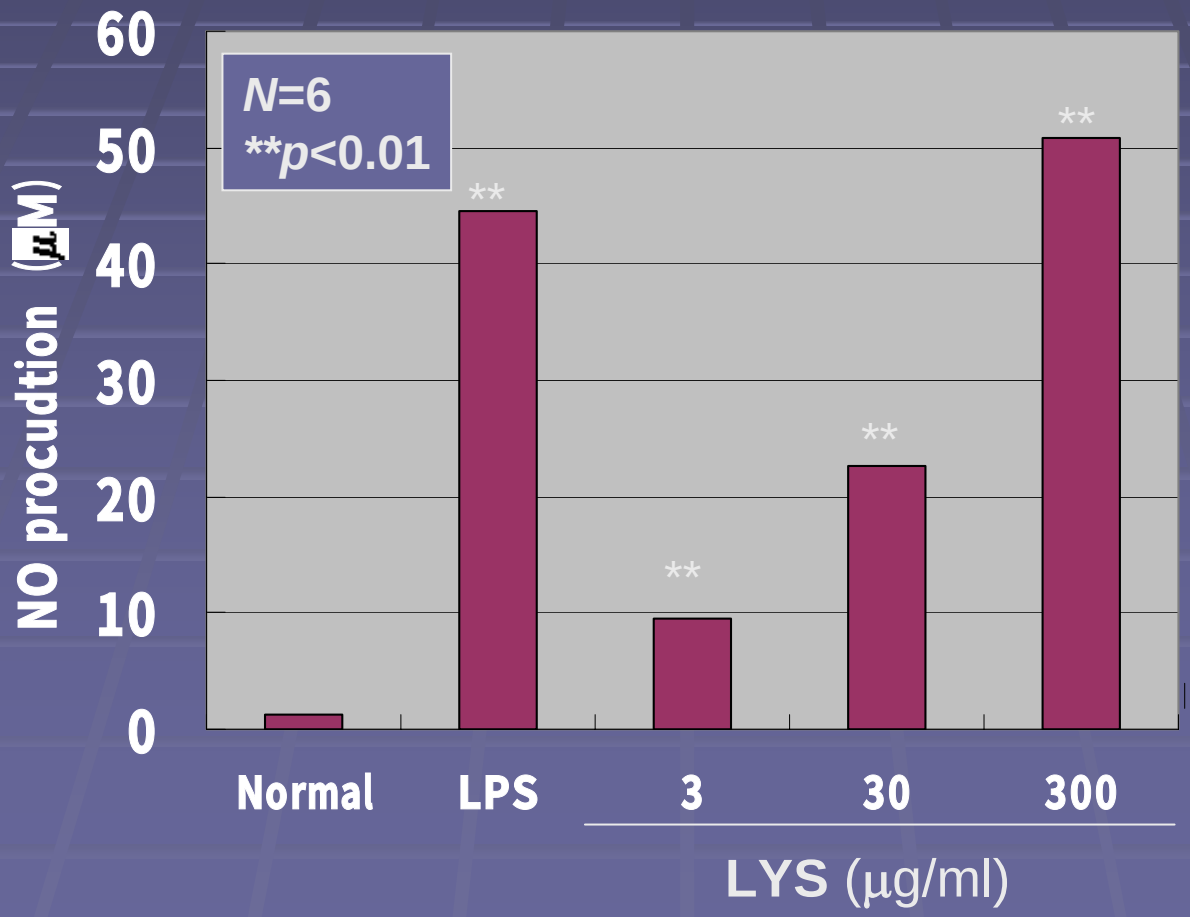
②Primary culture
LYS or LPS

Measurement of NO production by Griess reagent

Activation Marker

LPS; lipopolysaccharide from *S. aureus*

Effect of LYS on Macrophages Activation ②



Effect of LYS on Macrophages Activation ③

Mouse peritoneal macrophage

LYS (~300 μg/ml)
or
LPS (10 μg/ml)
37℃, 1 h

Fluorescence Beads for phagocytic activity

37℃, 1 h

Trypan Blue (quenching)

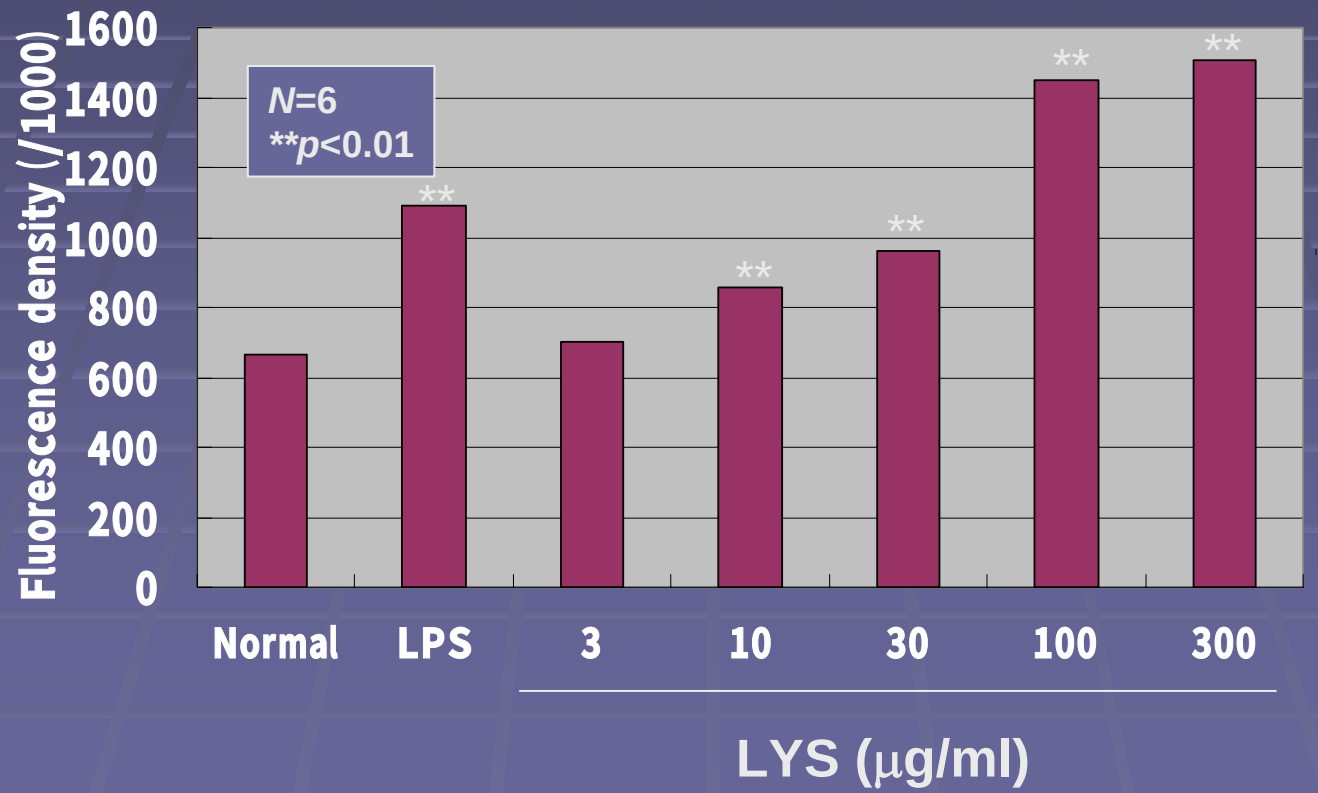
Measurement of fluorescence density of activated macrophage (Ex.532 nm, Em.526 nm)

①Collected from mouse peritoneal macrophage

②Primary culture LYS or LPS
③Bio-Beads (Fluorescence)

Measurement of fluorescence density

Effect of LYS on Macrophages Activation ③



Effect of LYS on Tumor Metastasis and Proliferation ①

Female C57/BL6 (4 weeks)

1 week

Normal diet
+
Water
or
1%, 2% LYS water
or
1%, 2% lipoprotein water

Injection (*i.v.*)
B16F10 melanoma, 10^5cells/mouse

2 weeks

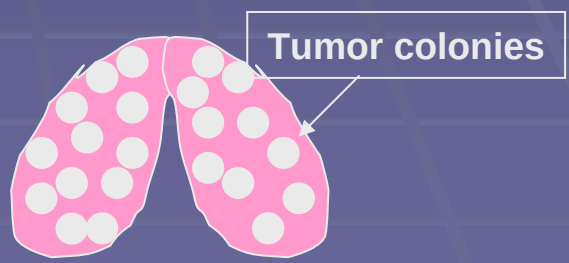
Same condition

Counting tumor colonies in lung

Lung

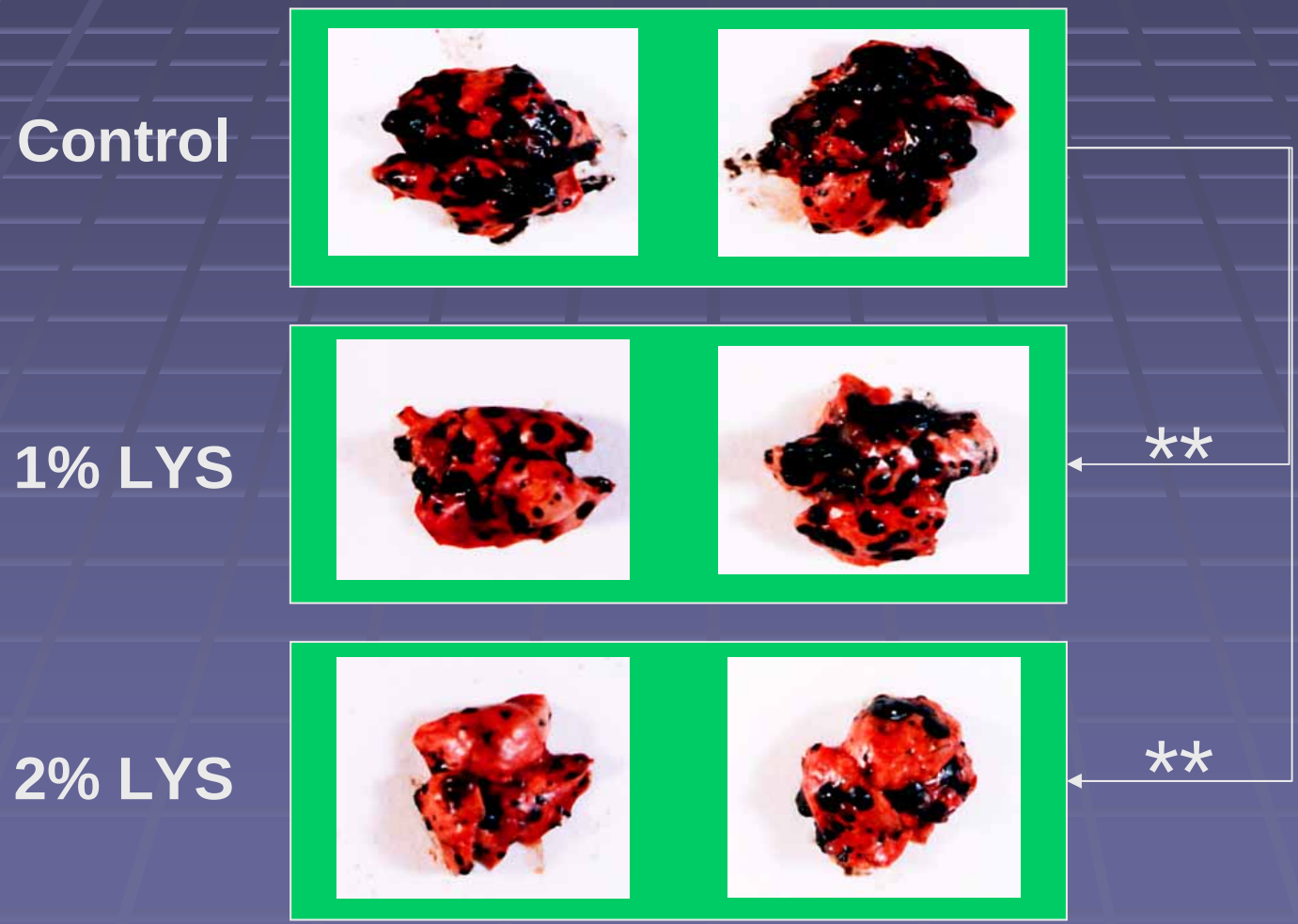
Melanoma

Injection

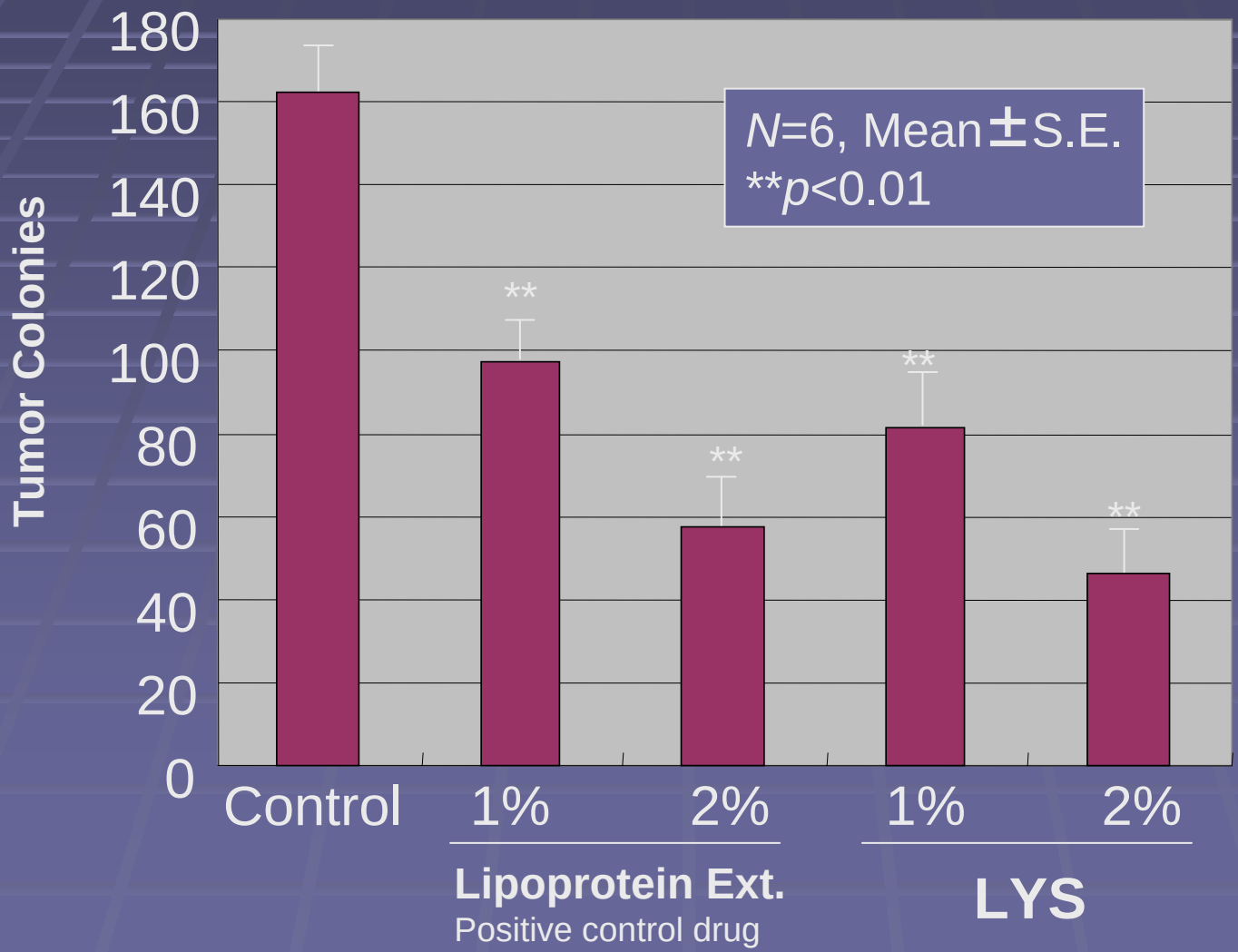


Metastasis and Proliferation

Effect of LYS on Tumor Metastasis and Proliferation ②



Effect of LYS on Tumor Metastasis and Proliferation ③



Conclusion

- By in vitro treatment with LYS, macrophages were significantly activated depending on LYS concentrations. By the addition of 0.3 mg/ml LYS, production of NO and phagocytic activities of macrophages were stimulated 15-fold and 3-fold, respectively.
- By in vivo, melanoma metastasis in lung was significantly suppressed by LYS according to its dose dependence. At dose level of 2% LYS, colonies of melanoma were decreased 1/3-fold. And anti-metastasis activity of LYS was 20% stronger than positive control drug of lipoprotein.
- These data indicates that LYS inhibits tumor metastasis and proliferation by stimulating the immune systems. The LYS, symbiotic Lacto bacterium- and Yeast-fermented soy extract, is considered to be one of the immune-response modifiers.

Anti-Tumor Metastasis and Proliferation Mechanisms of LYS

LYS
Symbiotic Lacto Bacterium- Yeast-fermented Soy Extraxt

Immune System
(Intestinal Immune System)

Stimulation
Activation

Immunocytes (Macrophage, leukocyte….) activation ↑

Production of
Cytokine, ILs, TNF

Phagocytosis

Inhibition of Tumor Metastasis and Proliferation

Prevention and Improvement of weakened Immune systems

Immunostimulator, Immunomodulator