TALAB Symposium
2007. 11. 9. National Taiwan Univ.

Cancer preventive effects of lactic acid bacteria

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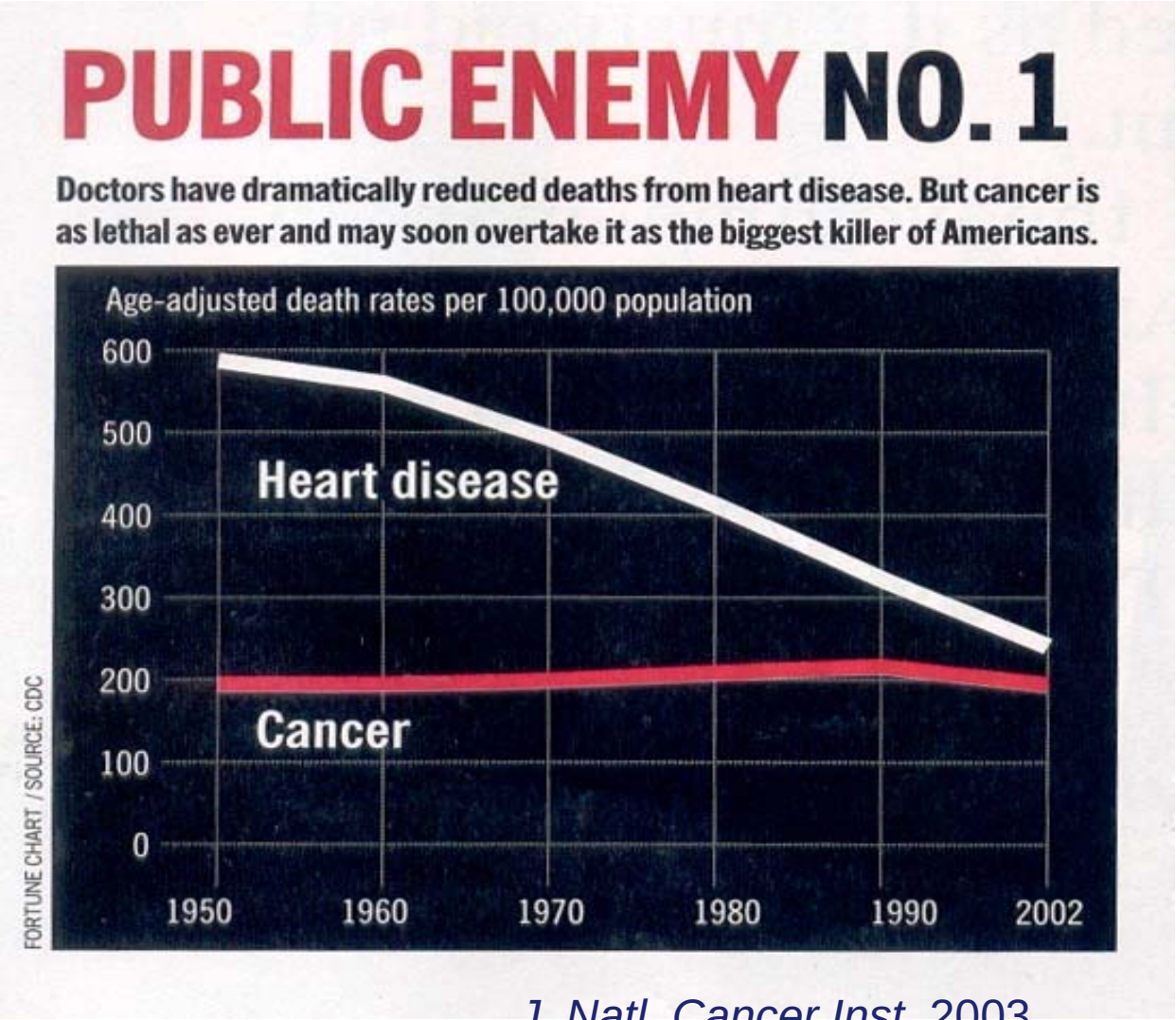
Total deaths from cancer and heart disease

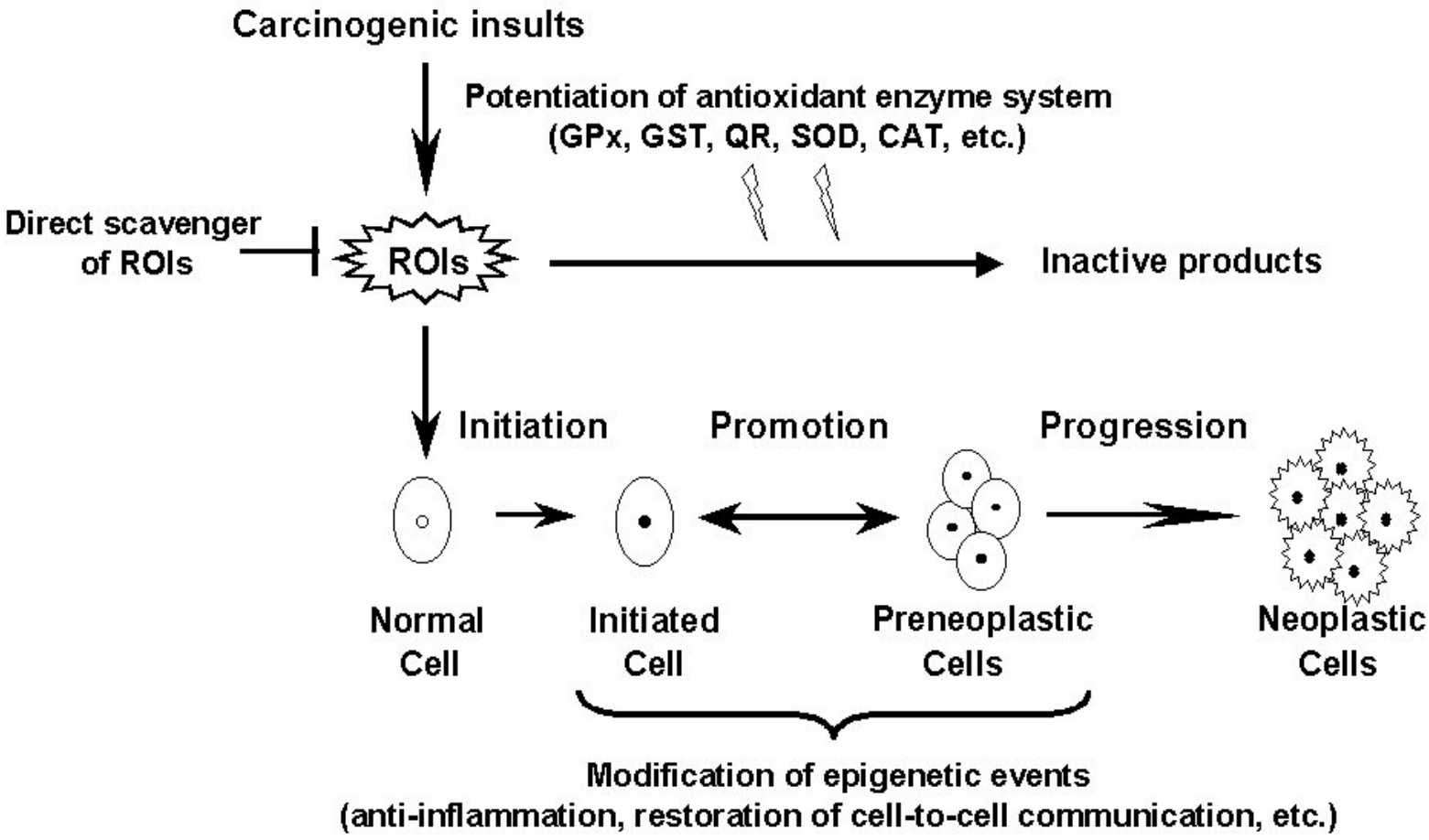


J. Natl. Cancer Inst. 2003

Major causes of cancer

Factor	Estimated % of all cancer deaths
Diet	**35**
Tobacco	30
Infection	10
Reproductive & sexual behavior	7
Occupation	4
Alcohol	3
Geophysical factors	3
Pollution	2
Industrial products	1
Medicines & medical procedures	1
Food additives	< 1

Cancer chemoprevention with food components



Lee HJ et al., *Am J. Clin. Nutr., 2003*

Health benefits of lactic acid bacteria (LAB)

- Improving the nutritional value of food
- Controlling gastrointestinal infections
- Controlling serum cholesterol levels
- Prevention of diarrhea and food allergy
- Controlling some types of cancer

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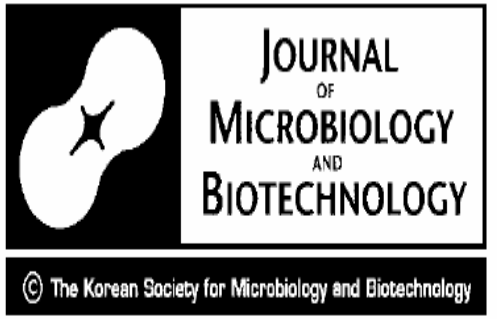
J. Microbiol. Biotechnol. (2007), **17**(8), 1227–1235



Cancer Chemopreventive Effects of Lactic Acid Bacteria

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LAB exhibited anticancer effects (1/2)

1. Colon cancer

Lc. lactis ssp. Lactis
Lb. acidophilus
Lb. rhamnosus GG
Bf. Lactis Bb12
Lb. plantarum
Lb. casei
Bf. longum

2. Bladder cancer

Lb. rhamnosus GG
Lb. casei – Shirota
Lb. casei

LAB exhibited anticancer effects (2/2)

3. Liver cancer

Lb. rhamnosus GG
Lb. rhamnosus LC705
Lb. acidophilus

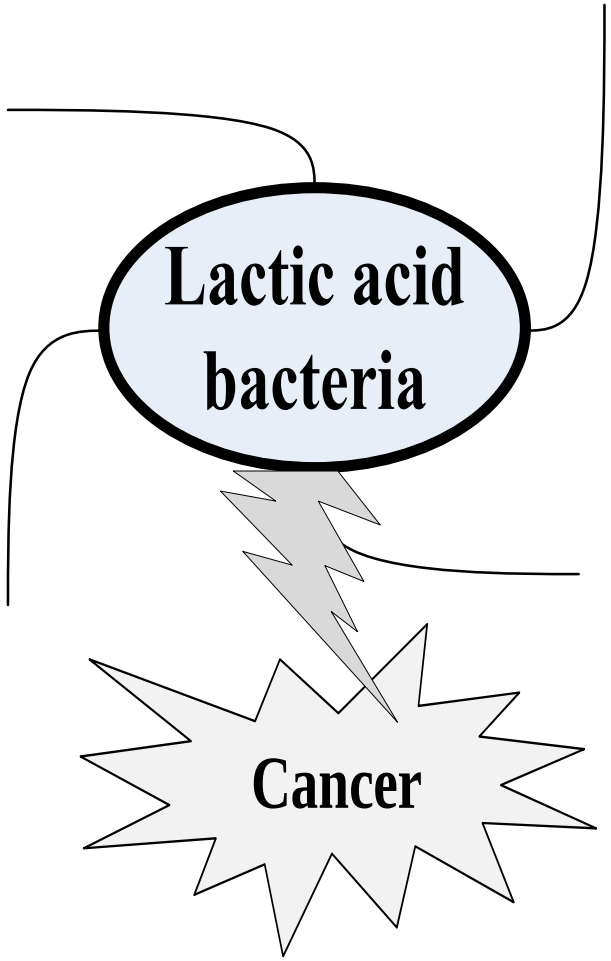
4. Breast cancer

Lb. acidophilus
Lb. helveticus
Lb. paracasei
Bf. Infantis, bifidum, animalis

5. Stomach cancer

Lb. plantarum
Lb. casei - Shirota

Mechanisms of anticancer activity of LAB



Antiproliferative activit

Biotechnology Letters **24:** 1431–1436, 2002.

Screening for antiproliferative effects of cellular components from lactic acid bacteria against human cancer cell lines

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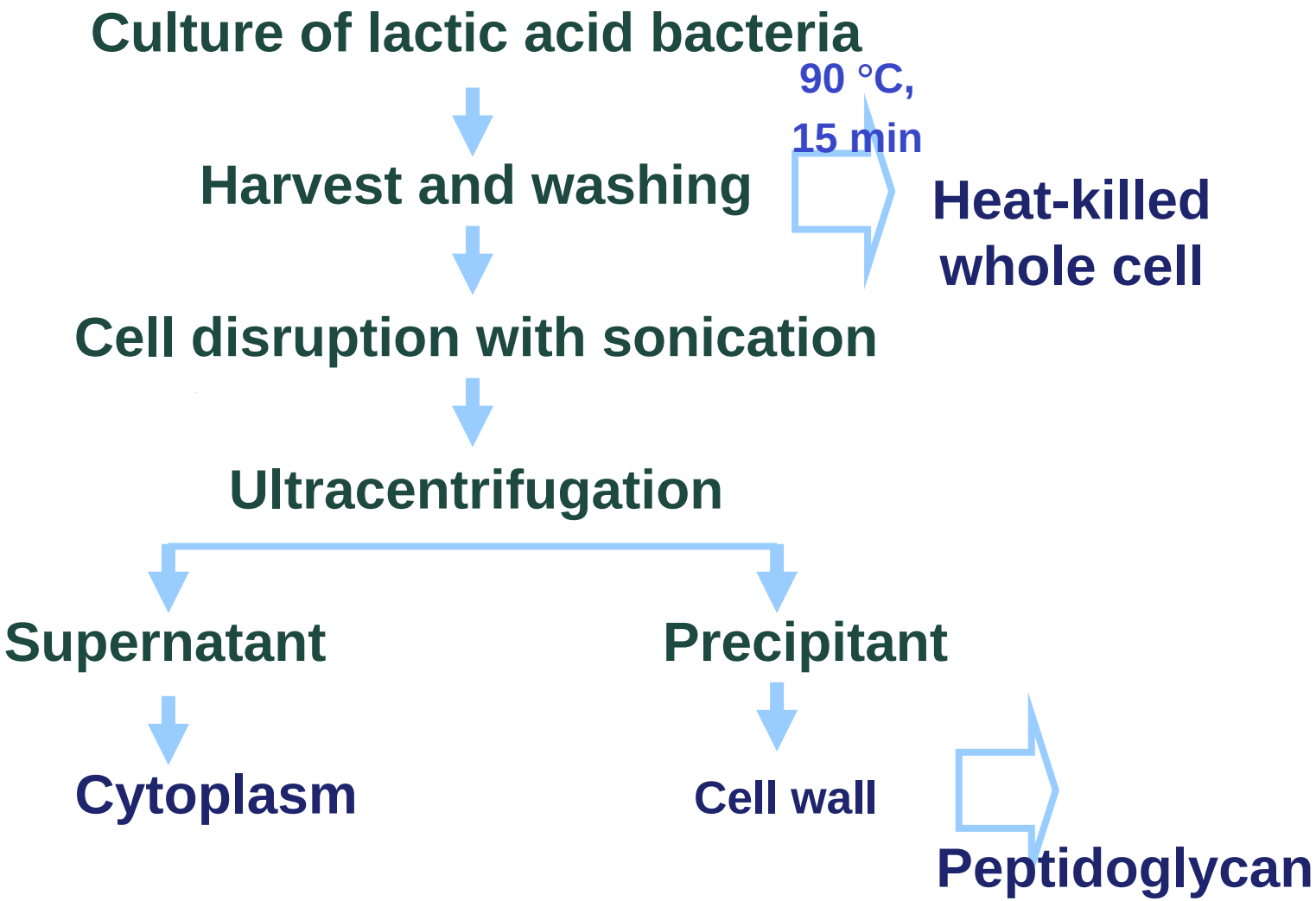
Lactic acid bacteria used for screening

- *Lactobacillus acidophilus* IAM 1084 (Laci)
- *Lactobacillus bulgaricus* KCTC 3188 (Lbul)
- *Lactobacillus casei* ssp. *casei* KCTC 3109 (Lcas)
- *Lactobacillus plantarum* KCTC 3099 (Lpla)
- *Streptococcus thermophillus* KCTC 2185 (Sthe)
- *Lactoccus lactis* ssp. *lactis* ATCC 7962 (Llac)
- *Lactococcus lactis* ssp. *cremoris* ML4 (Lcre)
- *Bifidobacterium adolescentis* ATCC 15730 (Bado)
- *Bifidobacterium breve* ATCC 15700 (Bbre)
- *Bifidobacterium longum* ATCC 1570 (Blon)

Fractionation into cytoplasm and cell wall



Human cancer cell lines used

Cell lines	Origin
SNU-1	Gastric cancer cell line
SNU-C2A	Colon adenocarcinoma cell line
DLD1	Colon adenocarcinoma cell line
K562	Leukemia cell line
A549	Lung carcinoma cell line
A498	Kidney carcinoma cell line
HT-1376	Bladder carcinoma cell line
HeLa	Cervix carcinoma cell line
MCF7	Breast adenocarcinoma cell line
HepG2	Hepatocarcinoma cell line
PC3	Prostate carcinoma cell line

Anticancer activity of cytoplasm

(% inhibition, 100 μg/ml)

Cell line \ LAB	*Laci*	*Lbul*	*Lcas*	*Lpla*	*Sthe*	*Bado*	*Bbre*	*Blon*	*Lcre*	*Llac*
SNU1	46	54	69	19	43	34	4	73	71	75
SNUC2A	44	73	75	**93**	42	29	87	**96**	64	**93**
DLD-1	34	33	25	29	33	2	8	–	15	37
K562	–	18	60	9	19	34	9	15	29	42
A549	8	–	–	26	–	3	52	53	–	–
A498	42	42	63	23	37	–	–	21	22	16
HT-1376	1	29	33	28	–	16	31	48	41	52
HeLa	–	–	16	–	–	–	–	–	–	–
MCF7	–	–	–	–	–	–	30	40	16	31
HepG2	19	12	72	23	14	22	44	11	–	–
PC3	–	–	–	–	–	–	–	–	–	29

IC_{50} values of cytoplasm fractions

(μg/ml)

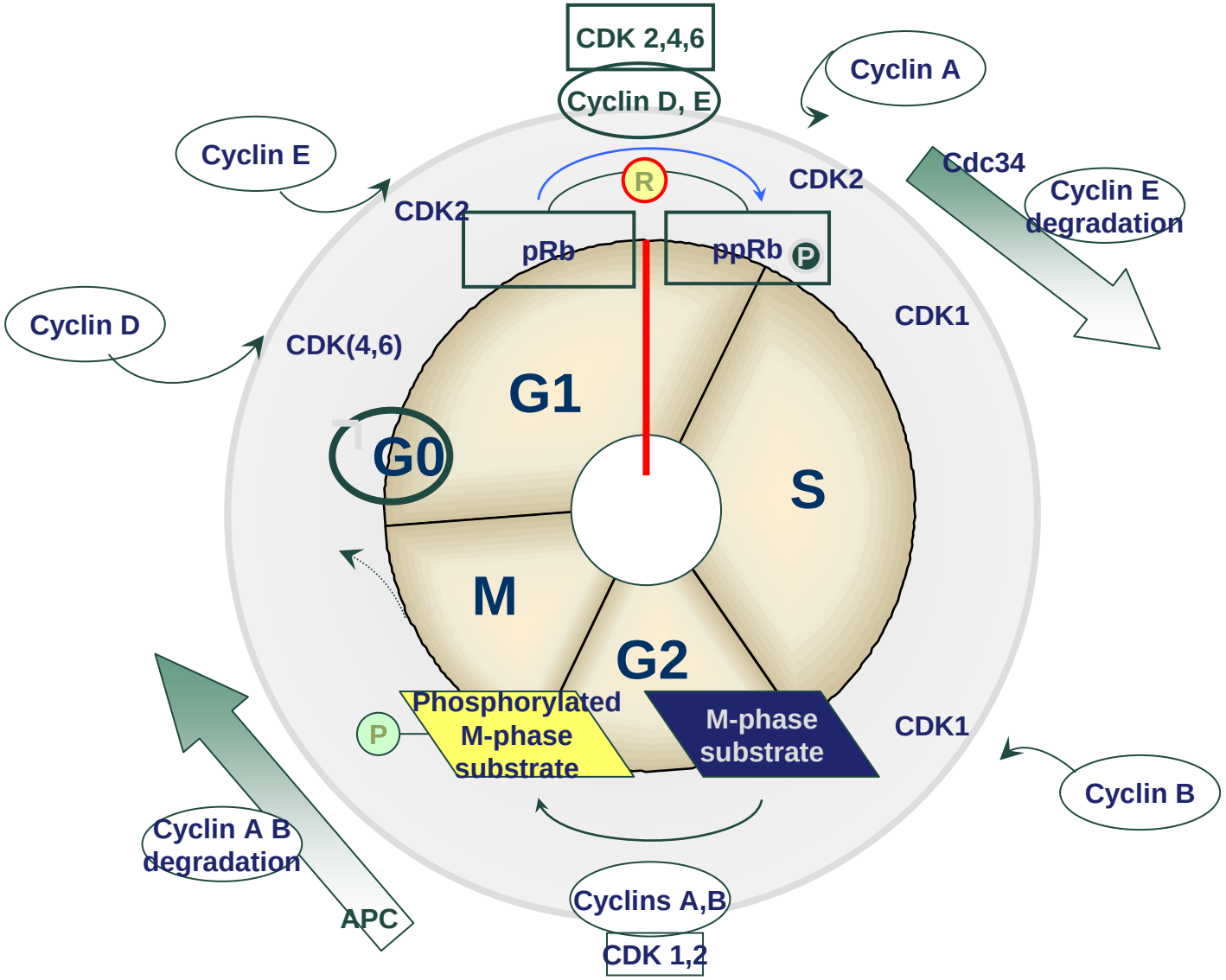
LAB / Cell line	*Laci*	*Lbul*	*Lcas*	*Lpla*	*Sthe*	*Bado*	*Bbre*	*Blon*	*Lcre*	*Llac*
SNUC2A	>100	50	53	36	>100	>100	43	33	75	23
SNU1	>100	94	>100	>100	>100	>100	43	17	54	11

NUTRITION AND CANCER, *46*(2), 197–201

Cell Cycle Dysregulation Induced by Cytoplasm of *Lactococcus lactis* ssp. *lactis* in SNUC2A, a Colon Cancer Cell Line

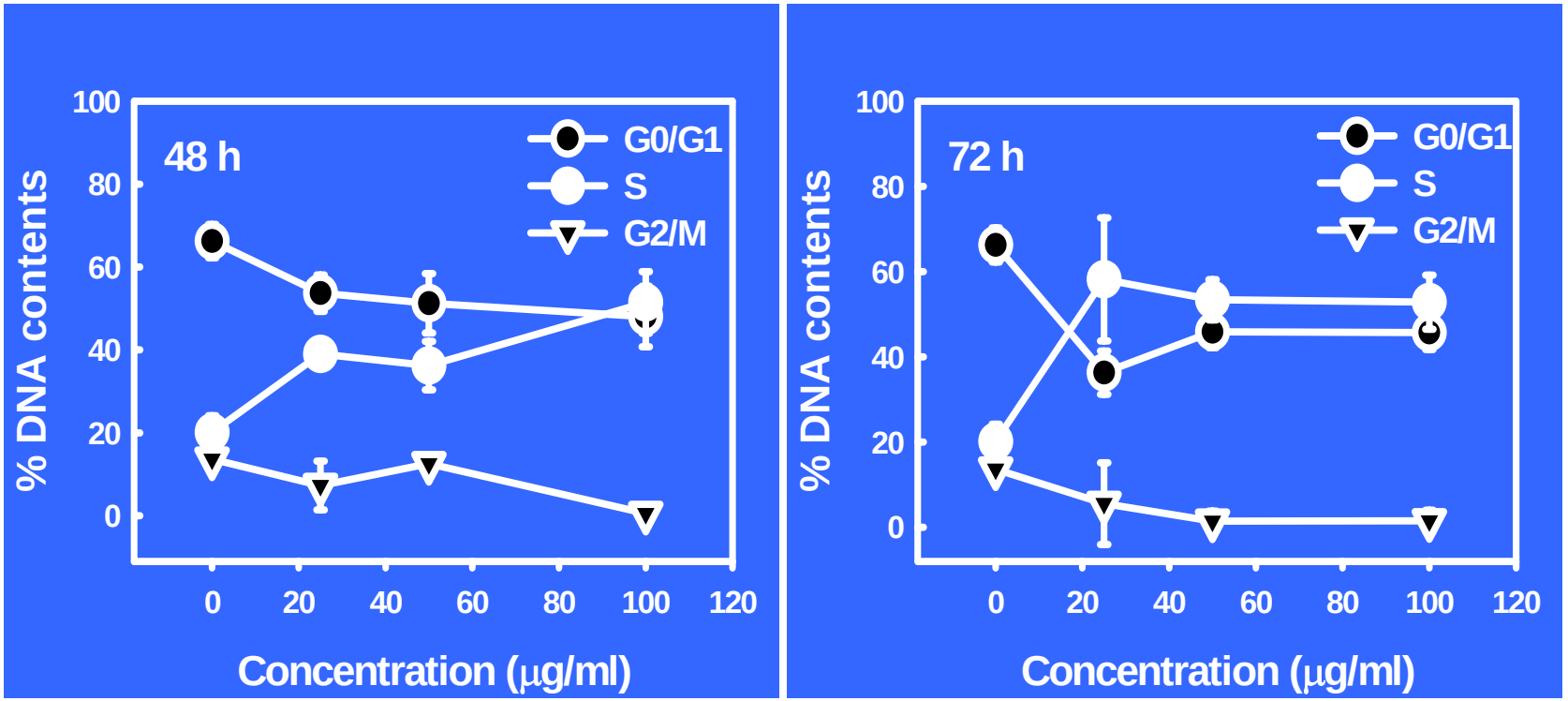
Ji Yeon Kim, Hee Jong Woo, Young-Suk Kim, Kyoung Heon Kim, and Hyong Joo Lee

Cell Cycle Control



Cell cycle analysis through flow cytometry

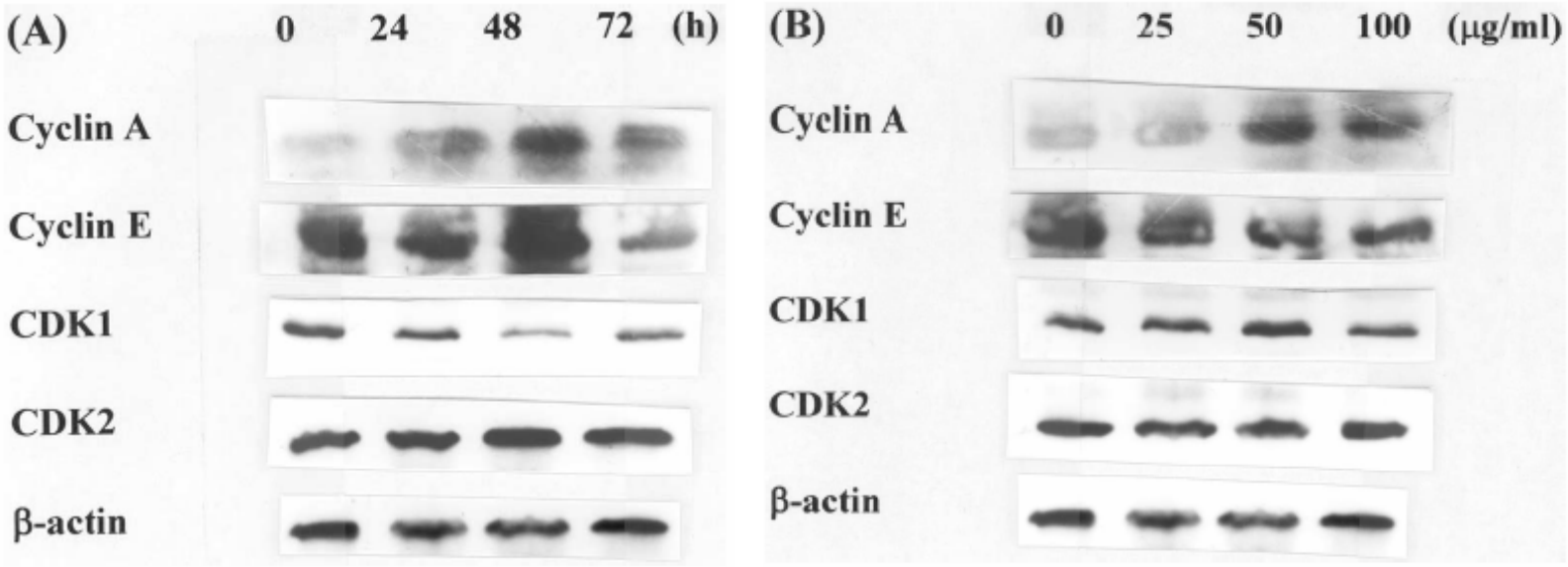
(*Llac* on SNUC2A, colon cancer cells)



S phase accumulation

Immunoblotting for cyclins and CDKs

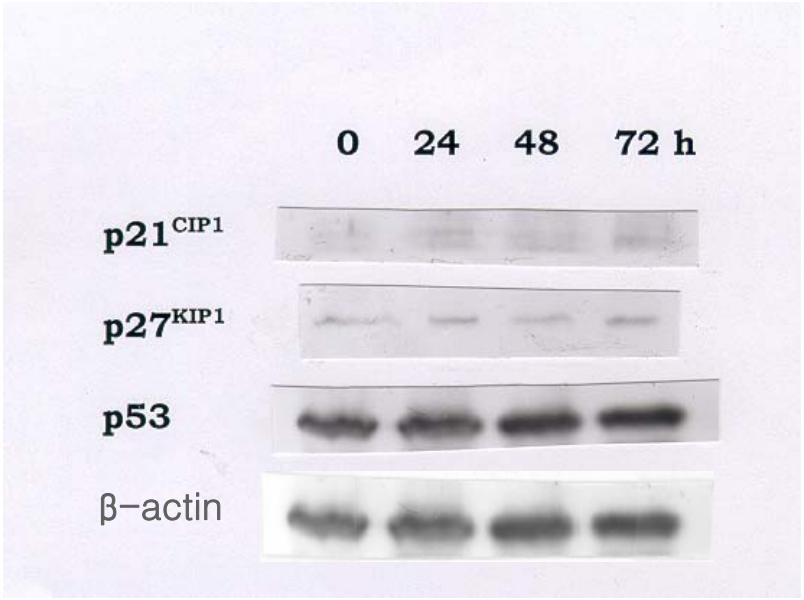
(*Llac* on SNUC2A, colon cancer cells)

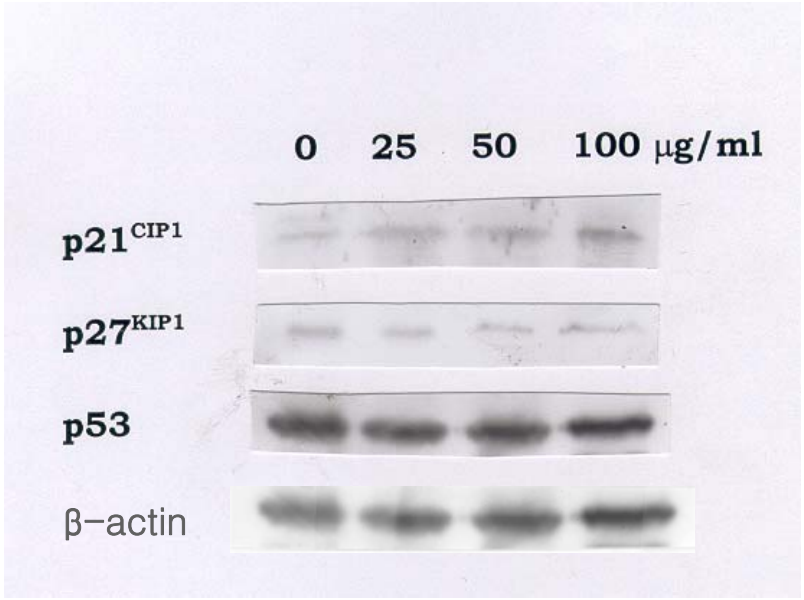


- Expression of Cyclin A increased, Cyclin E decreased
- No effect on CDK1 and CDK2

Immunoblotting for CDKIs and p53

(*Llac* on SNUC2A, colon cancer cells)

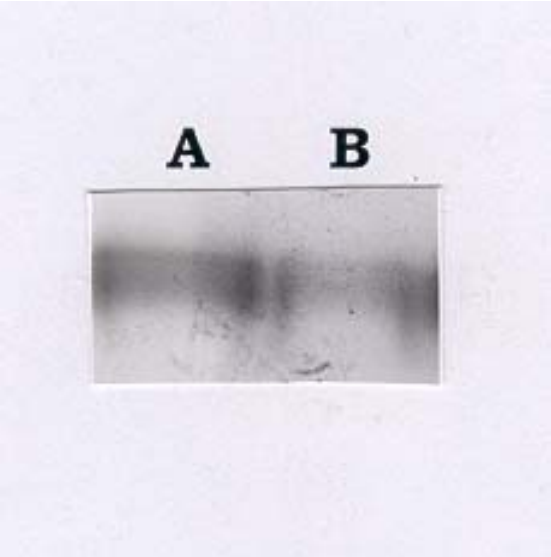




- $p21^{CIP1}$ increased
- No effect on $p27^{KIP1}$ and p53

Effect on CDK2 activity

(*Llac* on SNUC2A, colon cancer cells)



A; control,

B; cytoplasm treated (100 μg/ml, 72 h)

Inhibition of CDK2 activity, slightly

BioFactors 22 (2004) 119–122
IOS Press

Cytoplasmic fraction of *Lactococcus lactis ssp. lactis* induces apoptosis in SNU-1 stomach adenocarcinoma cells

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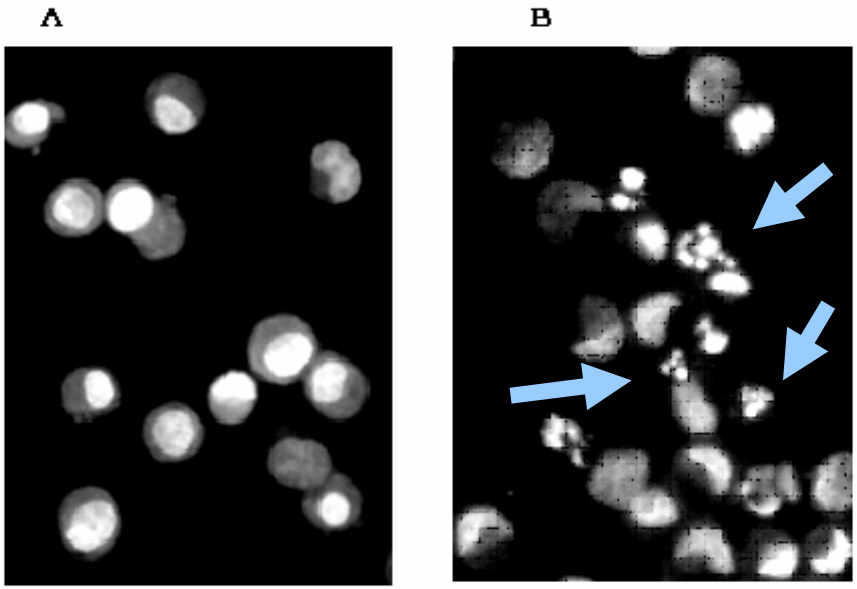
Department of Food Science and Technology, School of Agricultural Biotechnology, Seoul National University, Seoul 151-741, South Korea

Detection of apoptotsis in SNU-1 cells

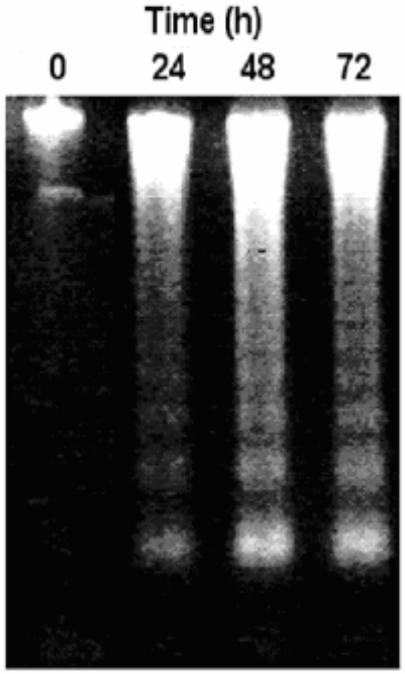
Nuclear fragmentation



A: control

B: *L. lac* CP treated (100 μg/ml)

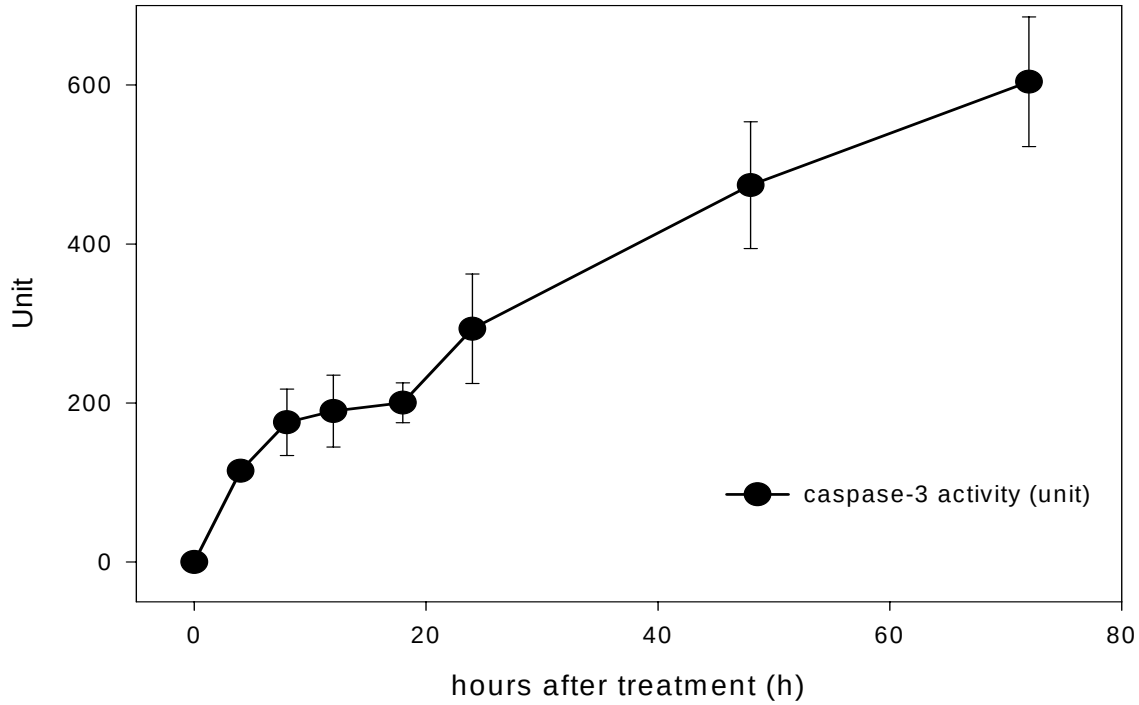
DNA ladder



Apoptosis induction

Effect on caspase-3 activity

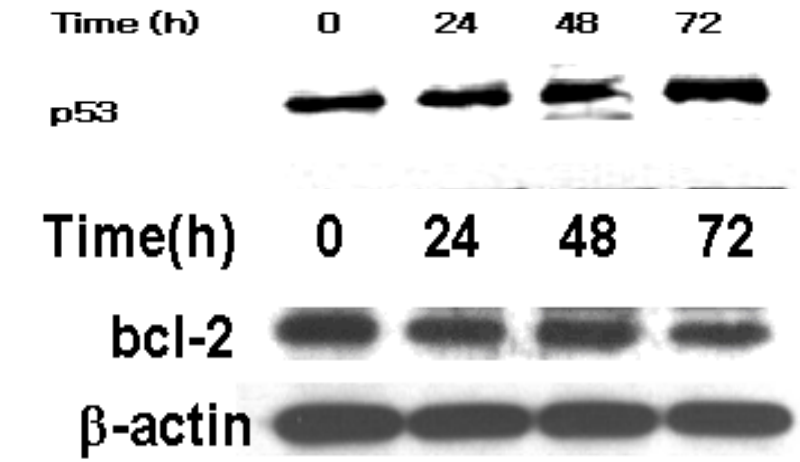
(*Llac* on SNU1, stomach cancer cells)



Increase of caspase-3 activity

Effect on apoptosis related proteins

(*Llac* on SNU1, stomach cancer cells)



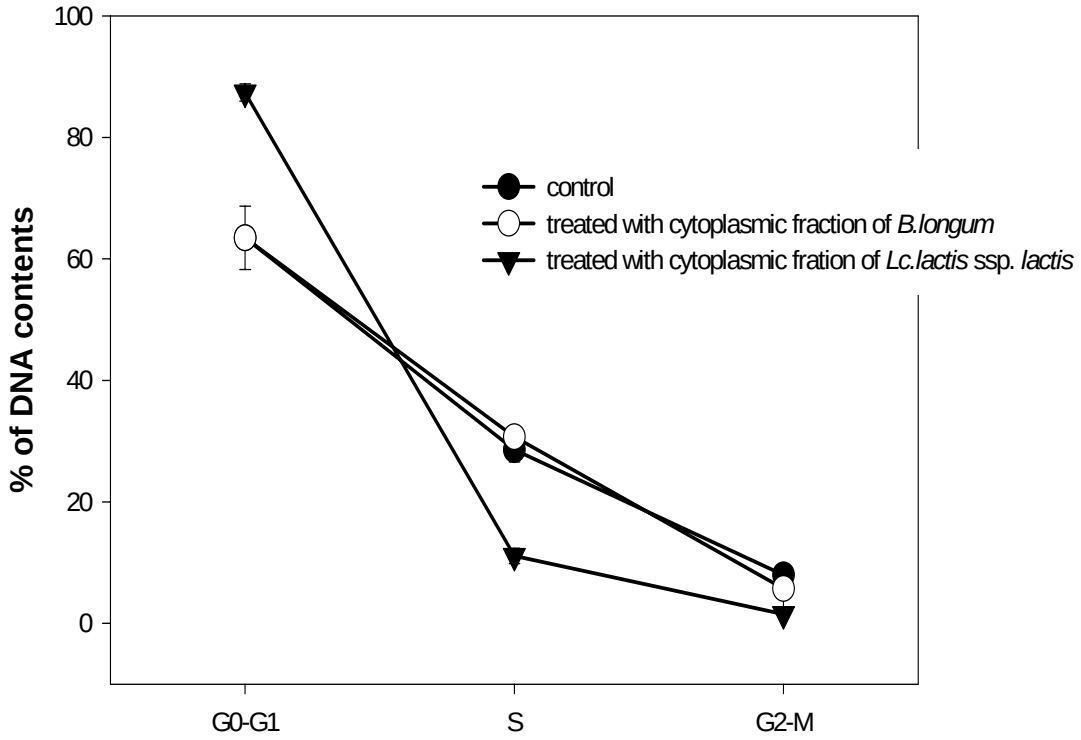
L. Lac CP treated (100 μg/ml)

Increase of p53 expression

Decrease of bcl-2 expression

Cell cycle analysis

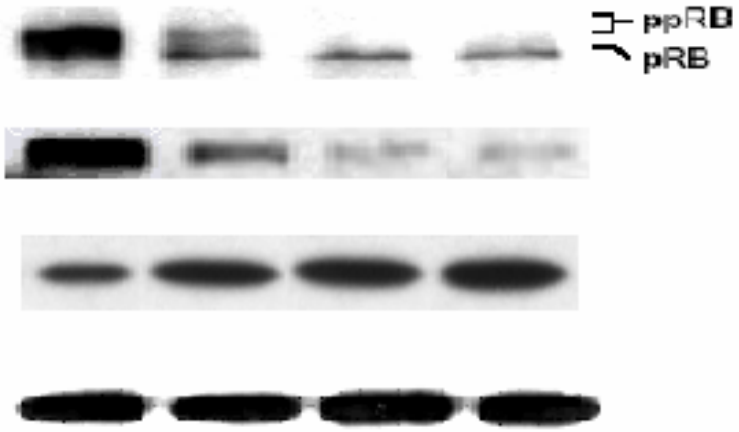
(*Llac* on SNU1, stomach cancer cells)



- G0/G1 phase accumulation

Proteins related to G0/G1 Cell cycle arrest

(*Llac* on SNU1, stomach cancer cells)



Decrease of phosphorylation of pRb
Decrease of cyclin D1 expression
Increase of p21 expression