TCM based botanical Formula **ProtectiVal™** (LCS101) and How It Can Be Used in Cancer-Care

DR. YAIR MAIMON

De NatuurApotheek
farmacie op maat

Vision

Bridging the gap between nature and science in cancer care


Immune
Anti-Cancer
Protection
Protectival
Protectival

Research -places Protectival ™ as one of the most scientifically validated botanical products in cancer care.

- Improve **Immunity** Increase Natural Killer Cell Activity by 400%

- Direct/ Selective Anti Cancer Effect

- Improving Quality of Life
- Reducing Hematological Toxicity

INTRODUCING THE TEAM

LCS101 (**ProtectiVal™**)

Holistic

Astragalus membranaceus
Huang Qi

Poria cocos
Fu Ling

Atractylodes macrocephala
Bai Zhu

Lycium chinense
Gou Qi Zi

Ligustrum lucidum
Nu Zhen Zi

Paeonia lactiflora
Bai Shao

Paeonia obovata
Chi Shao

Citrus reticulata
Chen Pi

Ophiopogon japonicus
Mai Men Dong

Milletia reticulata
Ji Xue Teng

Oldenlandia diffusa
Bai Hua She She Cao

Prunella vulgaris
Xia Ku Cao

Scutellaria barbata
Ban Zhi Lian

Glehnia littoralis
Bei Sha Shen

How we design and R&D the formula

- **Classic TCM knowledge**
  - Effect of herbs (temperature, organ, indication)
  - Understanding the complexity of cancer
  - Dui Yao
- **Modern research**
  - Mechanism of action
  - Research and results
  - The knowledge of chemo and drugs
  - Immunological and cancer research
- **Clinical experience**
  - Confirmation in our lab and research facilities.

Traditional Chinese medical knowledge

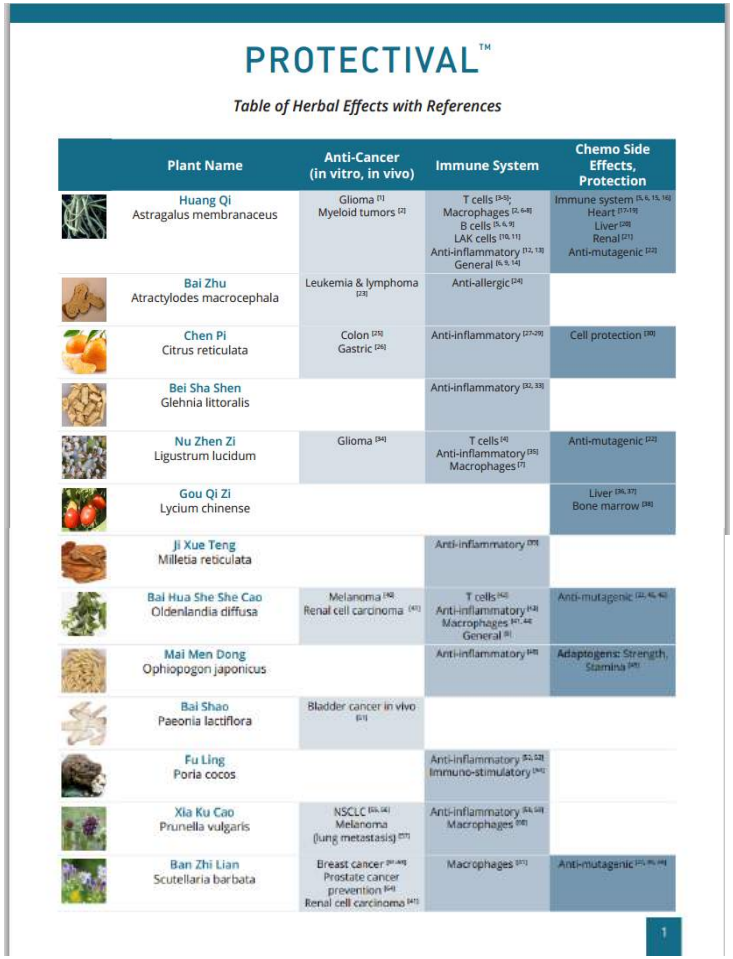
Based on TCM, the formula is constructed form different herbal categories and is acting in 3 different ways :

- **Tonifying** : QI , Blood and Yin
- Huang QI ,Bai zhu . Ji Xue Teng ,Gou Qi Zi ,Bai Shao , Niu Zhen Zhi ,Bei Sha Shen ,Mai Men Dong,
- **Harmonizing:** Qi and clearing Dampness and moving Blood

  Chi Shao ,Chen Pi ,Fu Ling
- **Clearing heat and Toxins:**

  Bai Hua She She Cao ,Ban Zhi Lian ,Xia Ku Cao.

Modern scientific research



PROTECTIVAL™

Table of Herbal Effects with References

Plant Name	Anti-Cancer (in vitro, in vivo)	Immune System	Chemo Side Effects, Protection
Huang Qi Astragalus membranaceus	Glioma [1] Myeloid tumors [2]	T cells [3-5]; Macrophages [2, 6-8] B cells [5, 6, 9] LAK cells [10, 11] Anti-inflammatory [12, 13] General [6, 9, 14]	Immune system [5, 6, 15, 16] Heart [17-19] Liver [20] Renal [21] Anti-mutagenic [22]
Bai Zhu Atractylodes macrocephala	Leukemia & lymphoma [23]	Anti-allergic [24]	
Chen Pi Citrus reticulata	Colon [25] Gastric [26]	Anti-inflammatory [27-29]	Cell protection [30]
Bei Sha Shen Glehnia littoralis		Anti-inflammatory [32, 33]	
Nu Zhen Zi Ligustrum lucidum	Glioma [34]	T cells [4] Anti-inflammatory [35] Macrophages [7]	Anti-mutagenic [22]
Gou Qi Zi Lycium chinense			Liver [36, 37] Bone marrow [38]
Ji Xue Teng Milletia reticulata		Anti-inflammatory [39]	
Bai Hua She She Cao Oldenlandia diffusa	Melanoma [40] Renal cell carcinoma [41]	T cells [42] Anti-inflammatory [43] Macrophages [41, 44] General [8]	Anti-mutagenic [22, 45, 46]
Mai Men Dong Ophiopogon japonicus		Anti-inflammatory [48]	Adaptogens: Strength, Stamina [49]
Bai Shao Paeonia lactiflora	Bladder cancer in vivo [51]		
Fu Ling Poria cocos		Anti-inflammatory [52, 53] Immuno-stimulatory [54]	
Xia Ku Cao Prunella vulgaris	NSCLC [55, 56] Melanoma (lung metastasis) [57]	Anti-inflammatory [53, 58] Macrophages [59]	
Ban Zhi Lian Scutellaria barbata	Breast cancer [60-62] Prostate cancer prevention [63] Renal cell carcinoma [47]	Macrophages [57]	Anti-mutagenic [22, 45, 46]

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2

Modern scientific research

PROTECTIVAL™

Table of Herbal Effects with References

	Plant Name	Anti-Cancer (in vitro, in vivo)	Immune System	Chemo Side Effects, Protection
	**Huang Qi** Astragalus membranaceus	Glioma [1] Myeloid tumors [2]	T cells [3-5]; Macrophages [2, 6-8] B cells [5, 6, 9] LAK cells [10, 11] Anti-inflammatory [12, 13] General [6, 9, 14]	Immune system [5, 6, 15, 16] Heart [17-19] Liver [20] Renal [21] Anti-mutagenic [22]
	**Bai Zhu** Atractylodes macrocephala	Leukemia & lymphoma [23]	Anti-allergic [24]	
	**Chen Pi** Citrus reticulata	Colon [25] Gastric [26]	Anti-inflammatory [27-29]	Cell protection [30]
	**Bei Sha Shen** Glehnia littoralis		Anti-inflammatory [32, 33]	
	**Nu Zhen Zi** Ligustrum lucidum	Glioma [34]	T cells [4] Anti-inflammatory [35] Macrophages [7]	Anti-mutagenic [22]
	**Gou Qi Zi** Lycium chinense			Liver [36, 37] Bone marrow [38]

Adaptogen

PROTECTIVAL™

BIOACTIVE COMPOUNDS

Table of Herbal Effects with References

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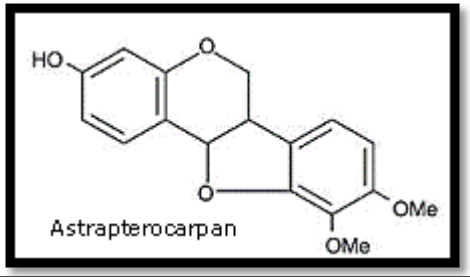
Flavonoids of the isoflavone type



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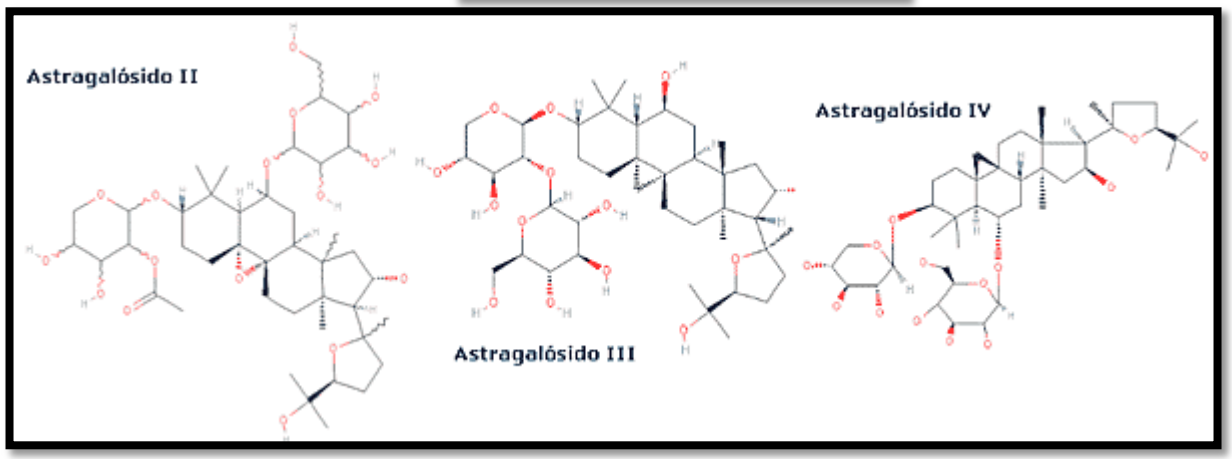

Hepatoprotective, antioxidant, immunstimulating, antiviral, cardiotonic,

PROTECTIVAL™

BIOACTIVE COMPOUNDS

Table of Herbal Effects with References

	Plant Name	Anti-Cancer (in vitro, in vivo)	Immune System	Chemo Side Effects, Protection
	Ban Zhi Lian Scutellaria barbata	Breast cancer [61-63] Prostate cancer prevention [64] Renal cell carcinoma [41]	Macrophages [41]	Anti-mutagenic [22, 45, 46]

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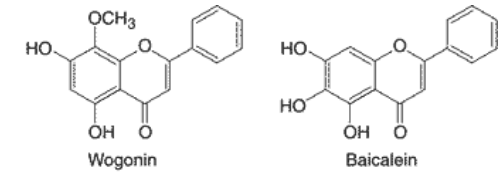
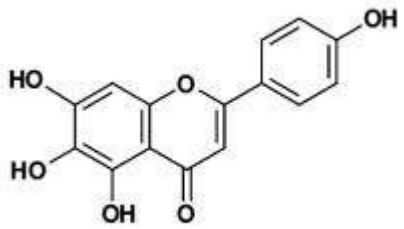
over 50 flavones isolated





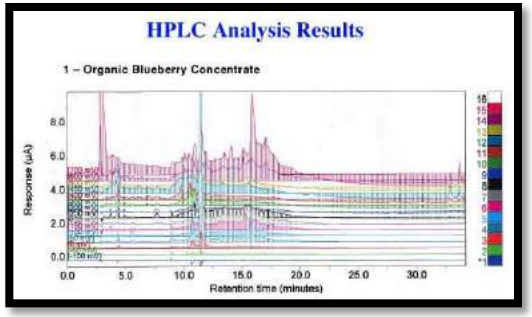
Batch to Batch Consistency

Identification

Cleanliness

Biological activity

HPLC



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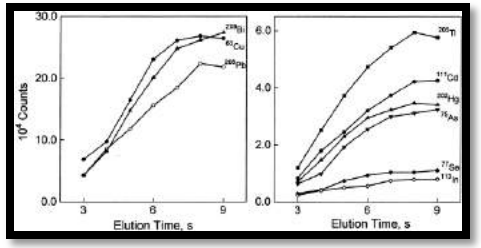
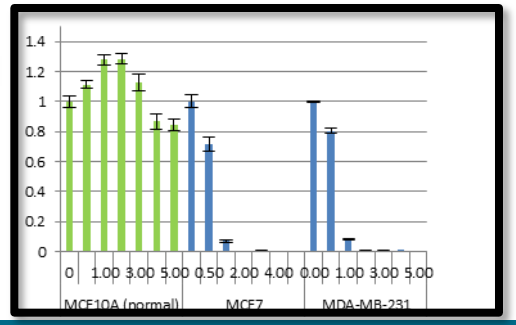


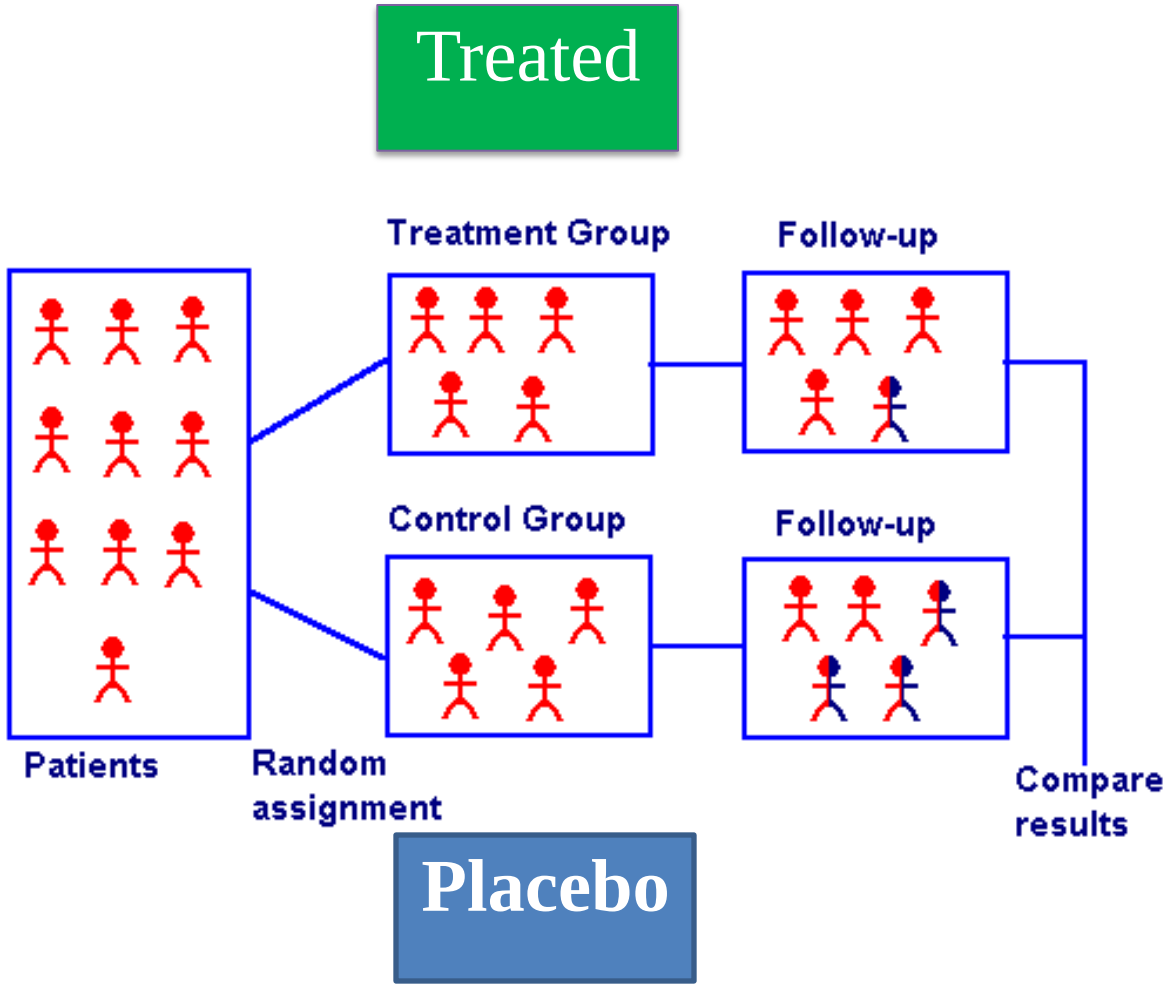


Protection and recovery

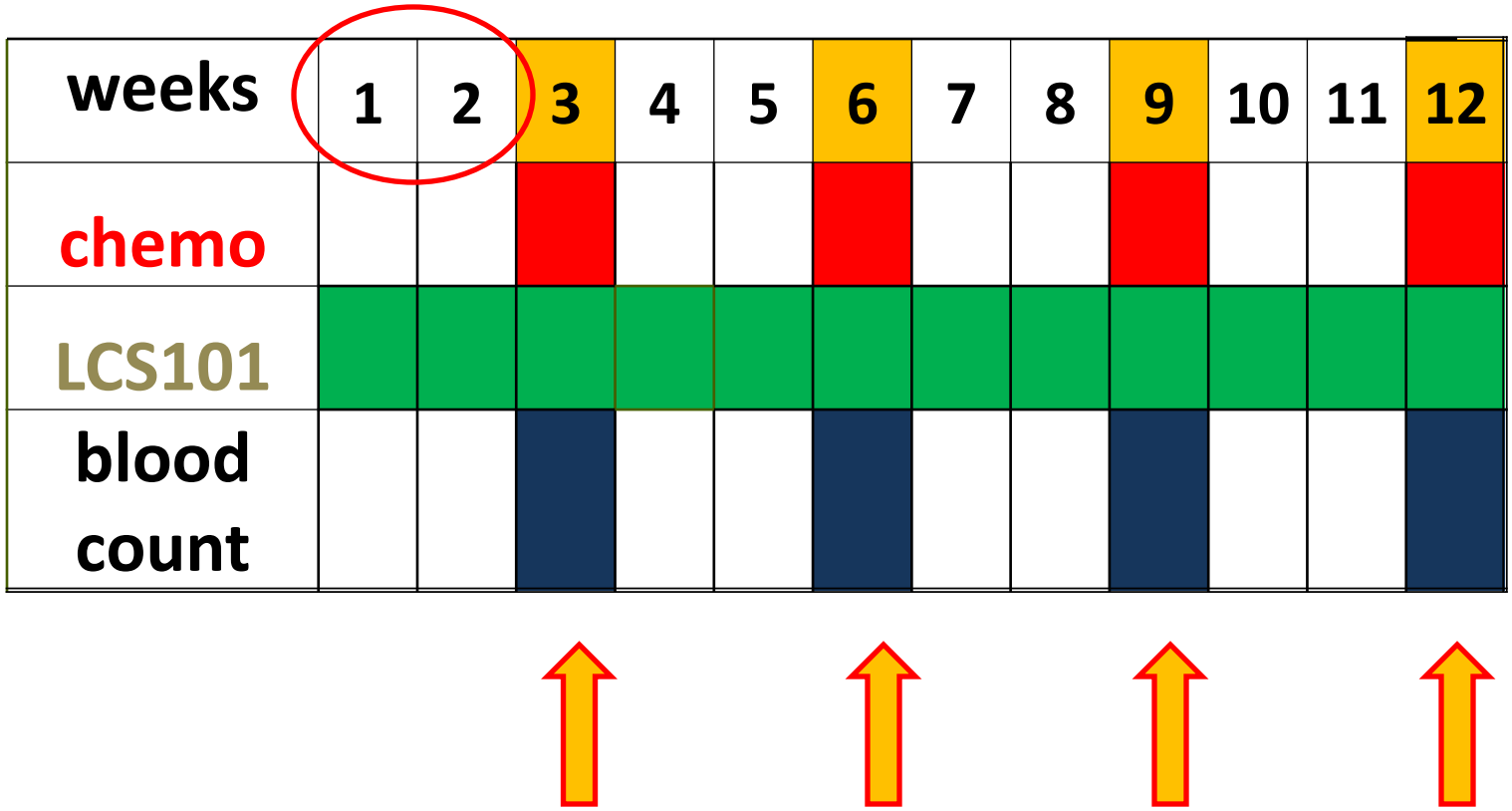
- Improving Quality of Life
- Reducing Hematological Toxicity

Human phase 2 research

Patients: Breast cancer during chemo

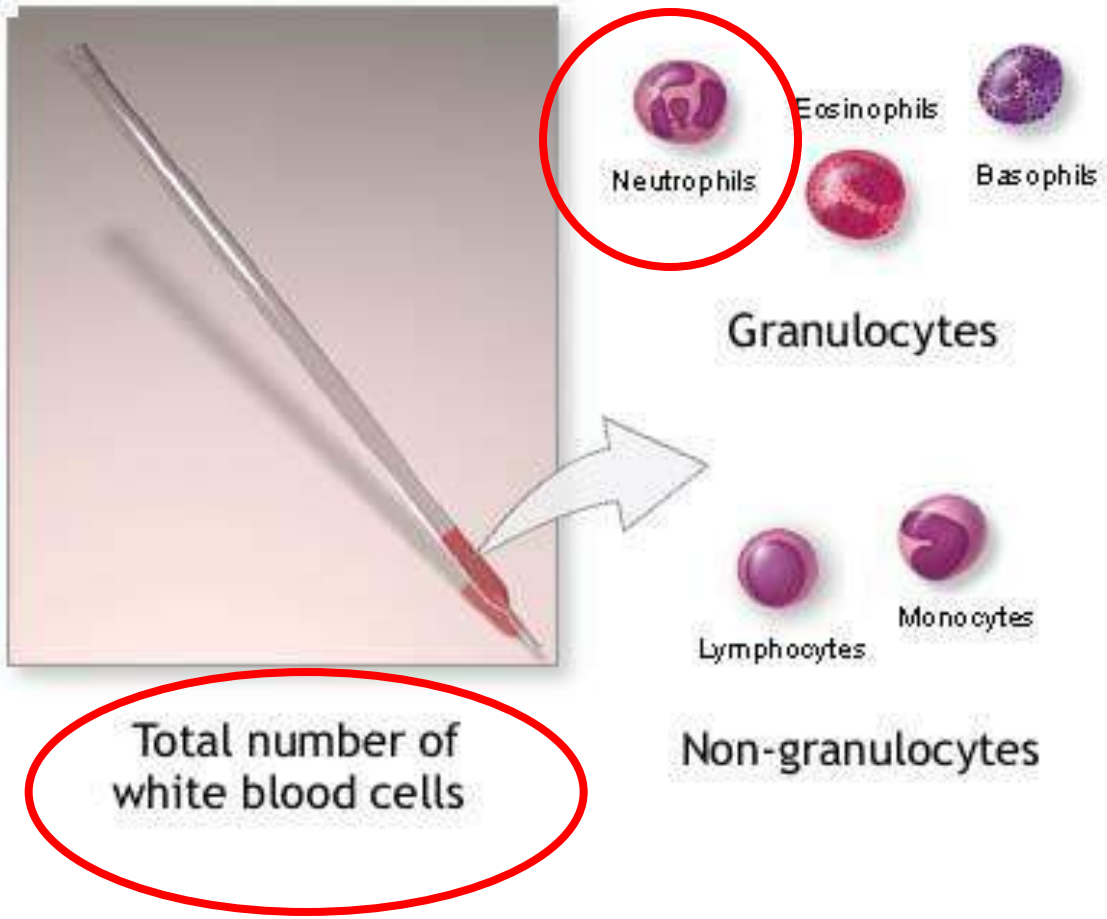


LCS101
research design



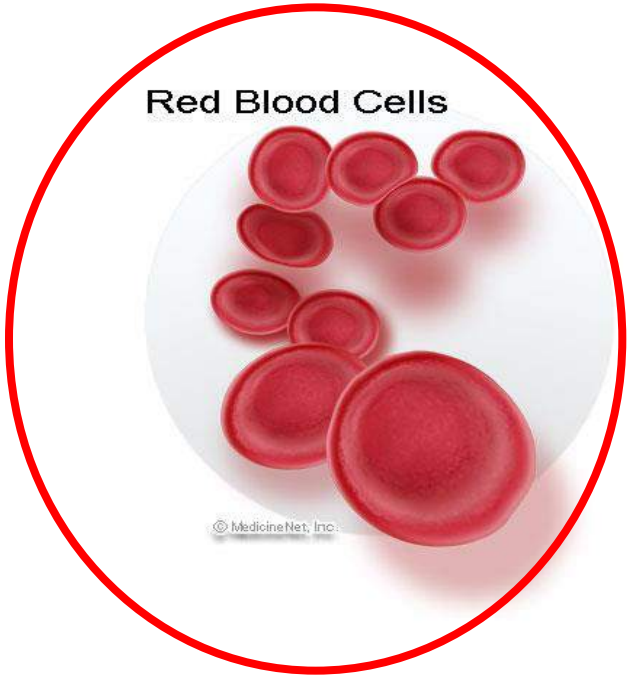
Complete Blood Count (CBC)

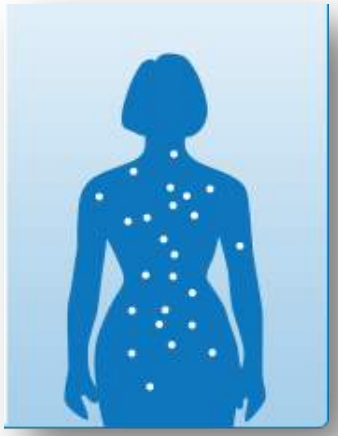
WBC



Total number of white blood cells

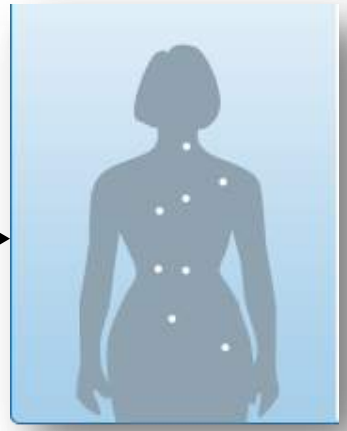
RBC



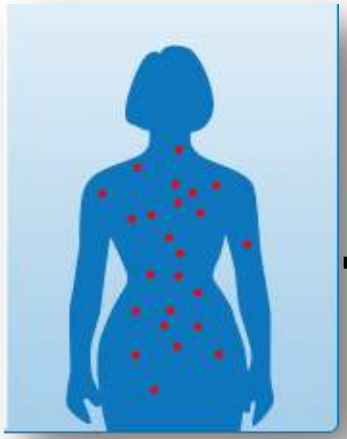


White Blood Cells

Chemotherapy

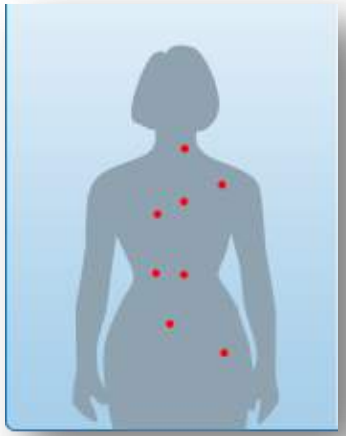


Leucopenia



Red Blood Cells

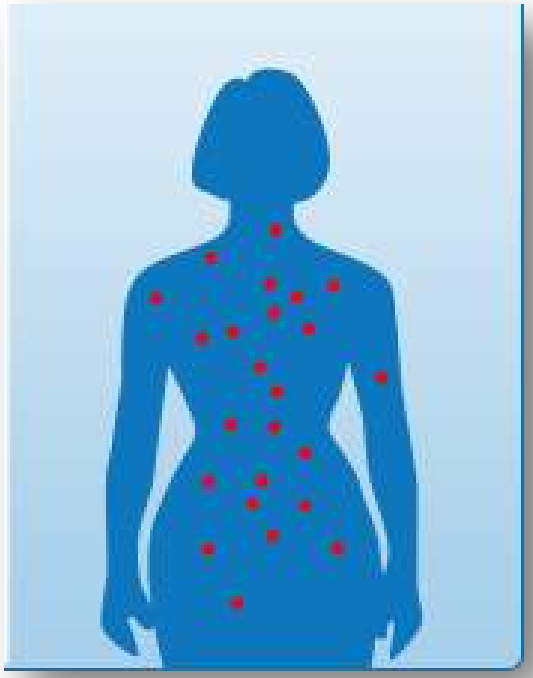
Chemotherapy

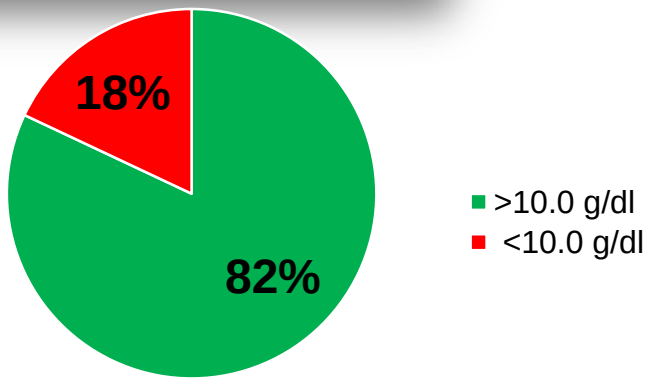


Anemia

Anemia

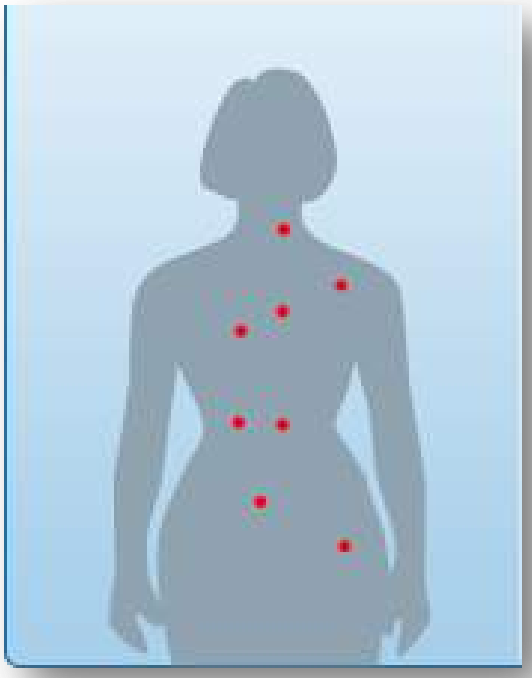
LCS101

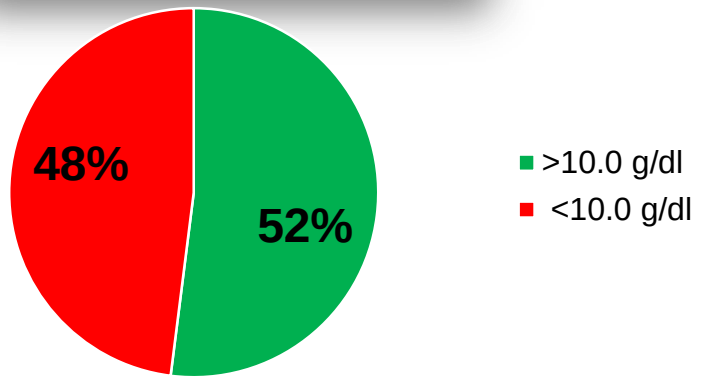




Reduction in hemoglobin count only 18%

Placebo



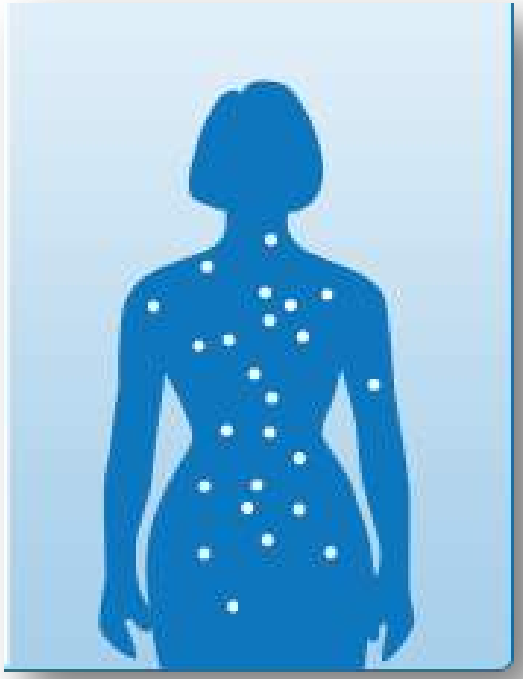


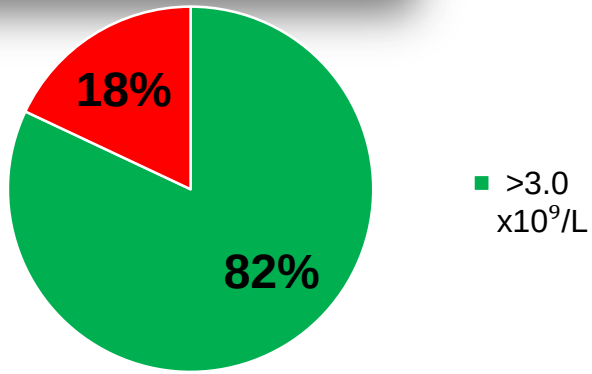
Reduction in hemoglobin count 48%

P –value 0.0081

Leucopenia

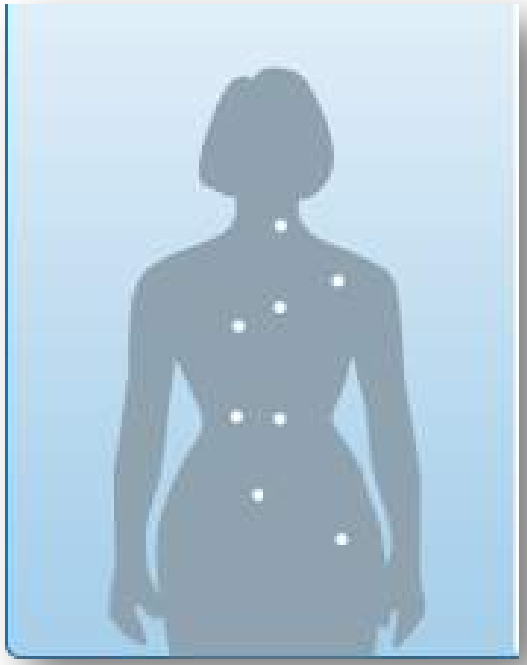
LCS101

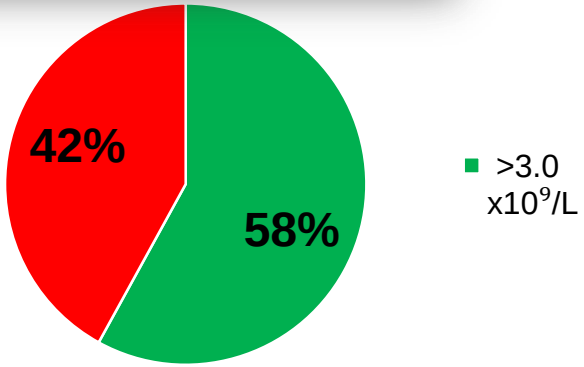




Drop in WBC only to 18 %
White blood cells under3000

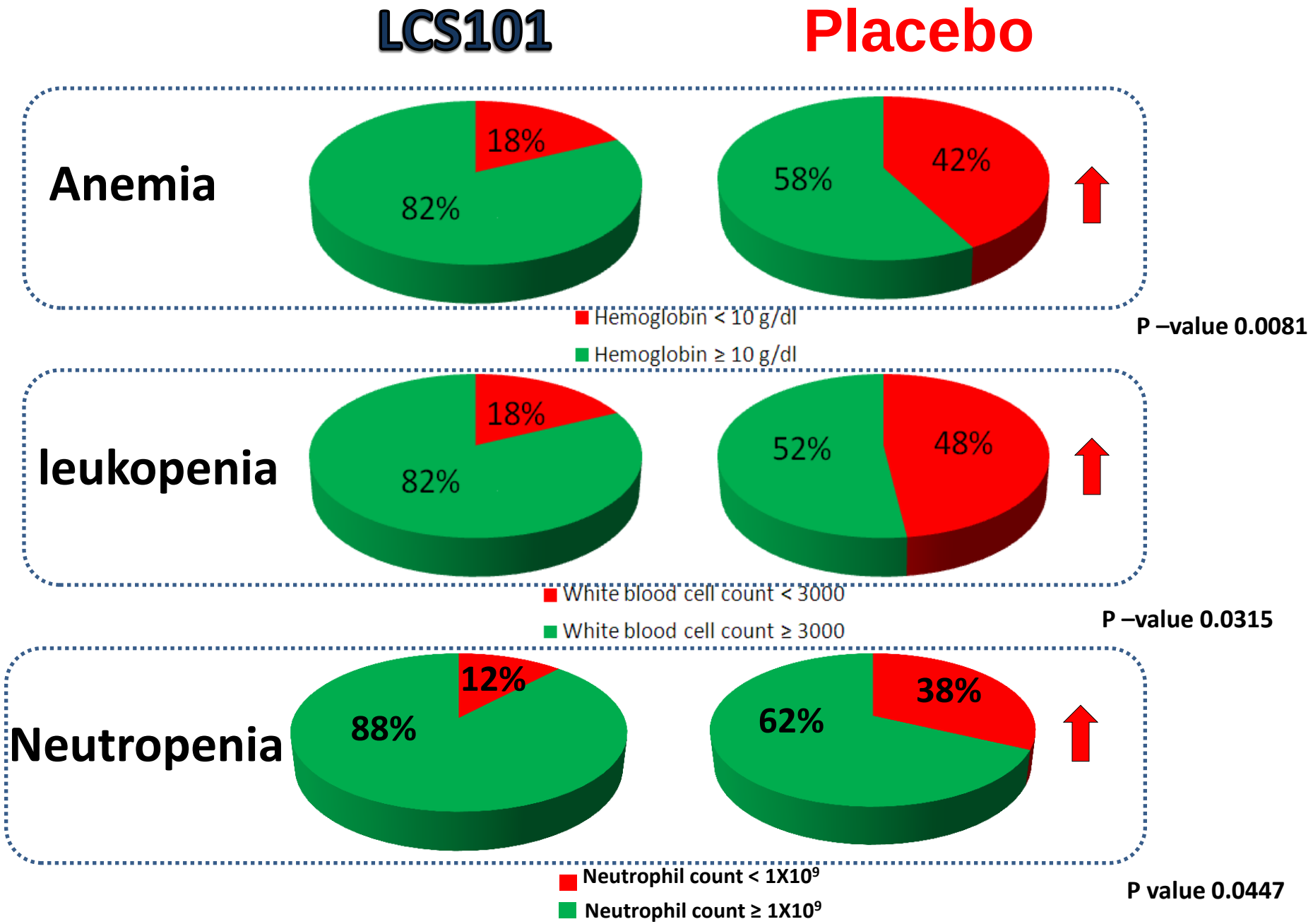
Placebo

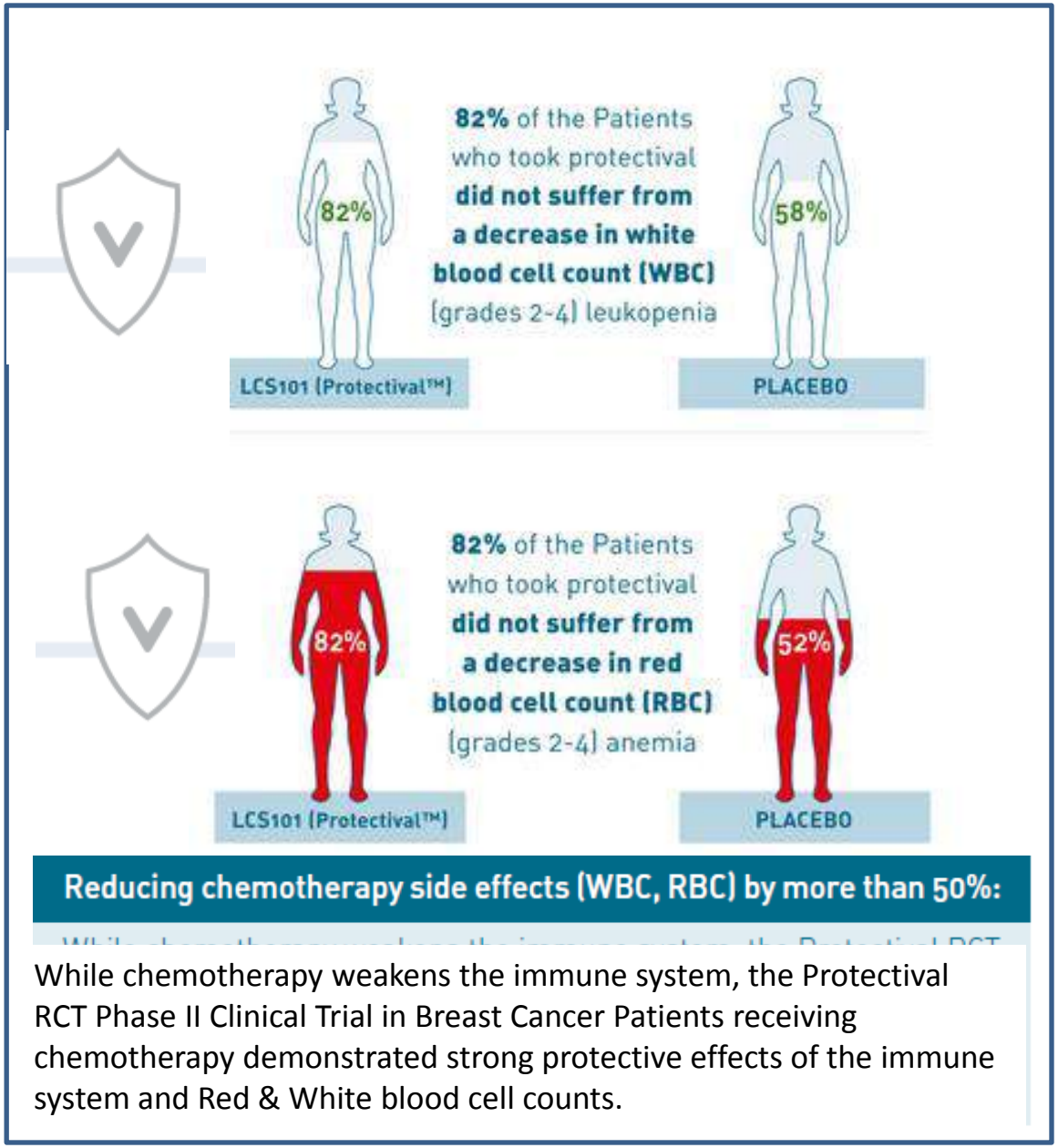




Drop in WBC to 42%
White blood cells under3000

P –value 0.0315


LCS101
Placebo
Anemia
18%
82%
58%
42%
Hemoglobin < 10 g/dl
Hemoglobin ≥ 10 g/dl
P –value 0.0081
leukopenia
18%
82%
52%
48%
White blood cell count < 3000
White blood cell count ≥ 3000
P –value 0.0315
Neutropenia
12%
88%
62%
38%
Neutrophil count < 1X10⁹
Neutrophil count ≥ 1X10⁹
P value 0.0447



While chemotherapy weakens the immune system, the Protectival RCT Phase II Clinical Trial in Breast Cancer Patients receiving chemotherapy demonstrated strong protective effects of the immune system and Red & White blood cell counts.

Publication

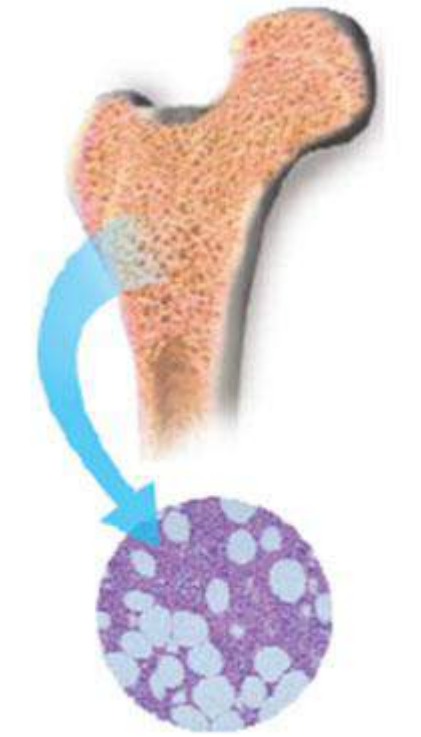
Study of the Botanical Compound Mixture LCS101 and it influence on reducing chemotherapy side effect .

Yaal-Hahoshen N, **Maimon Y**, Siegelmann-Danieli N, Lev-Ari S, Ron I, Sperber F, Samuels N, Shoham J, Merimsky O.

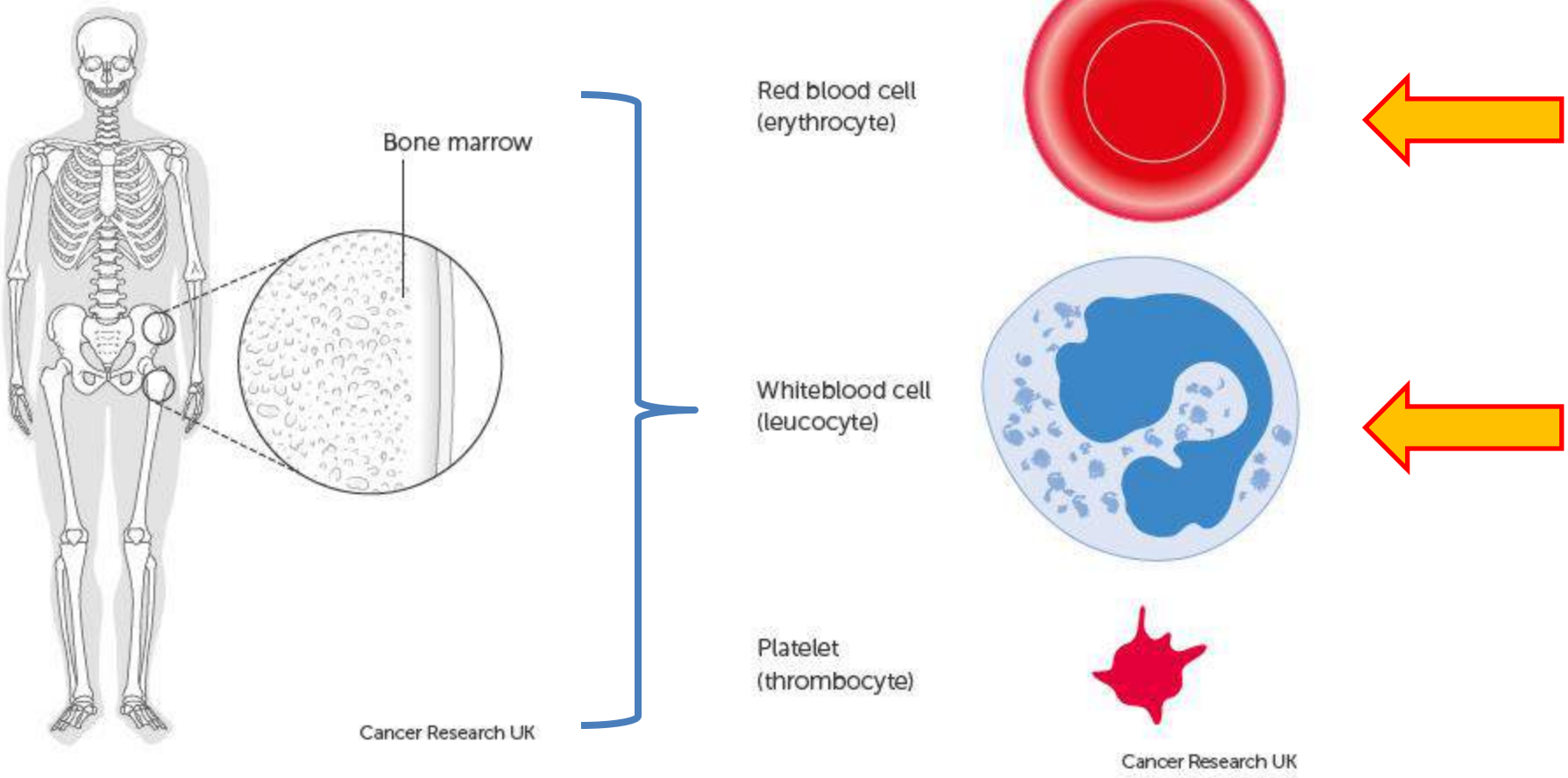
[The Oncologist 2011; 16: 1197-1202]

Hematological
Protection and recovery

- Bone Marrow Suppression leading to reduction in blood cell counts.
- **Red blood cells (RBC's)** transport oxygen. A low red blood cell count, called anemia, will generally give you fatigue.
- **White blood cells (WBC's)** help fight infection.



Blood cells are produced in bone marrow


Bone marrow
Cancer Research UK
Red blood cell
(erythrocyte)
Whiteblood cell
(leucocyte)
Platelet
(thrombocyte)
Cancer Research UK

What are the advantage ?

- **During chemo:**
  - Complete the chemo
  - Prevent secondary infection
  - Improve Quality of Life
  - Protect

- Long term – protection….

Helping to avoid compromising the treatment by delaying or decreasing chemotherapy.

- chemotherapy dose may need to be lowered, or the treatment delayed, to avoid dangerously impairing the ability of the bone marrow to produce blood cells.

Preventing secondary infections

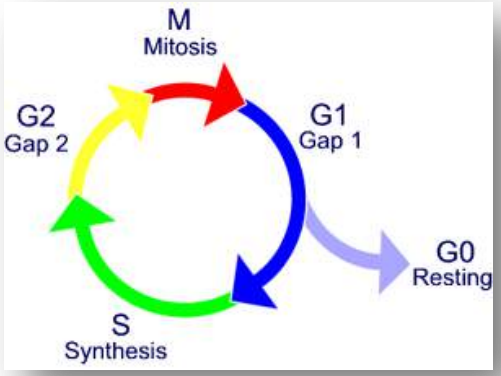
- When the white blood cell count is low, the body may not be able to fight off infections.
- Most infections come from bacteria normally found on the skin, in the intestines, and in the genital tract.

- Immune system- immune modulation

Side effects

- Although chemotherapy is given to kill cancer cells, it also can damage normal cells. The normal cells most likely to be damaged are those that divide rapidly, for instance:

- **Bone marrow/blood cells**
- **Cells of hair follicles**
- **Cells lining the digestive tract**



Quality of life:

Nausea, vomiting, appetite

dryness, fatigue, sleep disorders

Chemotherapy and cancer patient TCM view

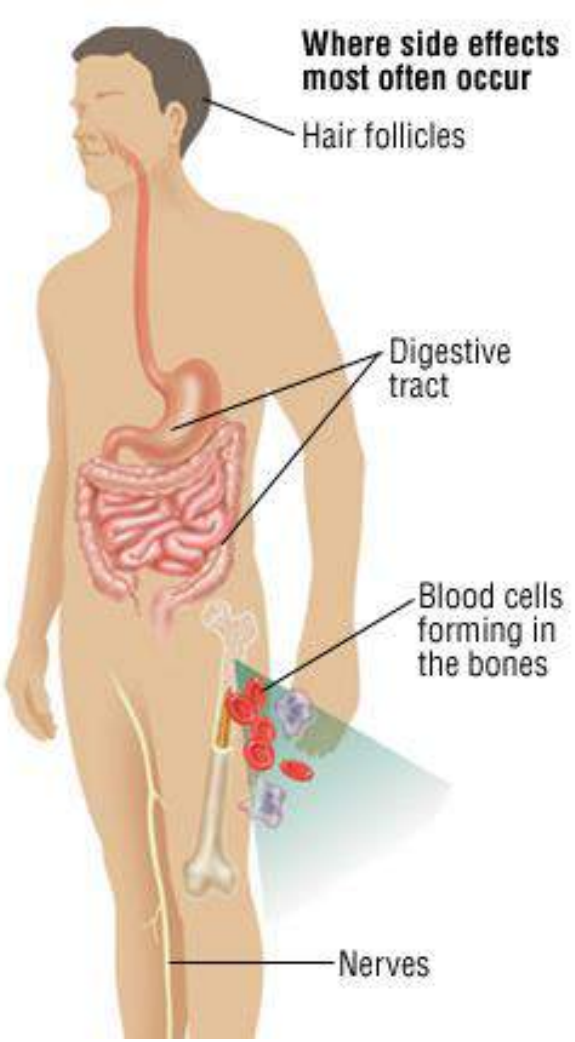
- ***Deficiency*** – Blood, Qi, wei Qi, Jing
- ***Eccess*** – phlegm, heat, heat and toxins (phlegm)
- ***Deficiency of organs*** – spleen, liver-blood, kidney.

How it is used in the clinic ?

- Treatment during chemotherapy
- Addressing QoL issues
- **Hematological**
- **Non hematological**

Side effects of chemotherapy and radiation

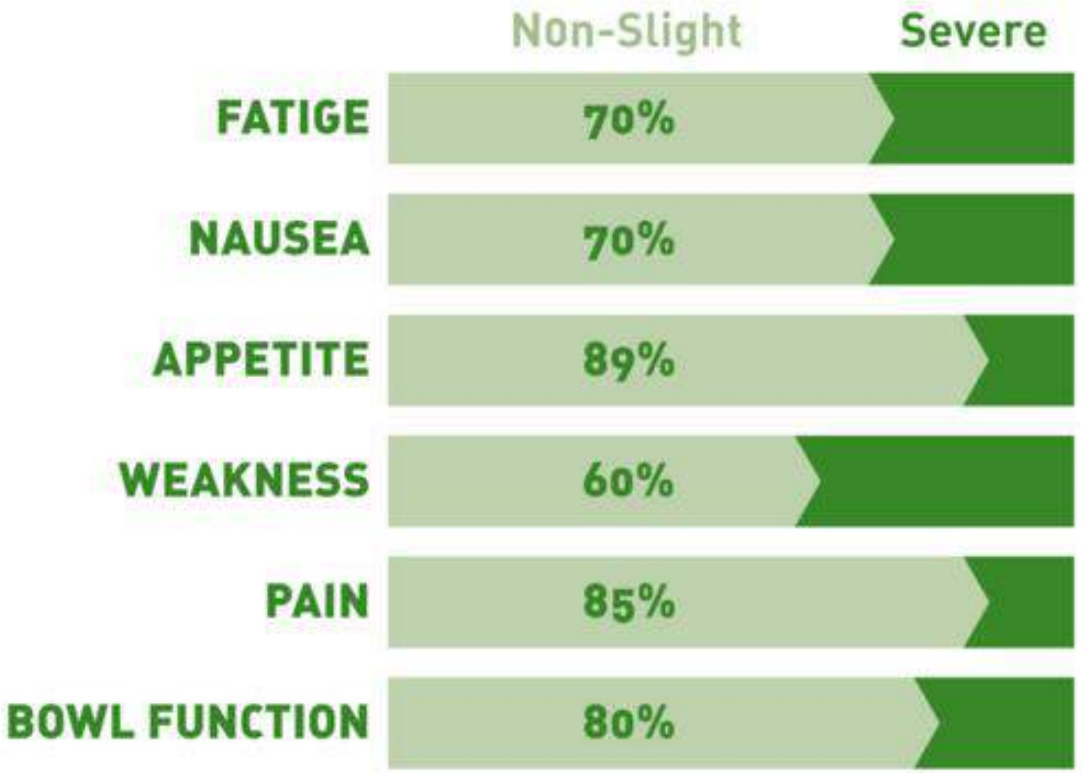
- Fatigue (also chemo brain)
- Loss of appetite
- Nausea , vomiting
- Diarrhea



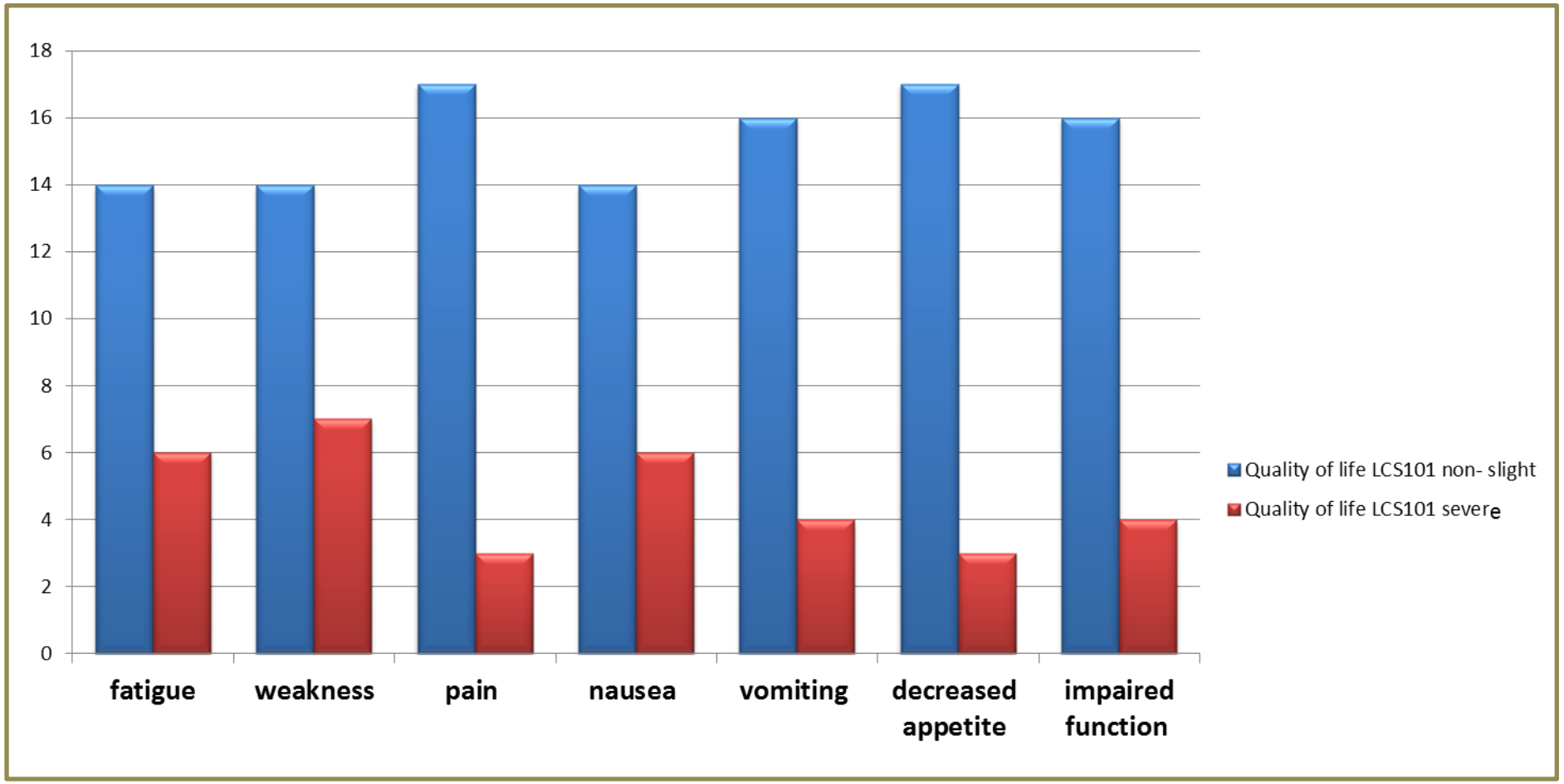
- More serious – low blood counts, infections

Improves Quality Of Life

85% of the Patients who took protectival reported that they felt that **Protectival™ helped reduce their symptoms**



Effect of the Botanical Compound LCS101 on Chemotherapy-Induced Symptoms in Patients with Breast Cancer: A Case Series Report



Example : Fatigue

Expected: 81.7% reported significant fatigue*. Observed: 30 %

Janz NK, et al. *J Women Health* 2007; 16:1348–1361

Clinical- Human Research Results

Effect of the Botanical Compound LCS101 on Chemotherapy-Induced Symptoms in Patients with Breast Cancer: A Case Series Report

Noah Samuels, MD
Yair Maimon, PhD
Rachel Y Zisk-Rony, RN, MPH, PhD

Published in peer-reviewed Journal

Integrative Medicine Insights **2013:8 1–8**

For Nausea or Vomiting

- Stomach spleen supporting herbs
- Add- fresh ginger

- **Research**
- 0.5 ginger in capsules x 3.

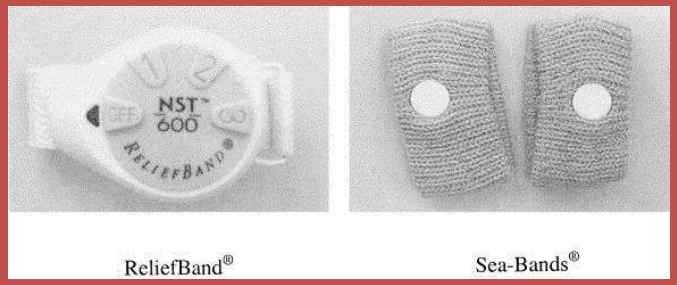
start every 8 hours start at the day of chemo

continue 5 days.

Acupressure for chemotherapy induced nausea and vomiting

- **PC-6**

- **PC-6**
- ACUPRUSHER
- **ACUPUNCTURE**



- Press needle

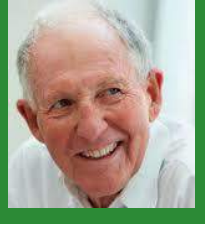
case 1, follow up 3 years

Female 42 breast cancer stared treatment with **ProtectiVal™** during chemo

- Increase in her WBC and RBC
- Minor side effects.

- **Maintenance**: prevention dosage for 2 years
- Feels well

Case 2, follow up 5 years



Male 62 Lung caner

- Started taking **ProtectiVal™** after lung **surgery**

✓ Fast recovery , elevation of WBC (fighting well throat infection).

- Continue **during chemotherapy**

✓ good Quality of life (Acupuncture helped with depression and insomnia)

- **Maintenance** :Now still on full dose for recovery

Dosage:

A bottle of ProtectiVal™ contains 90 tablets.

There are 2 dosages recommendation:

- **Full dose: 2 tab. X 3 times daily**

- **Maintenance dose: 1 tab. X 3 times daily**

  (some patients prefer twice a day than

  2 in the morning and 1 in the evening)

Dosage:

- **During chemotherapy**: Full dose

(recommended to start 2 weeks before chemo).

- **After chemotherapy**: For 3 month maintain full dose then Maintenance dose

- **Past cancer** : For 3 month maintain full dose then Maintenance dose

- **For patient with active cancer**: full dose all the time

How it is used in the clinic ?

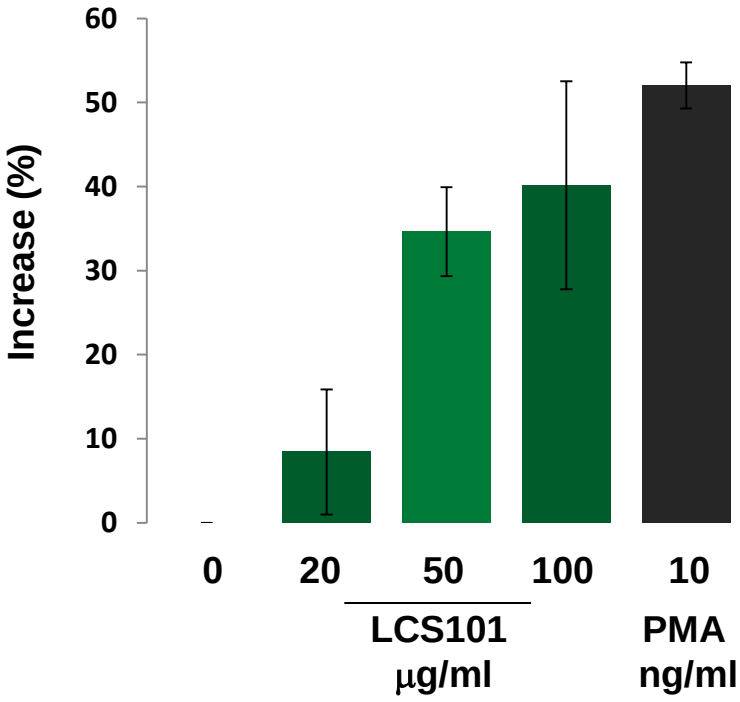
- **Reducing conventional medicine side effect:**
  - During Chemotherapy
  - After chemo for recovery
  - Anti hormonal therapy (breast, prostate Ca)
  - Radiation
  - Surgery

Immune

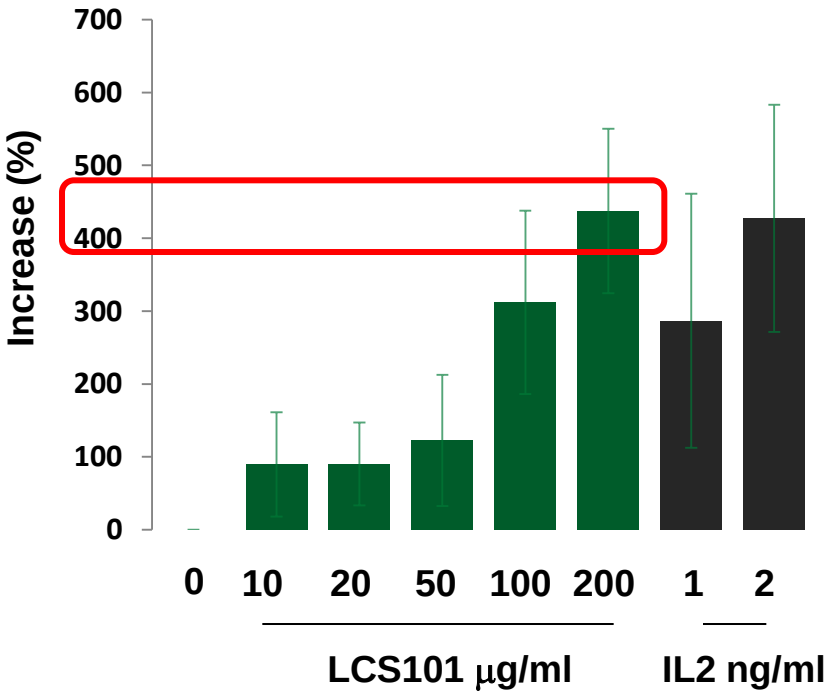
- **Improve Immunity Increase Natural Killer Cell Activity by 400%**

Activation of the Immune System

Activates T cells



Activates NK cell



400% activation of NK cells

- **Immuno-modulatory Effects of the Botanical Compound LCS101: Implications for Cancer Treatment,**

OncoTargets and Therapy 2013:6 437–445

Case 3

M 72 Colon cancer after chemo

- Low blood counts after Chemo
- Recurrent lung infractions

- Also: fatigue, lack of appetite

Female 66 metastatic Breast cancer (triple negative)

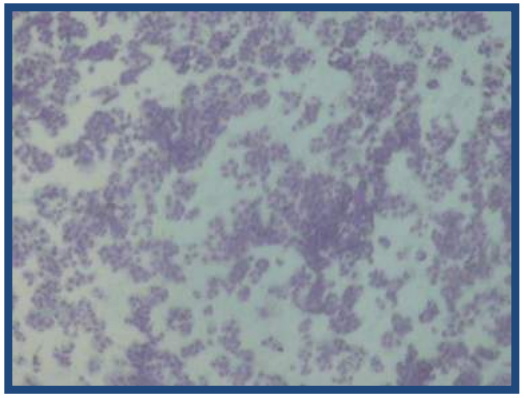
- Low blood WBC counts
- Throat infections (on antibiotic for the 4th time)
- Low Neutrophil count.

- very weak

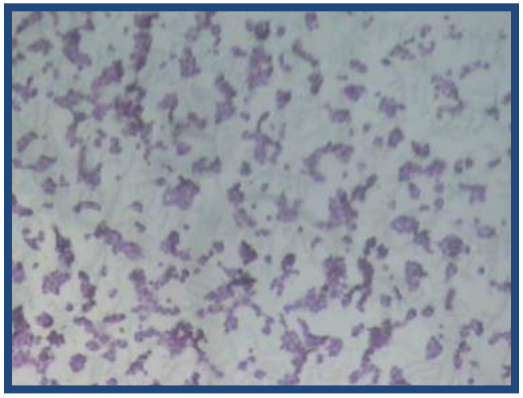
- **Direct/ Selective Anti Cancer Effect**

Breast cancer cell survival after 72 hours

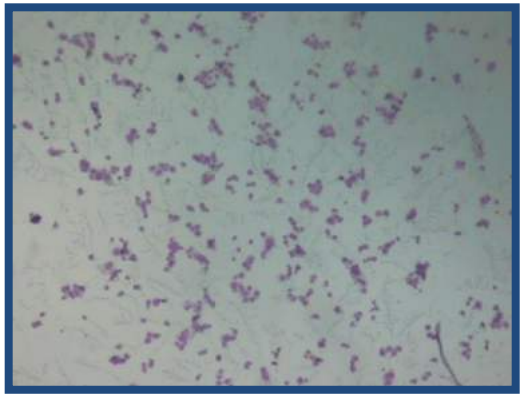
Effect of LCS101 on
Breast Cancer adenocarcinoma cell line (T47D)



Control



LCS101 (3mg/ml)



LSC101 (50 mg/ml)

Effect of Chinese herbal therapy on breast cancer adenocarcinoma cell lines.

Maimon Y, Karaush V, Yaal-Hahoshen N, Ben-Yosef R, Ron I, Vexler A, Lev-Ari S.

J Int Med Res. 2010;38:2033-9.

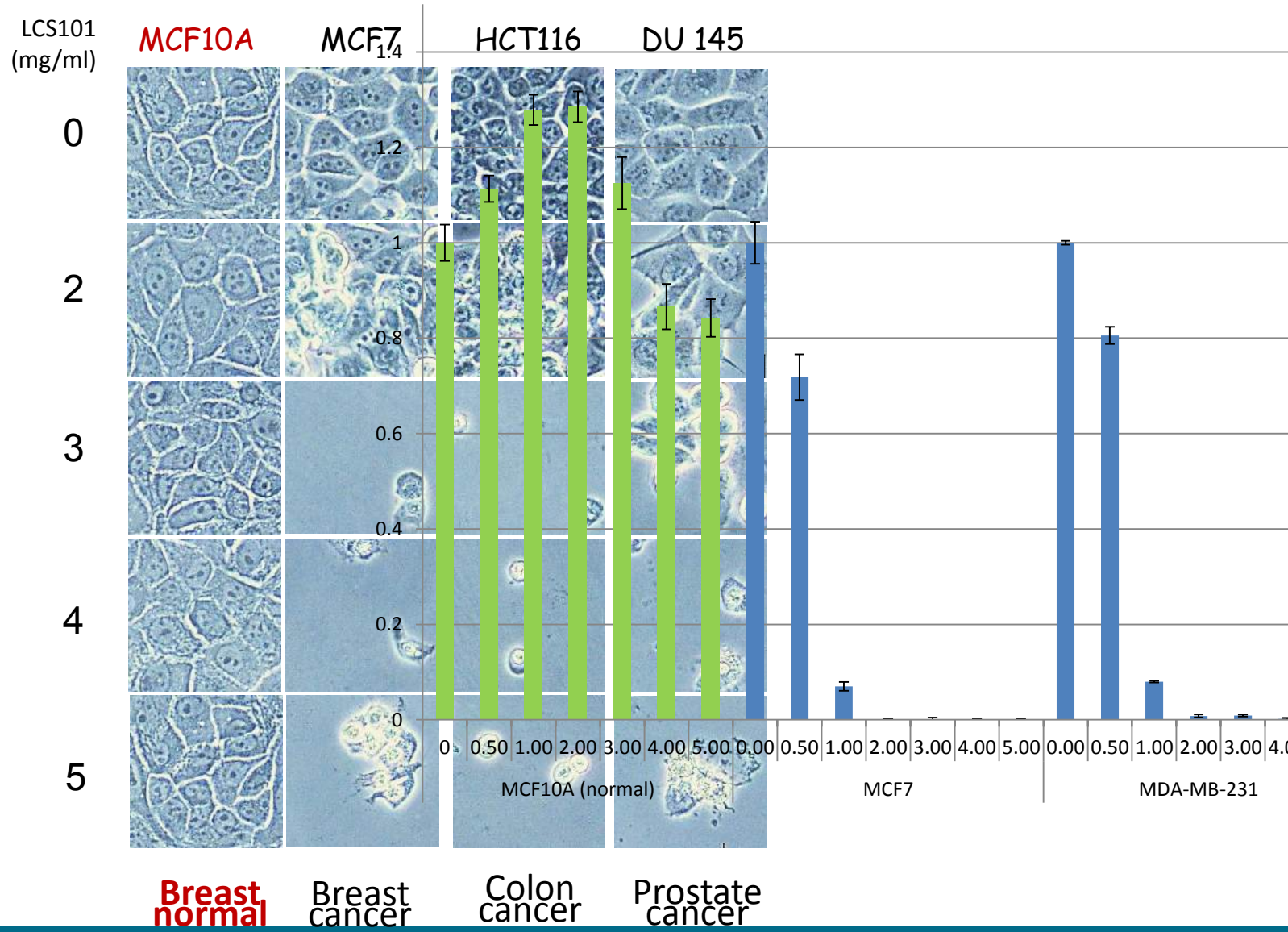
Chemotherapy

Non Selective

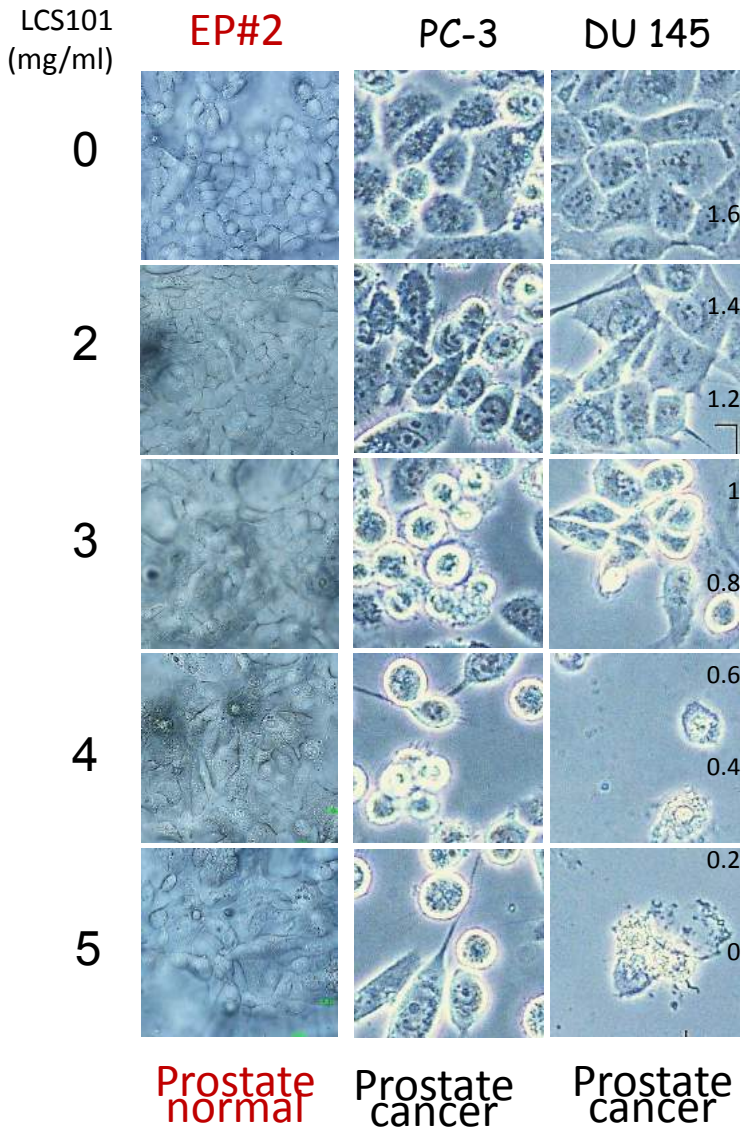
is the formula selective?

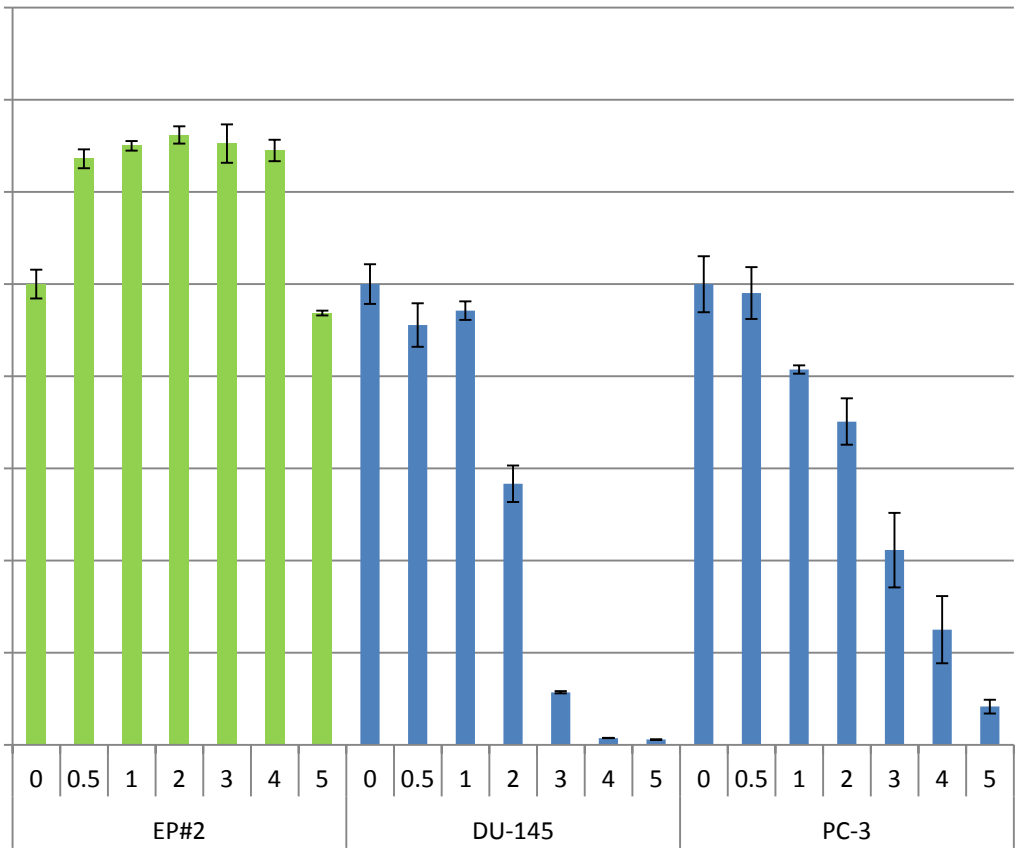
Selective

LCS101- selective killing effect



LCS101- selective killing effect



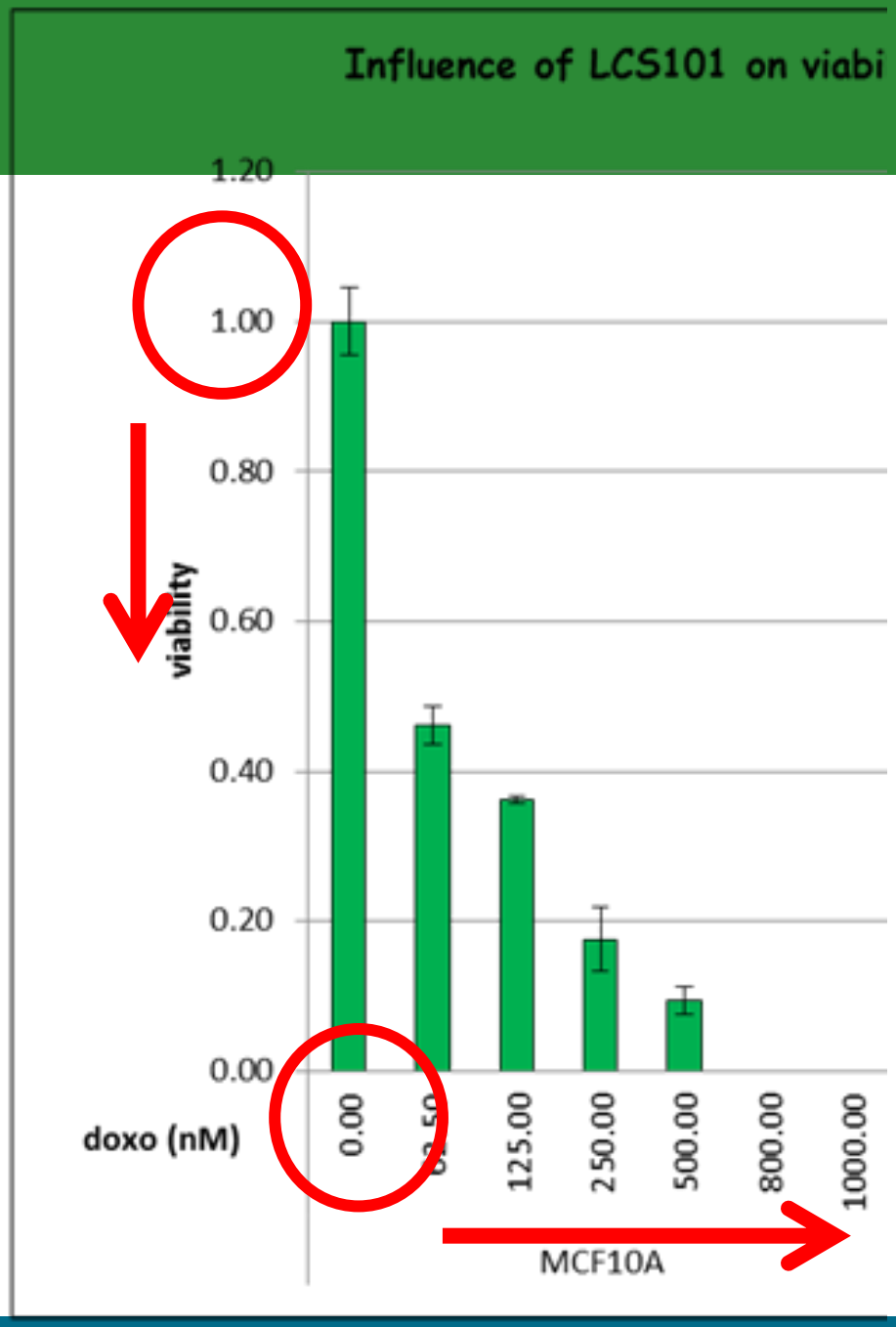


Protection


CAUTION
CHEMOTHERAPY

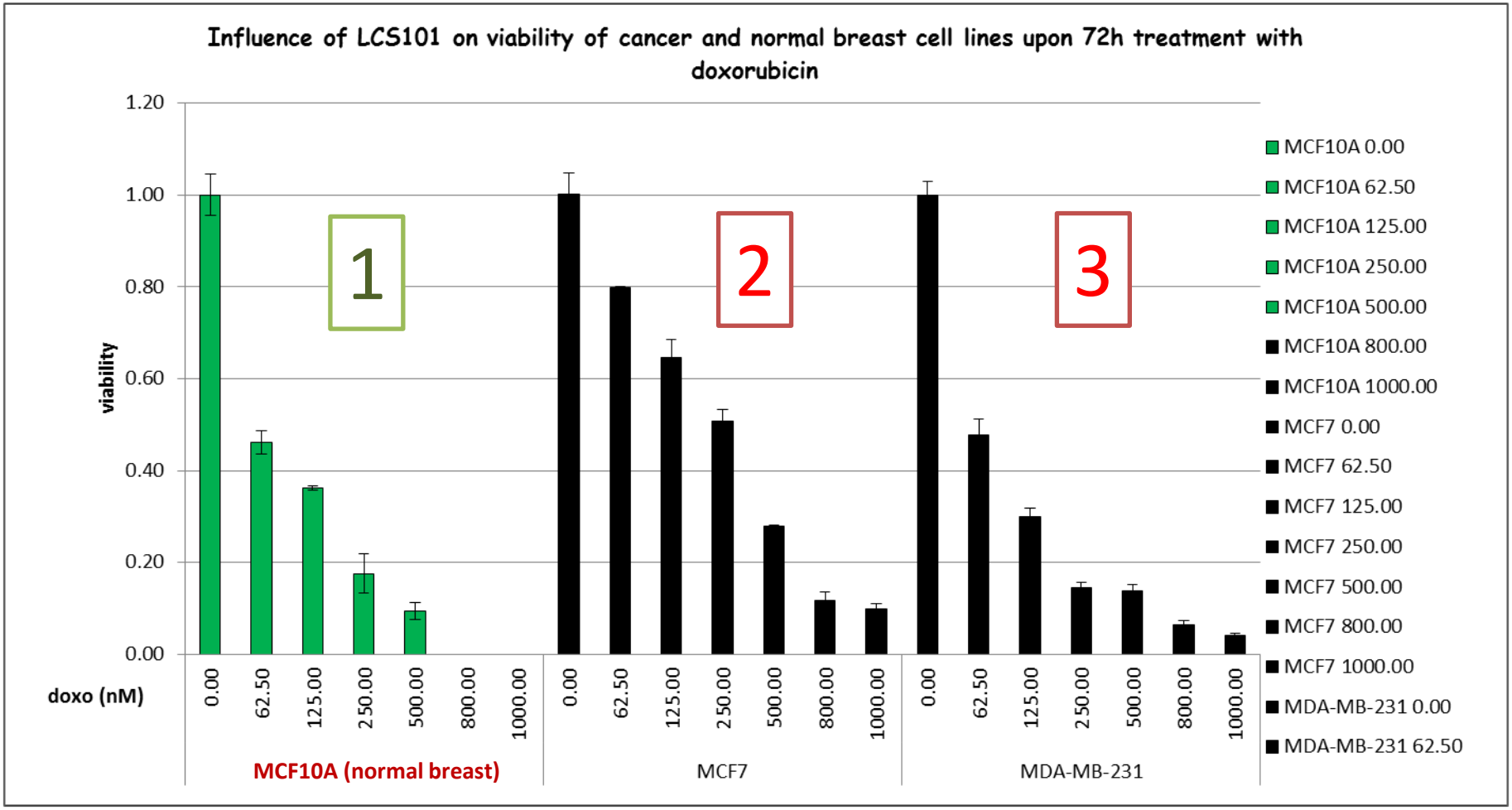

Protectival
The Active Shield


Good
Bad

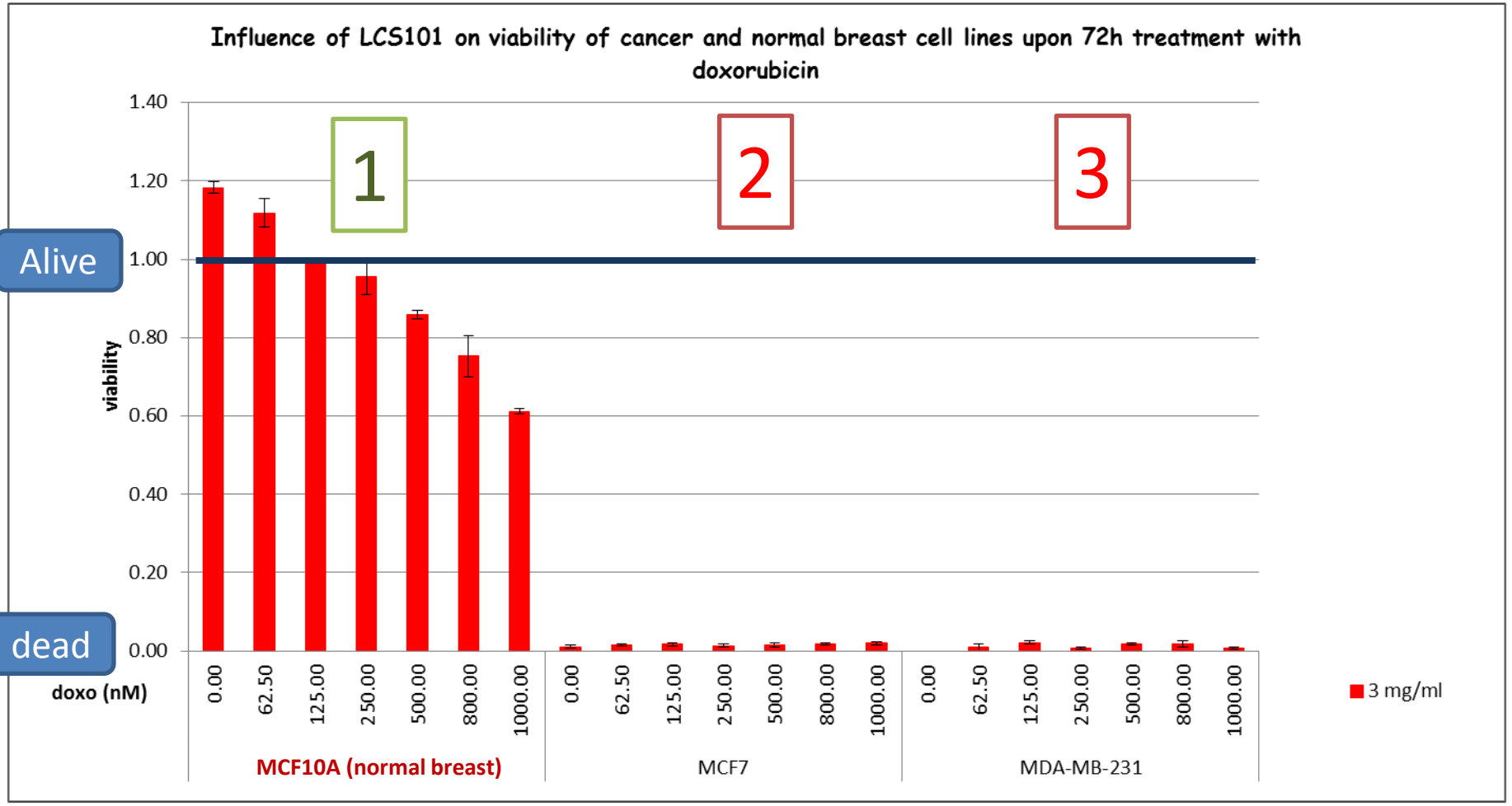

Influence of LCS101 on viabi
1.20
1.00
0.80
0.60
0.40
0.20
0.00
viability
doxo (nM)
0.00
125.00
250.00
500.00
800.00
1000.00
MCF10A

Doxo alone – non selective

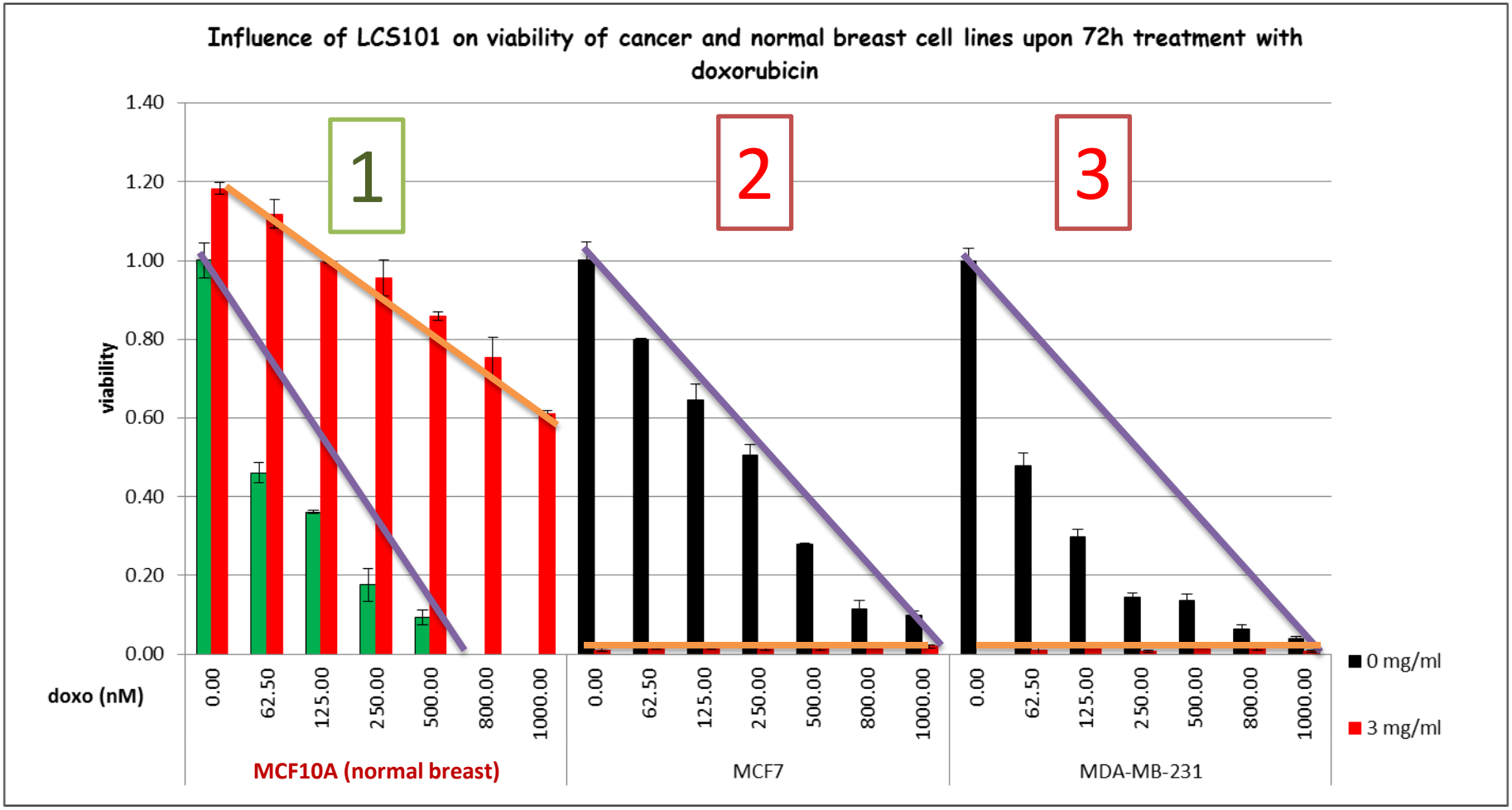
CAUTION
CHEMOTHERAPY



Doxo + LCS101- selective

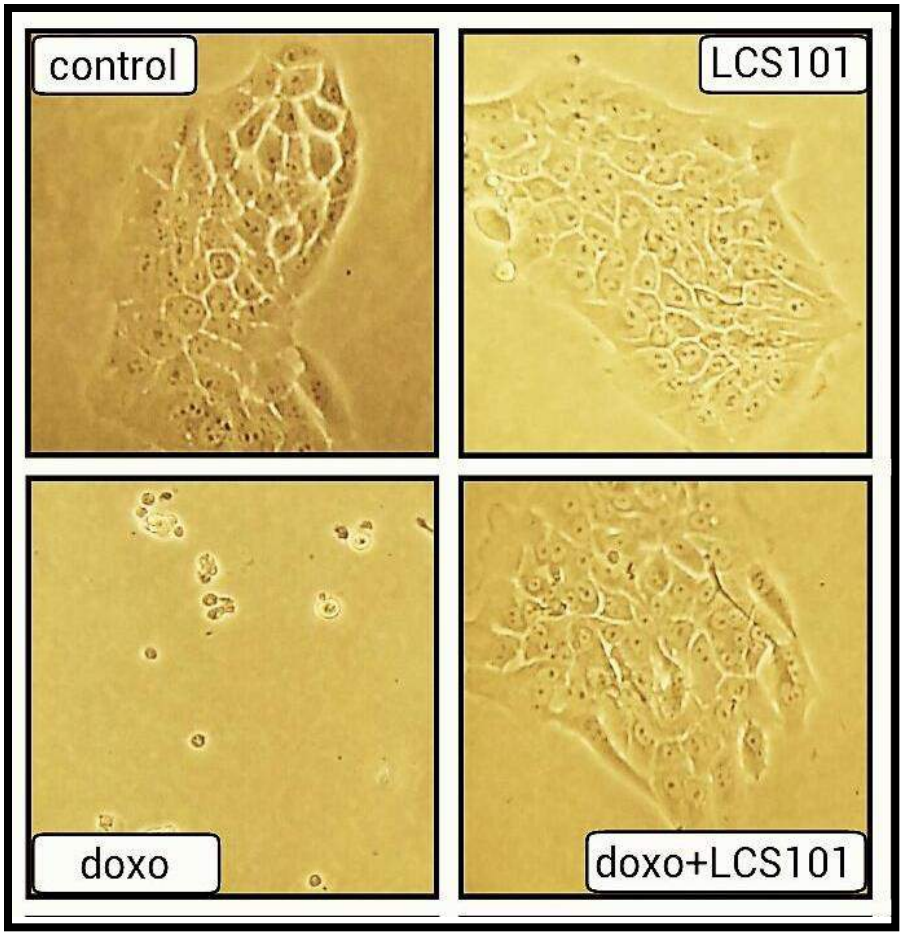


Selective effect of LCS101 on doxorubicin breast cancer and normal cells

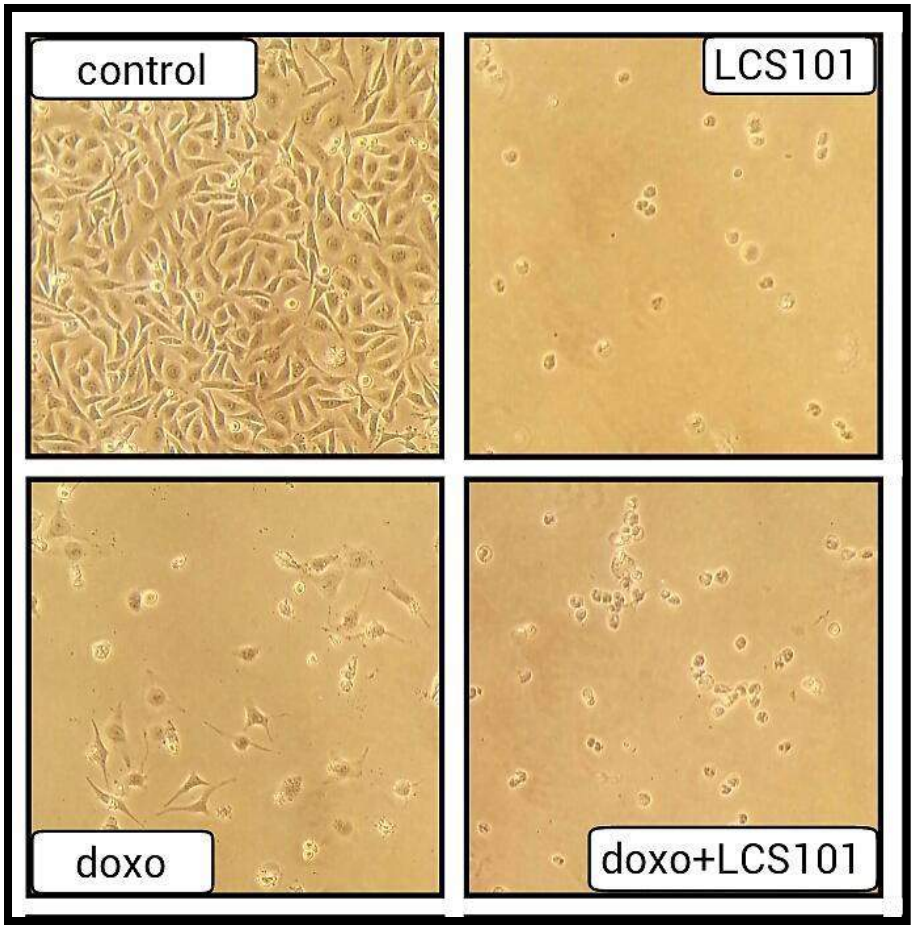


Selective protection of non-cancer cells

Non-cancer MCF10A cells



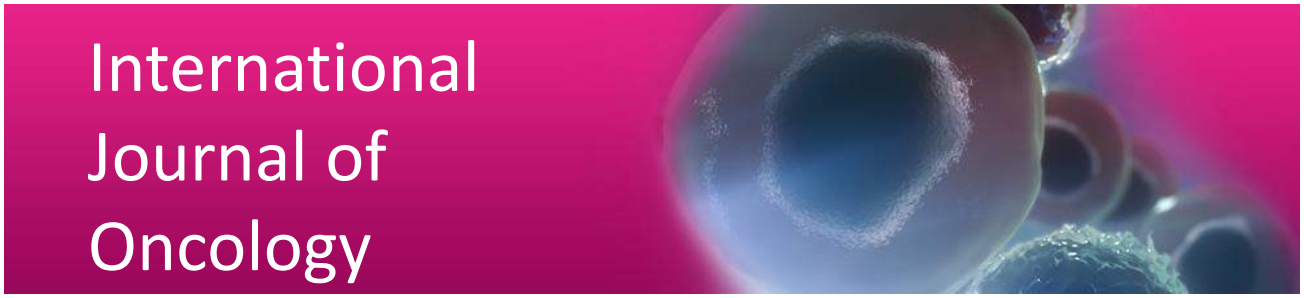
Cancer MDA-MB-231 cells



Selective anticancer effects and protection from chemotherapy by the botanical compound LCS101: Implications for cancer treatment.

Zoya Cohen ,Yair Maimon, Merav Yoeli-Lerner , Peiying Yang, Noah Samuels, Raanan Berger

Published in the international journal of oncology



Case 4: Female 84 Metastatic breast cancer

Taking **ProtectiVal™** for **8 years** along with the anti hormonal Medicine. Started with Tamoxi, than Femara

Excellent Quality of life
Improvement in sweating, hot flashes and sleep, vitality

Reduction in palpable tumor, reduce markers

TCM:
Sp Qi Xu
Kid Ql Xu, jing-yin Xu

Prevention of growth through
Tonifiying deficiency

Case 5: Male 67 metastatic Prostate cancer

Taking **ProtectiVal™** over 2 years

- Better Quality of life
- Less fatigue
- Return of sexual drive and ability

- Dosage full dosage :

2 X 3

Cancer

Original Article

Adjunctive Traditional Chinese Medicine Therapy Improves Survival in Patients With Advanced Breast Cancer

A Population-Based Study

Yuan-Wen Lee, MD[1,2,3]; Ta-Liang Chen, MD, PhD[2,3]; Yu-Ru Vernon Shih, PhD[4]; Chu-Lin Tsai, MD, ScD[5]; Chuen-Chau Chang, MD, PhD[2,3]; Hung-Hua Liang, MD[6,7]; Sung-Hui Tseng, MD, PhD[8]; Shu-Chen Chien, PharmD[1]; and Ching-Chiung Wang, PhD[1]

BACKGROUND: Traditional Chinese medicine (TCM) is one of the most common complementary and alternative medicines used in

Among the frequently used TCMs, those found to be most effective (lowest HRs) in reducing mortality were **Bai Hua She She Cao, Ban Zhi Lian, and Huang Q**

tion between the use of TCM and patient survival. **RESULTS:** A total of 729 patients with advanced breast cancer receiving taxanes were included in the current study. Of this cohort, the mean age was 52.0 years; 115 patients were TCM users (15.8%) and 614 patients were TCM nonusers. The mean follow-up was 2.8 years, with 277 deaths reported to occur during the 10-year period. Multivariate analysis demonstrated that, compared with nonusers, the use of TCM was associated with a significantly decreased risk of all-cause

CONCLUSIONS: The results of the current observational study suggest that adjunctive TCM therapy may **lower the risk of death in patients with advanced breast cancer….**

Research Database, taxane.

http://onlinelibrary.wiley.com/doi/10.1002/cncr.28579/epdf Cancer May 1,2014

Research conducted at 4 Medical Centers and university caner laboratories in Israel and the US with renowned oncologists and scientists .

- ***Phase II clinical study*** *conducted at* ***Ichilov Hospital*** **.**

Pre-clinical *conducted at:*

- ***Bar-Ilan University's Cancer Research Center;***
- ***Sheba Hospital Tal center integrative Oncology research unit; Ichilov Hospital biology laboratories;***
- ***Miami Children Hospital Pathology laboratories;***
- ***Future research planed at MD Anderson Laboratories.***

TLC side effect :)

IF THE HEART HAS NO WORRIES, THE BODY HAS NO LIMIT.

Sun Simiao

Thank you

Be good stay healthy

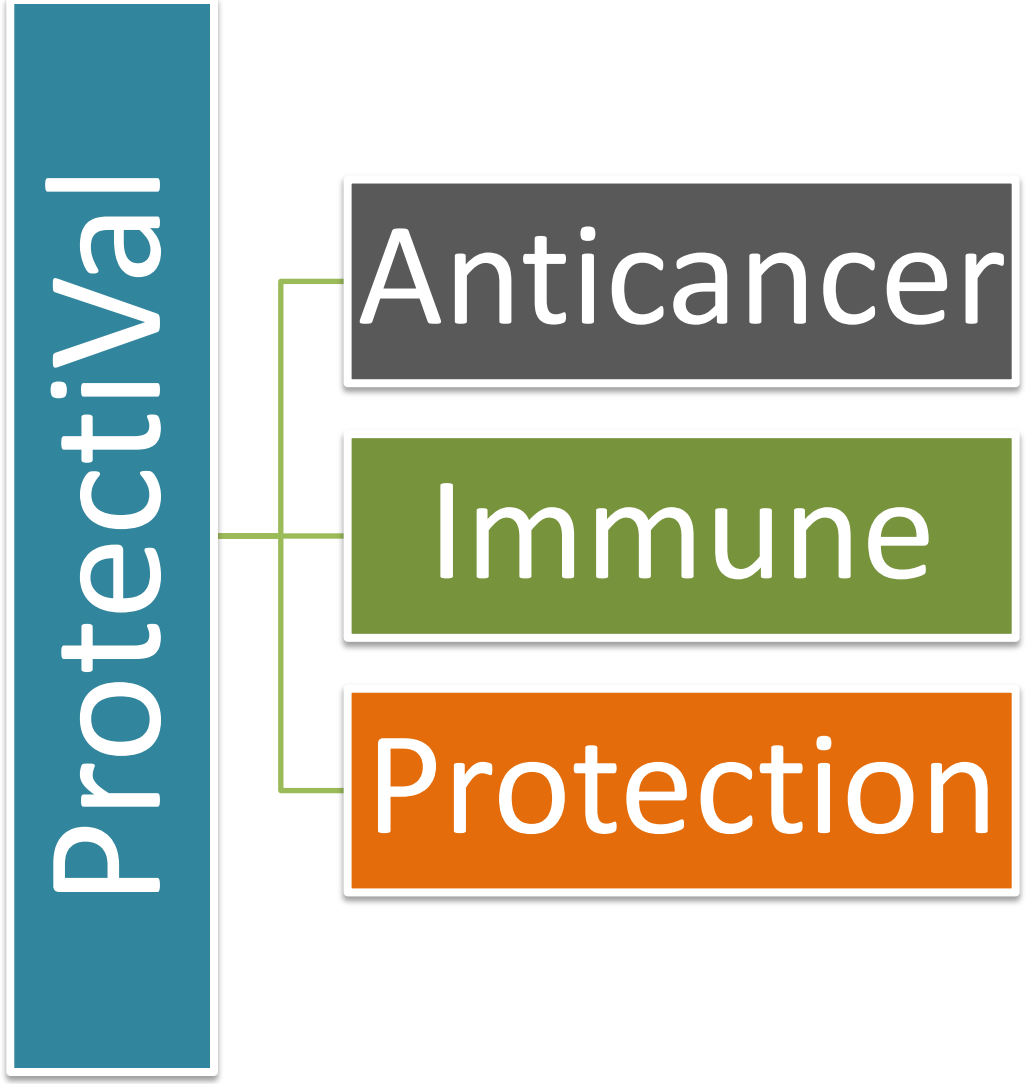
Life Biotic®

More information :

lifebiotic.com

De NatuurApotheek®
farmacie op maat

natuurapotheek.com
natuurapotheek.eu


ProtectiVal
Anticancer
Immune
Protection

Future investigation

- **Protection**: of non-cancer cell lines from chemotherapy-induced damage

- **Selectivity** : Growth inhibition and apoptosis induction in cancer vs non-cancer cell lines

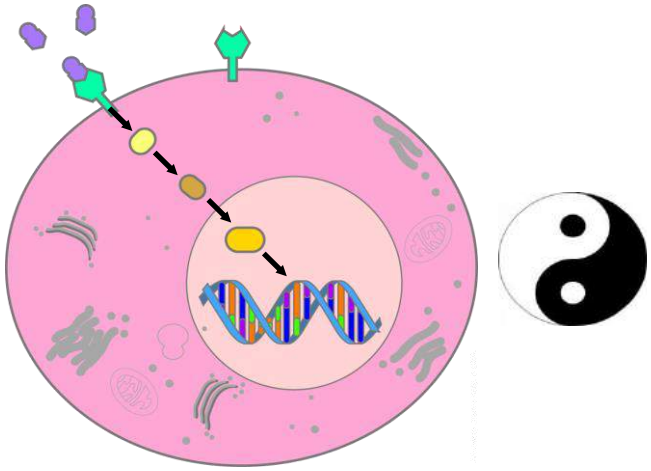
- **Synergy** : Synergy with chemotherapy in breast, colon and lung cancer cell lines

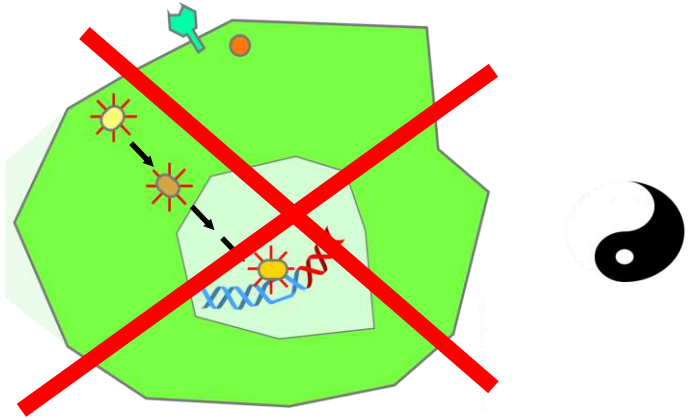
The future- clever selective medicine

Shen

Life

Jing





Thank you for your attention

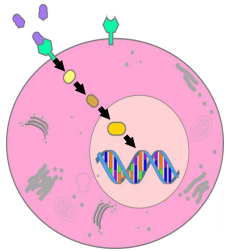
Question? yair@tcm.org.il

More Information: **lifebiotic.com**

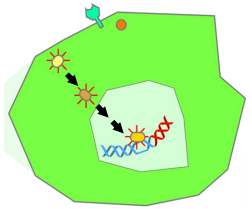
Design a team- TCM logic

- Balanced formula :

- Yang promoting life aspect (LifeBiotic) **protecting**.



- Yin cancer – **killing cancer**



Protecting

- Balanced formula :
- Yang promoting life aspect  (LifeBiotic) **protecting**.
- Yin cancer – **killing cancer** 

Protection

LCS 101

Protectival™


Map
Satellite
Hybrid
Sea of Galilee
Jordan River
Dead Sea
20 mi
50 km
©2007 Google - Imagery ©2007 TerraMetrics - Terms of Use

Life

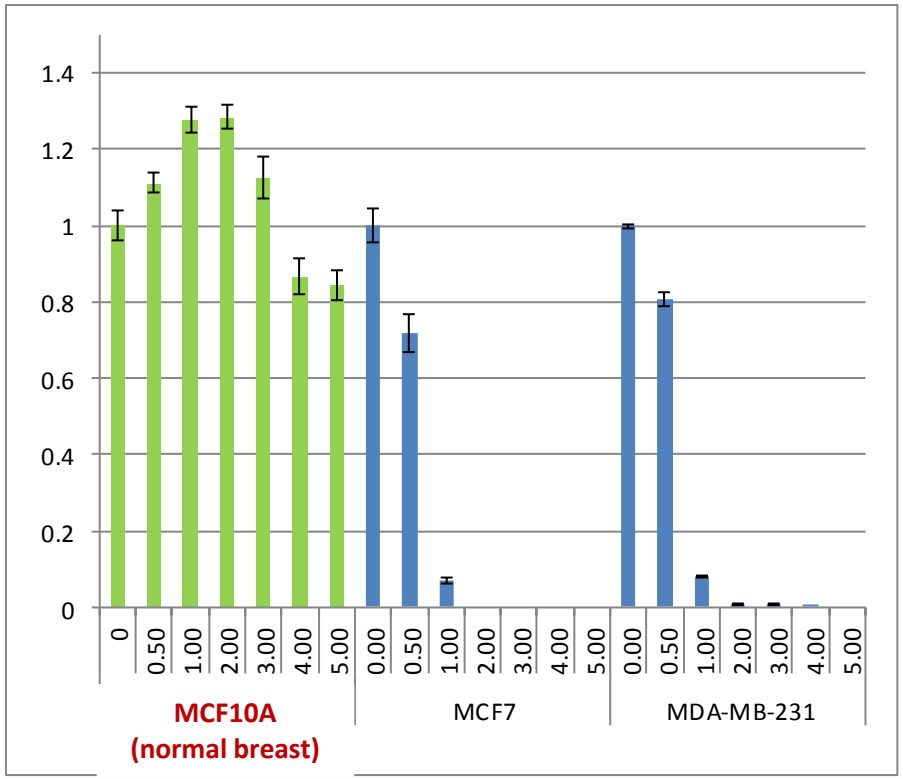
Death

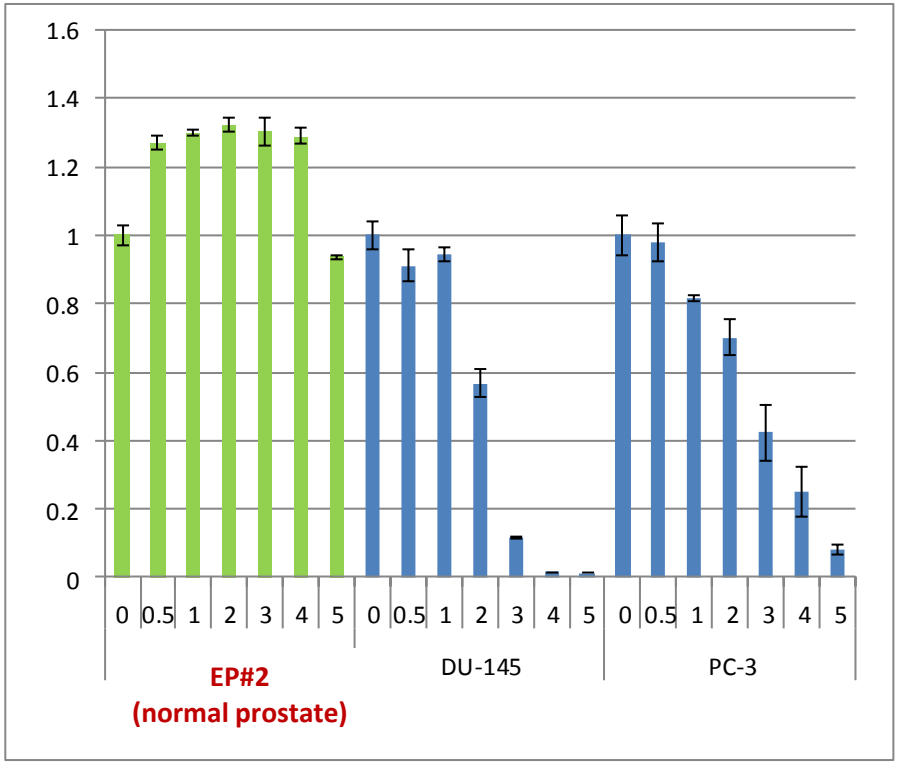
Activity

- The herb formulations are not simply a mixture of herbs, as with many products of low efficacy on the market today.
- R&D results created a unique proprietary with outstanding production and Quality Control process .
- we utilize cutting-edge technologies in extraction, isolation and purification.
- resulting in multi-herbal extract has maximum efficacy, potency, purity, bio availability

LCS101- selective killing effect

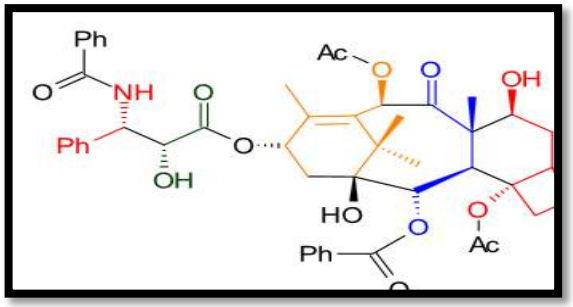
Kills the cancer but not normal breast / prostate cells





Selective protection

Taxol



+

Astragalus

Poria cocos

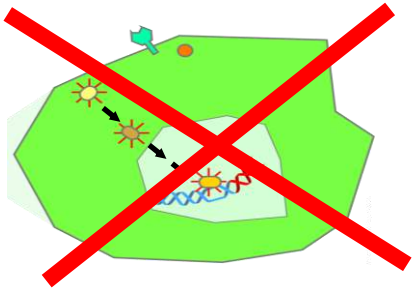
Lycium chinense

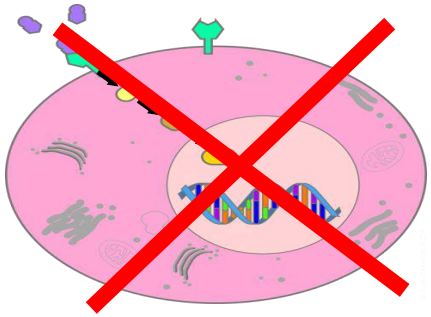
Ligustrum lucidum

Paeonia lactiflora

Scutellaria barbata

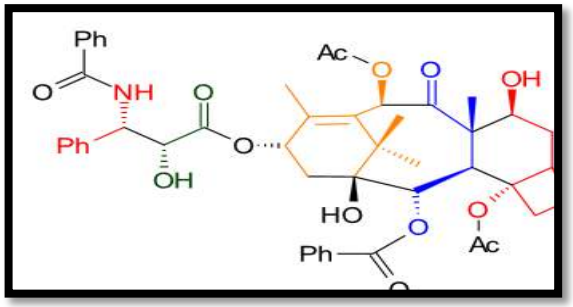
Atractylodes macrocephala





Selective protection

Taxol



+

Astragalus

Poria cocos

Lycium chinense

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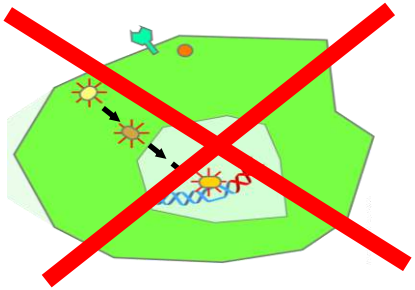
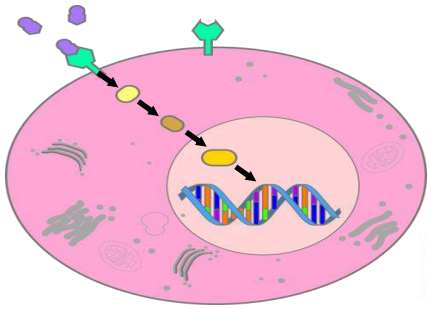
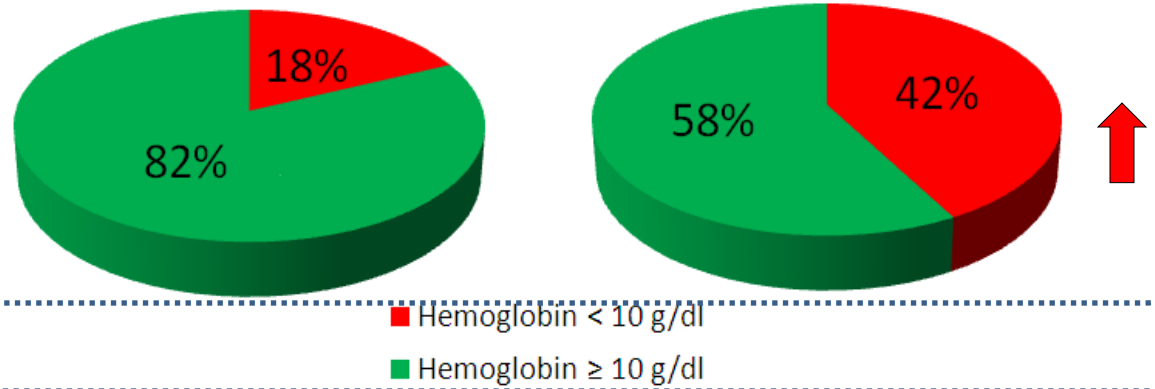




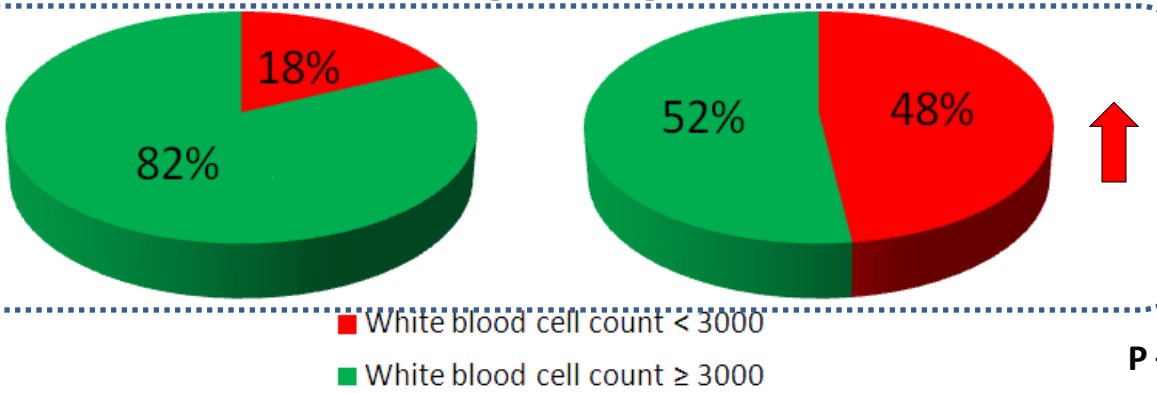
LCS101 Placebo

Anemia



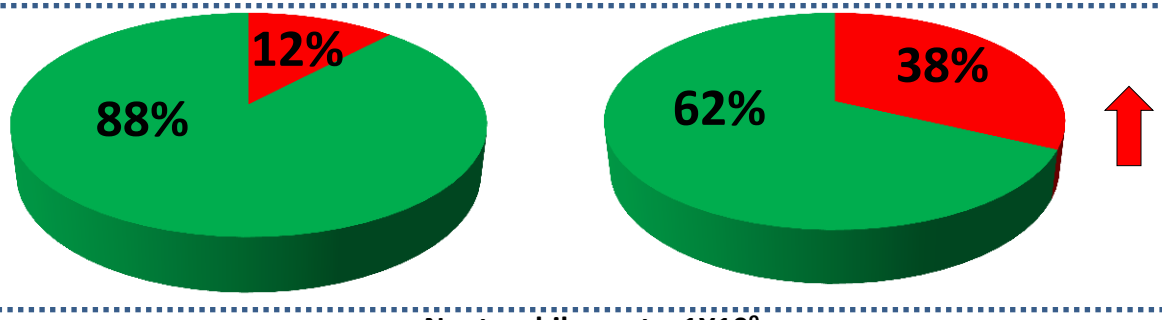
P –value 0.0081

leukopenia



P –value 0.0315

Neutropenia



P value 0.0447

PROTECTIVAL™

Scientific Background & Research Summary:

Protectival™ is a unique, multi-targeted, natural, bio-active, botanical compound, which is based on many years of clinical experience and research. There have been over 200 pre-clinical studies conducted on Protectival™ with renowned oncologists and scientists in Medical Centers in Israel and the US and at the Bar Ilan University Cancer Research Laboratories. A Randomized Controlled Clinical Trial (RCT) on Protectival™, carried out in the Oncology Department of a leading Hospital in Israel demonstrated safety and efficacy.

The Protectival™ (LCS101) Formula is proprietary and patented – both regarding the ingredient concentration and the unique Product Development and Production Process – which are essential to Product Safety & Efficacy. The outstanding safety & efficacy are the result of 15 years of intensive Scientific Research & Development and should not be provided in any other form.

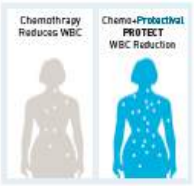
Protectival™'s multi-targeted action has been shown to be effective in:

1. **Protection** from chemotherapy side effects;
2. **Killing** of cancer cells;
3. **Immune** enhancement;
4. **Quality** of life

This broad spectrum activity - with such ample scientific support - **is outstanding.**

1. Protection from chemotherapy side effects:

Reducing chemotherapy side effects by more than 50%. Protectival™ (Research Name LCS101) was clinically tested in a study conducted at the Tel Aviv Sourasky Medical Center Oncology Department. This breakthrough study demonstrated that breast cancer patients undergoing chemotherapy and using Protectival™ showed an increased recovery rate, improved quality of life and enhanced immune system.

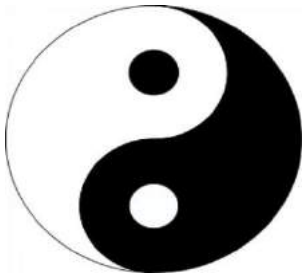


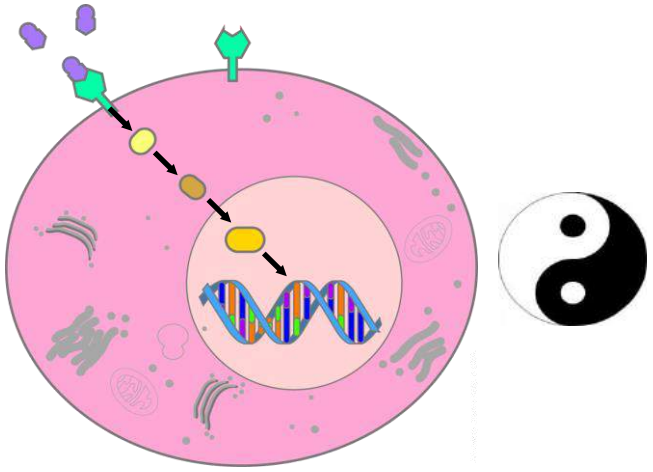
Reducing chemotherapy side effects (WBC, RBC) by more than 50%:
While chemotherapy weakens the immune system, the Protectival™ demonstrated strong protective effects of the immune system (red & white blood cell counts).

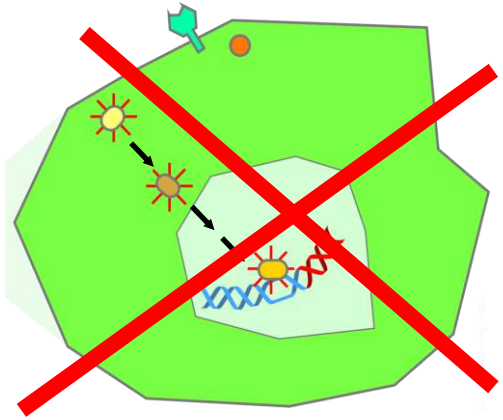
In further pre-clinical studies, Protectival™ has been shown to protect healthy cells from the effect of various chemotherapeutic drugs, while killing cancer cells (pancreatic, breast, colon and prostate cancer cells - in fact every solid cancer tumor tested).

The clinical trial was published in "The Oncologist" 2011;16(9): 1197-1202)

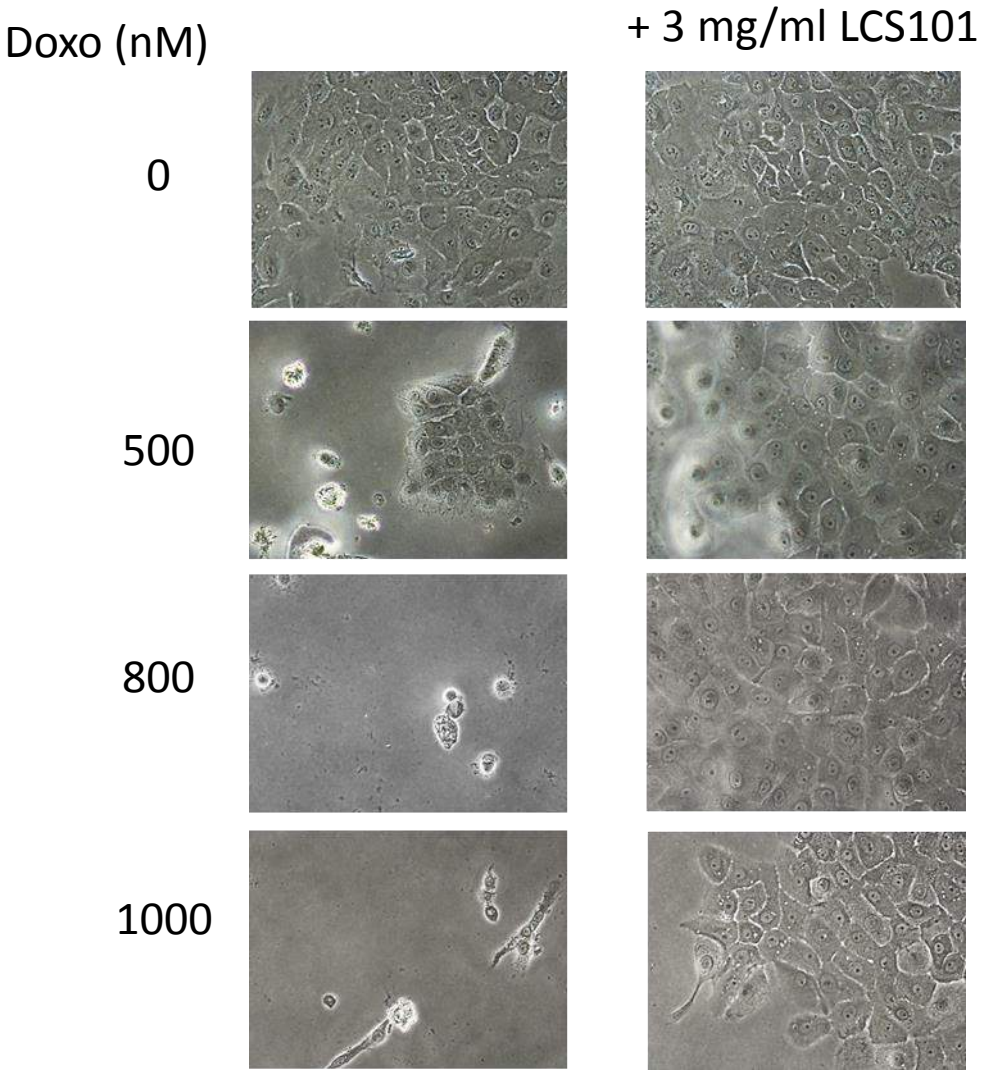
The future- selective medicine







Protection of MCF10A cells from doxorubicin-induced death

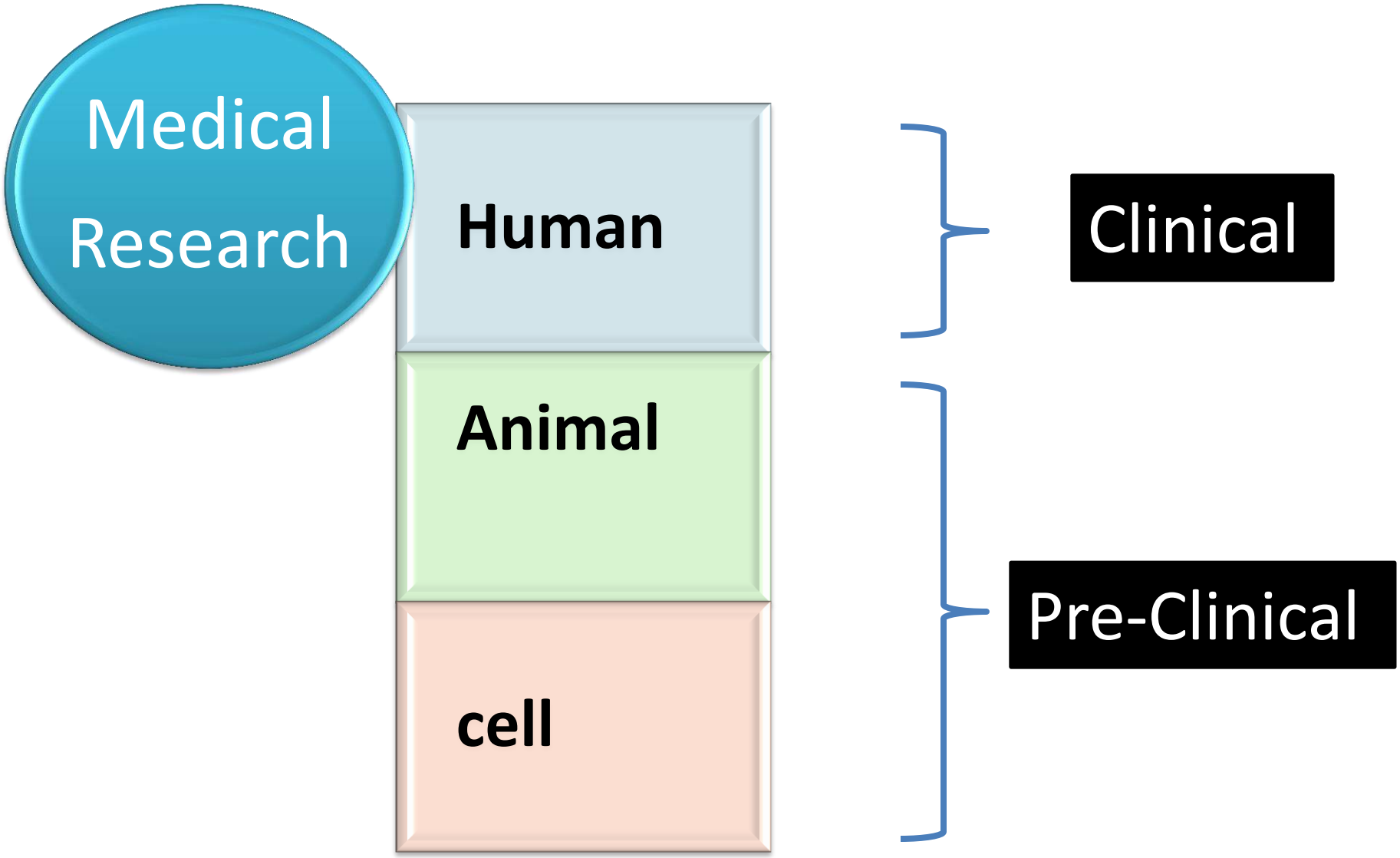


belief or Proof

Study of the Botanical Compound Mixture LCS101 and it influence on reducing chemotherapy side effect .

Yaal-Hahoshen N, **Maimon Y**, Siegelmann-Danieli N, Lev-Ari S, Ron I, Sperber F, Samuels N, Shoham J, Merimsky O.

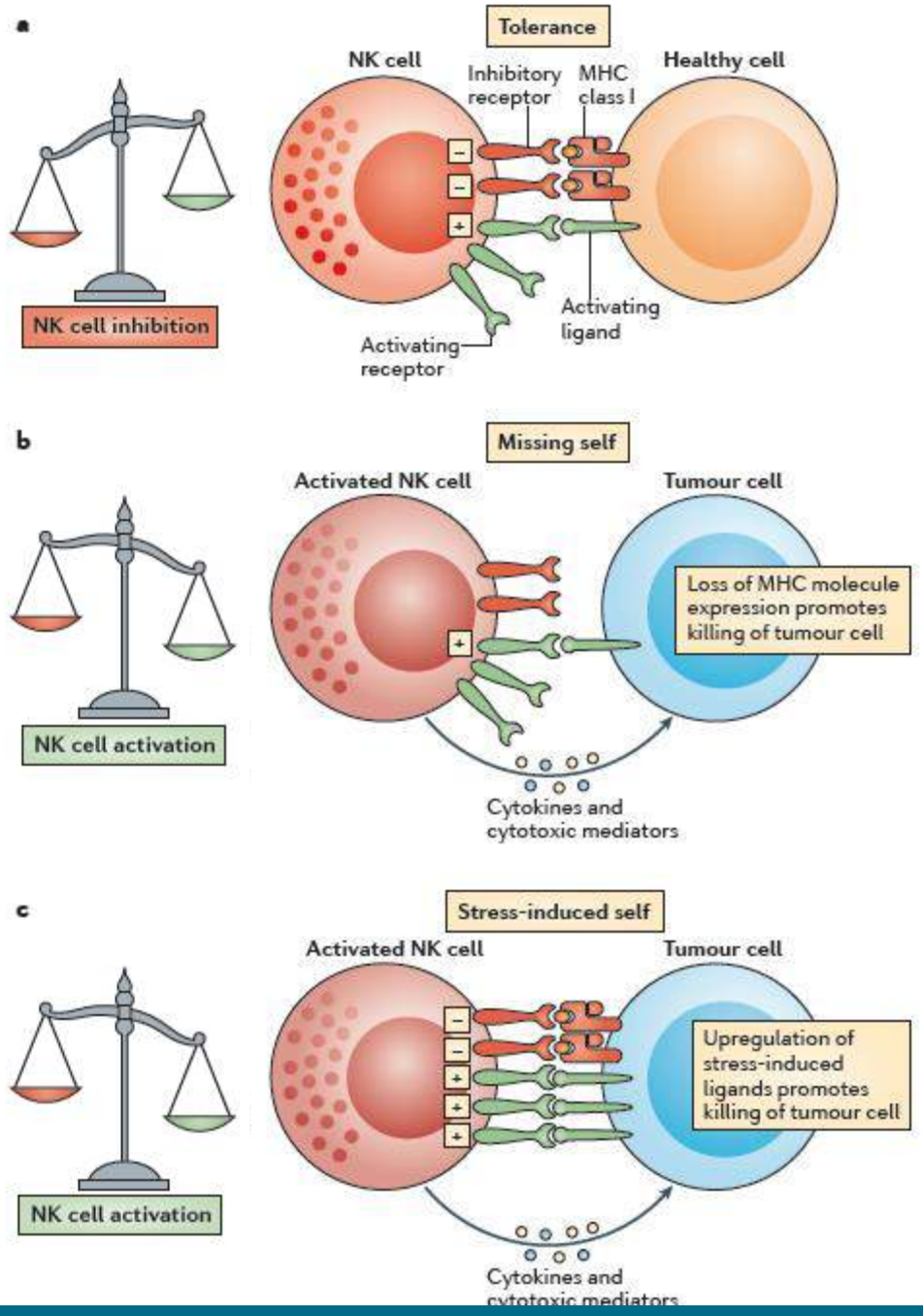
[The Oncologist 2011; 16: 1197-1202]


Medical Research
Human
Animal
cell
Clinical
Pre-Clinical

Background: LCS101

- Capsule form (0.4g)
- Good Manufacturing Practice (GMP) conditions
- batch-to-batch consistency
- analysis with chemical /physical identification
- high performance liquid chromatography (HPLC)
- free of: heavy metals, microbial contamination, pesticide residues, mycotoxins.

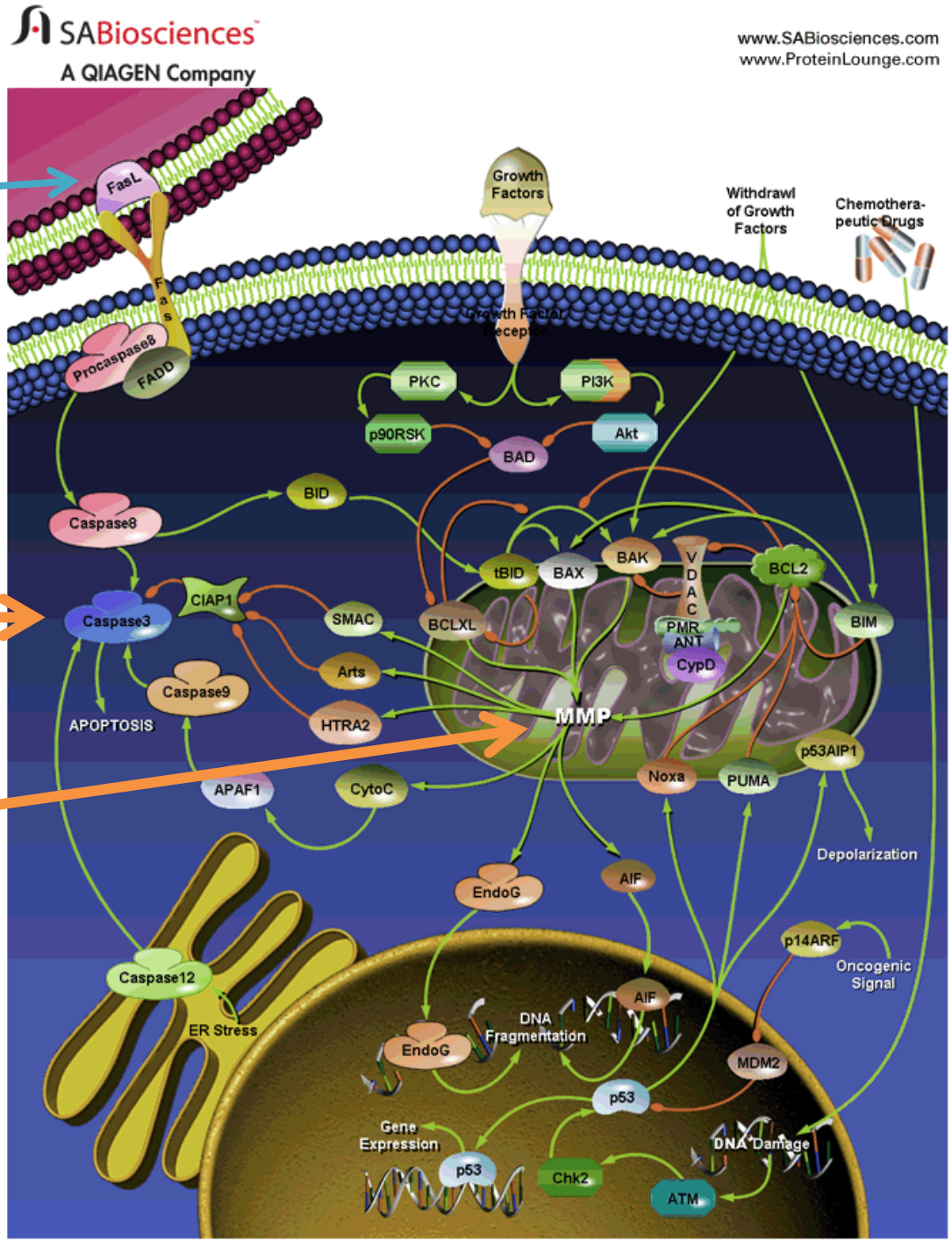
- Placebo capsules: bread crumbs (0.4 g)
- = LCS101capsules (texture, appearance, smell and taste)


a
Tolerance
NK cell
Inhibitory receptor
MHC class I
Healthy cell
NK cell inhibition
Activating ligand
Activating receptor
b
Missing self
Activated NK cell
Tumour cell
Loss of MHC molecule expression promotes killing of tumour cell
NK cell activation
Cytokines and cytotoxic mediators
c
Stress-induced self
Activated NK cell
Tumour cell
Upregulation of stress-induced ligands promotes killing of tumour cell
NK cell activation
Cytokines and cytotoxic mediators

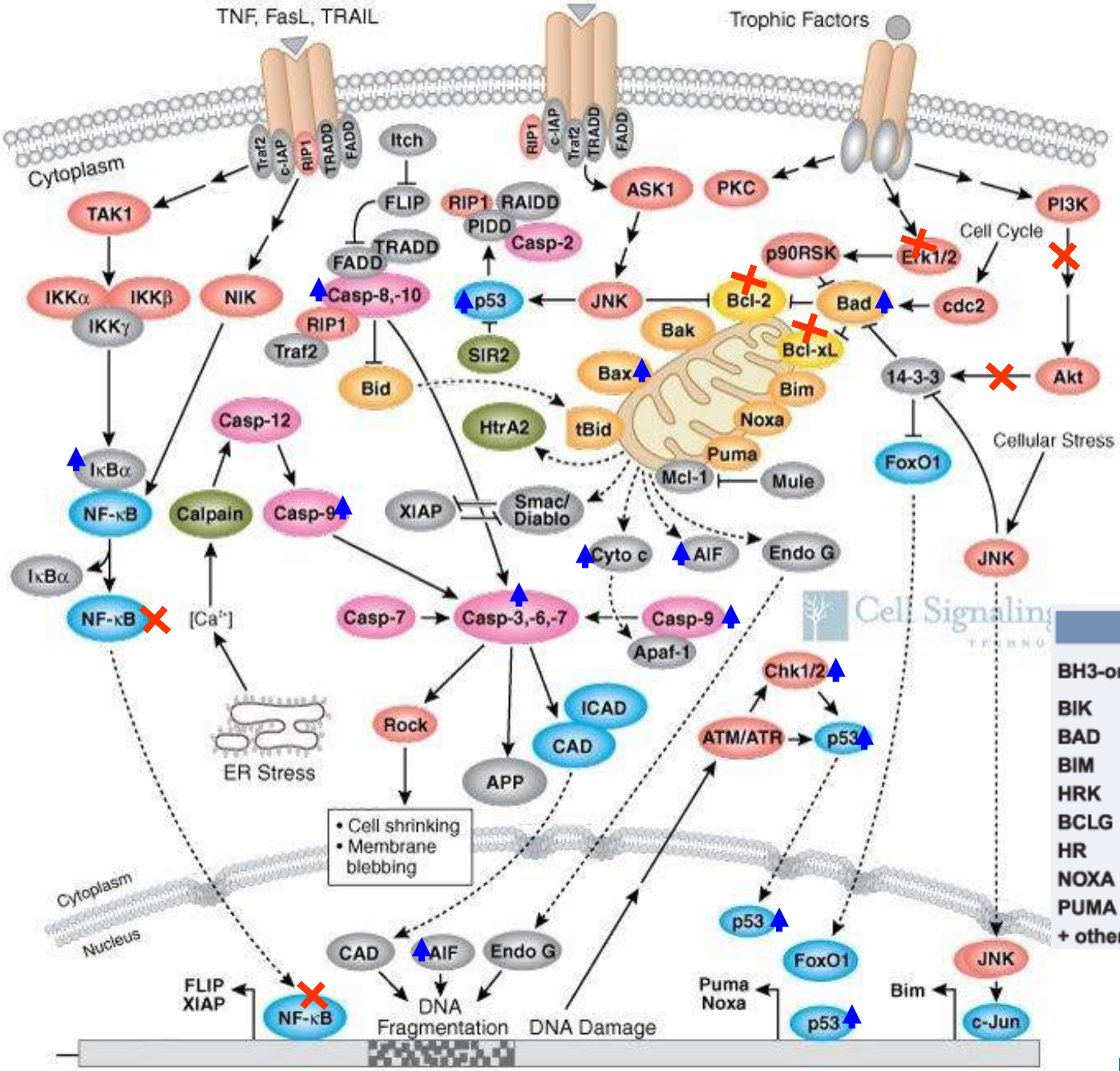
Apoptosis

Extra-cellular

Intra-cellular

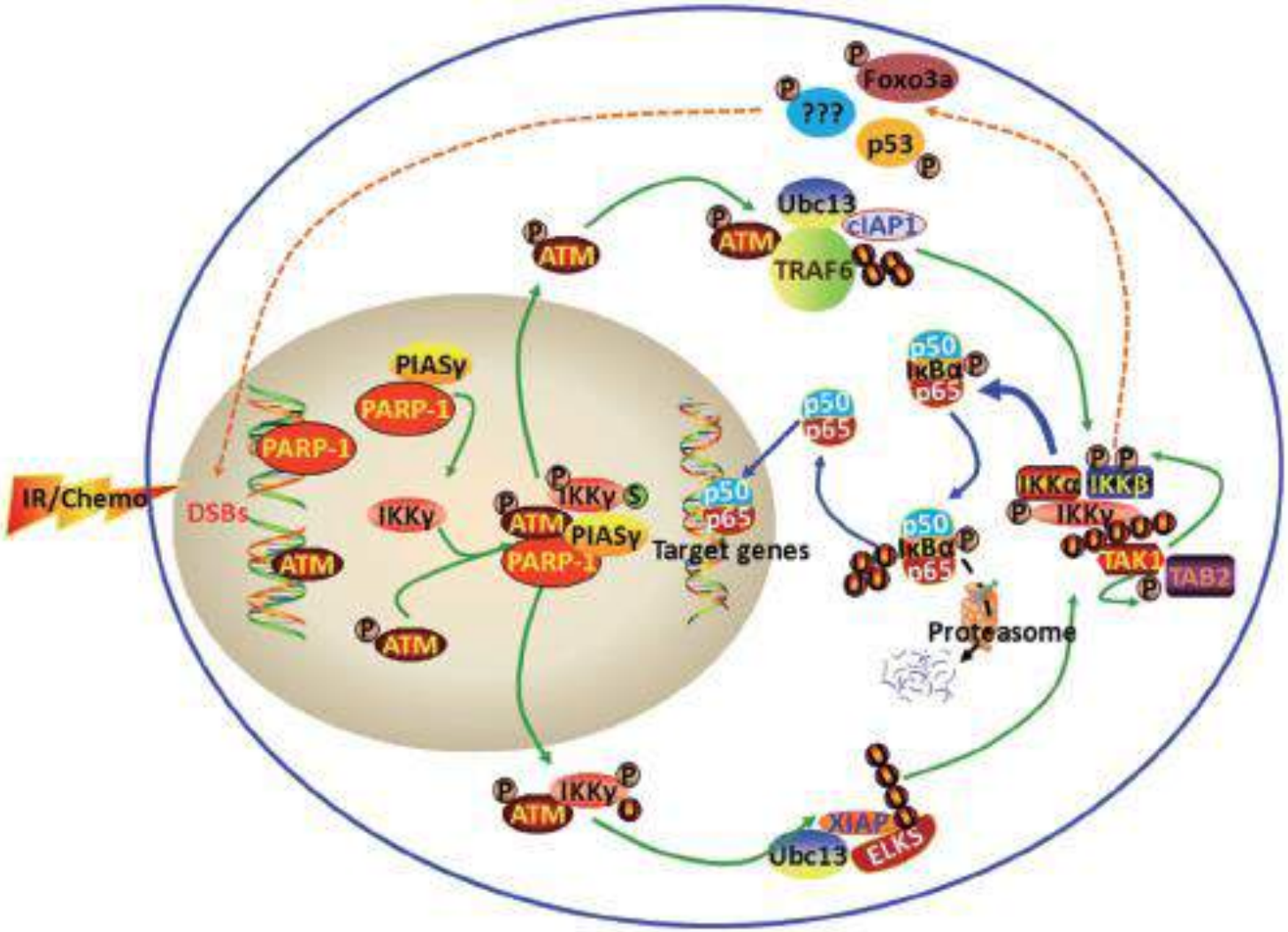


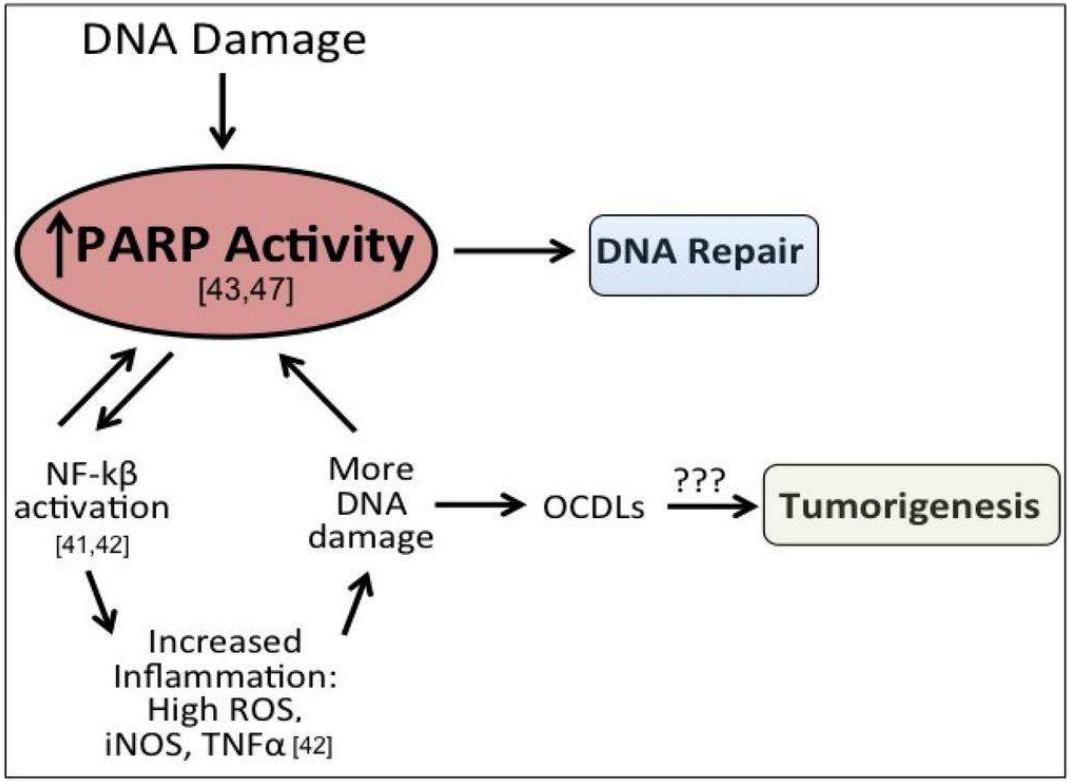
Bai Zhu
Fu Ling
Xia Ku Cao
Nu Zhen Zi
Ji Xue Teng
Bai Hua She
She Cao
Bai Shao
Bei Sha Shen

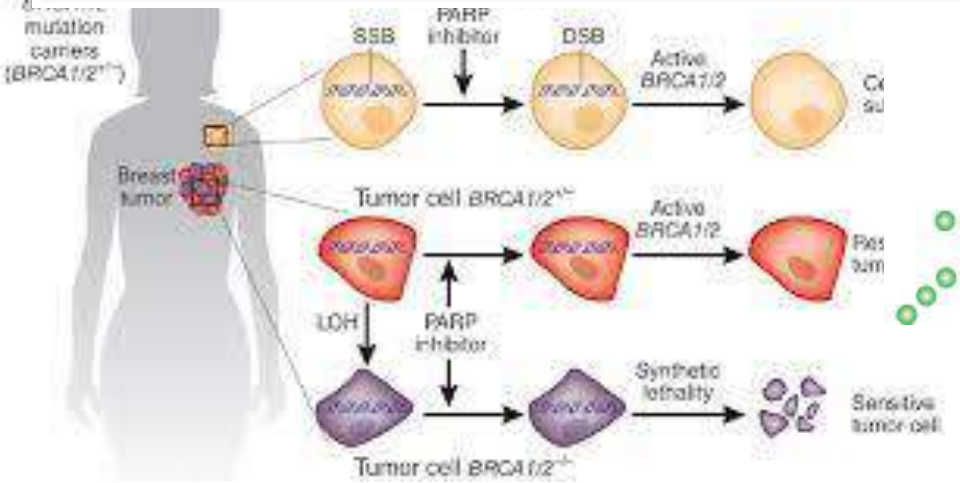


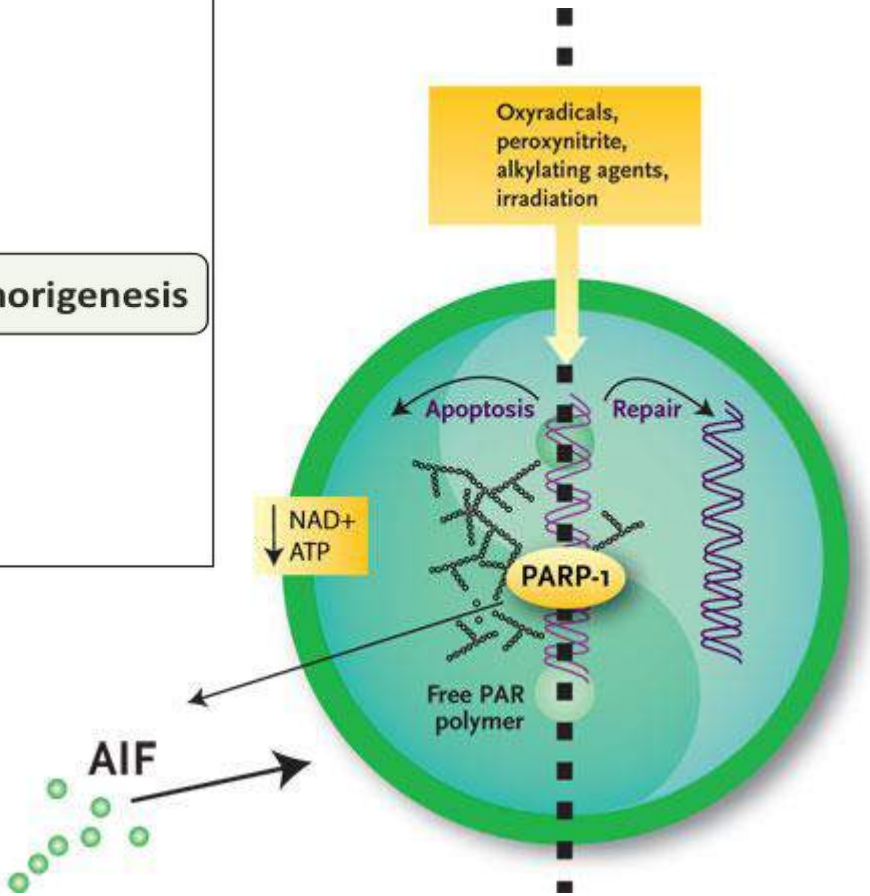
Anti-apoptotic
BCL-2
BCL-X_L
BCLW
MCL1
BCLB

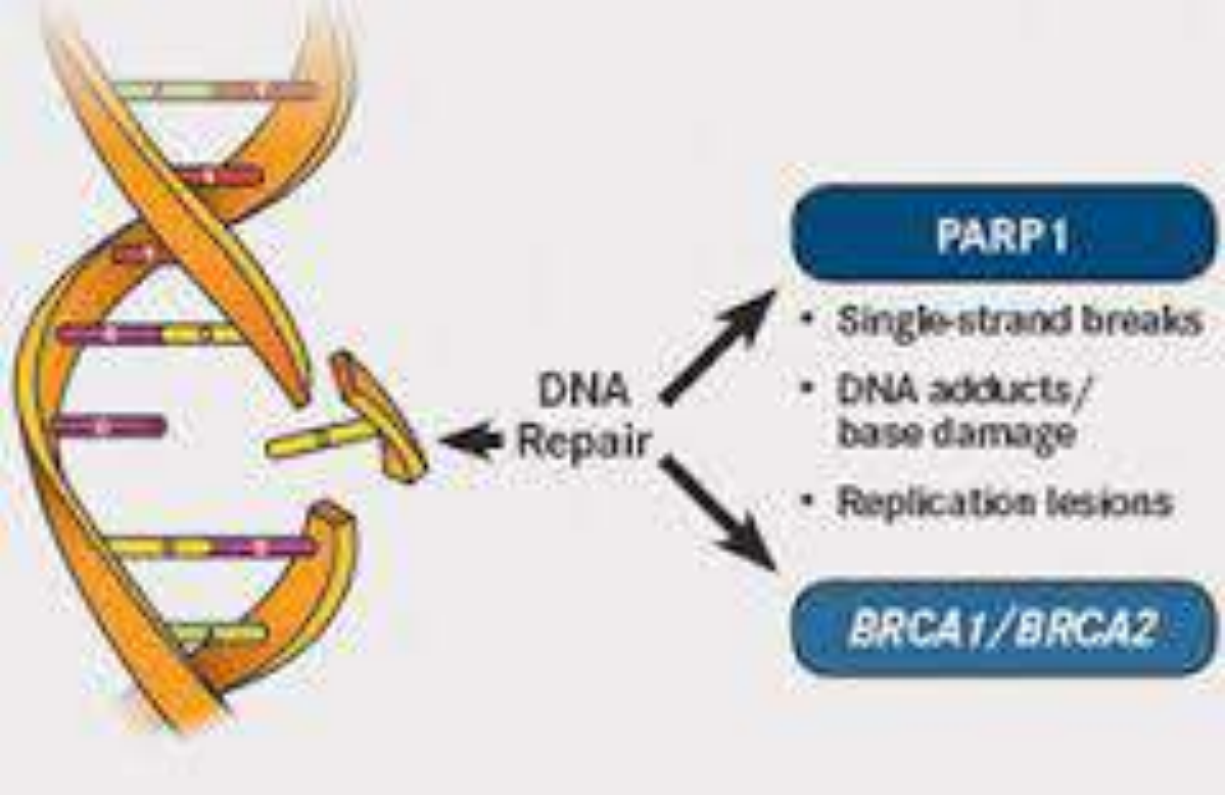
Pro-apoptotic	
BH3-only proteins	Multidomain (Bl
BIK	BAX
BAD	BAK
BIM	BOK
HRK	BOO
BCLG	BCLG
HR	BCLB
NOXA	BCL-RAMBO
PUMA	
+ others	

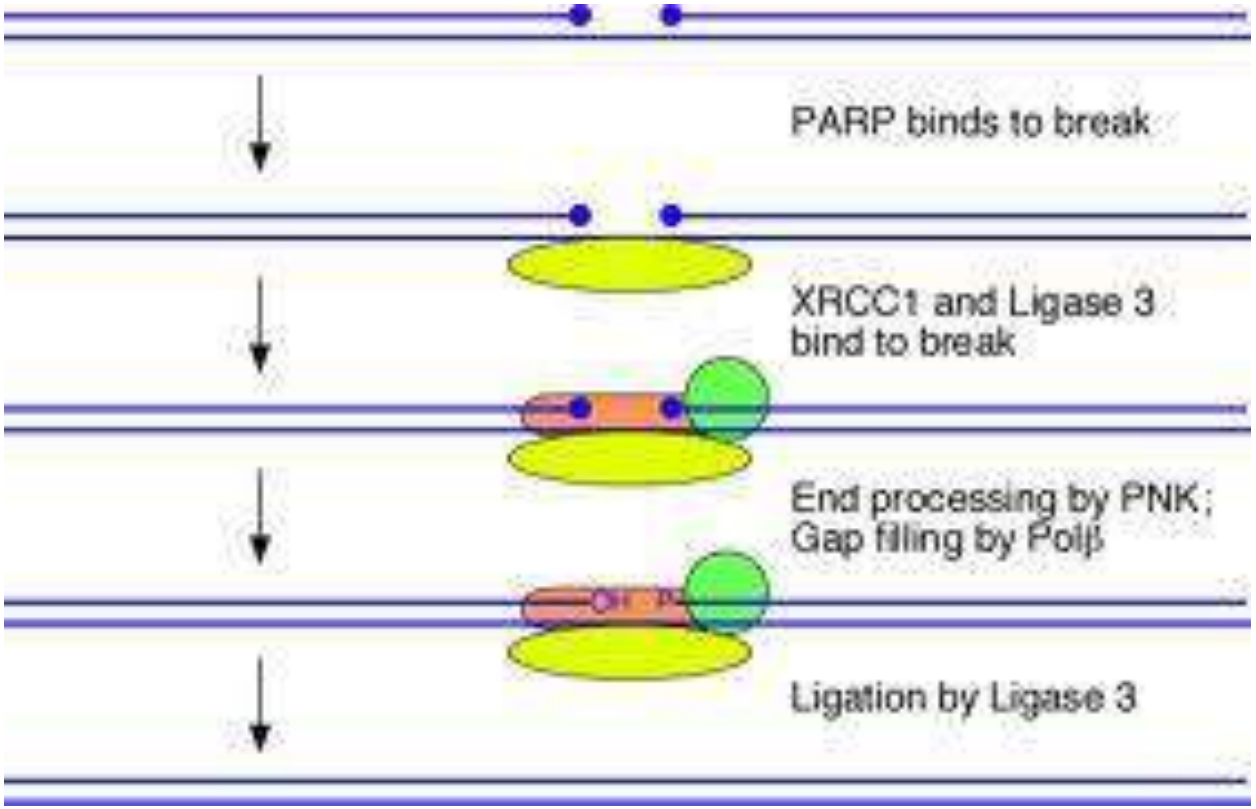

Foxo3a
???
p53
Ubc13
cIAP1
ATM
TRAF6
PIASγ
PARP-1
IR/Chemo
DSBs
IKKγ
Target genes
p50
p65
IκBα
IKKα
IKKβ
TAK1
TAB2
Proteasome
XIAP
ELKS


DNA Damage
↑PARP Activity
[43,47]
DNA Repair
NF-kβ activation
[41,42]
More DNA damage
OCDLs
???
Tumorigenesis
Increased Inflammation: High ROS, iNOS, TNFα [42]


SSB
PARP inhibitor
DSB
Active BRCA1/2
Tumor cell BRCA1/2+/-
Active BRCA1/2
LOH
PARP inhibitor
Synthetic lethality
Tumor cell BRCA1/2-/-


Oxyradicals, peroxynitrite, alkylating agents, irradiation
Apoptosis
Repair
NAD+
ATP
PARP-1
Free PAR polymer
AIF


DNA
Repair
PARP1
• Single-strand breaks
• DNA adducts/
base damage
• Replication lesions
BRCA1/BRCA2


PARP binds to break
XRCC1 and Ligase 3
bind to break
End processing by PNK;
Gap filling by Polβ
Ligation by Ligase 3

Metastatic breast cancer

Sp Qi Xu
Kid QI Xu
Prevention of growth through
Tonifiying deficiencey
+ LCS101 (Protectival


SPORTS WEAR

Believe or proof

- Ancient text
- Complexity

- Modern research
- Reductionism

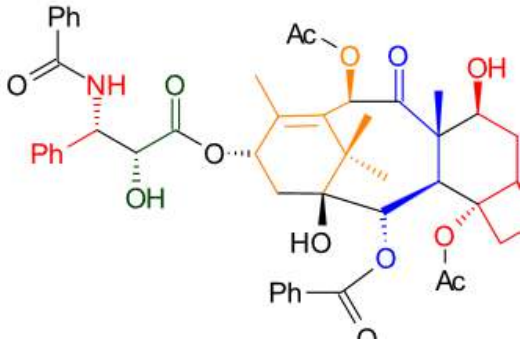
- Chinese person

- Research person
- Statistics

2 different methods of medicine

Taxus brevifolia **(Pacific Yew)**

Taxol



Lycium chinense

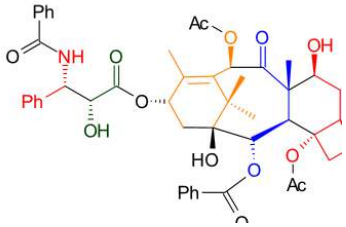
Ligustrum lucidum

Paeonia lactiflora

Scutellaria barbata

Reductionism

Complexity



Taxol

Reductionism

Complexity

The future

Reductionism Complexity

Will win

In the fight for prevention and treatment of cancer

Don’t stop dreaming

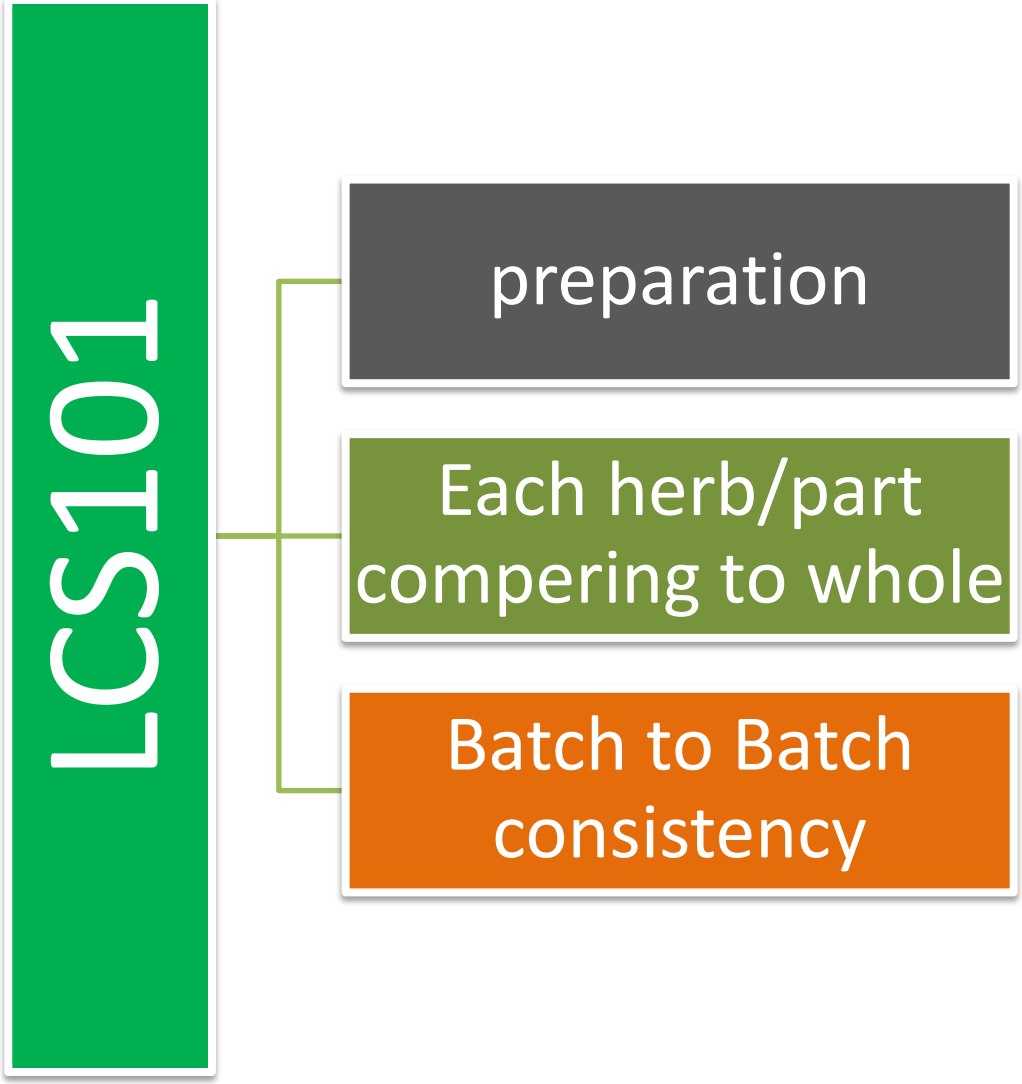
Only very few things are really impossible.

Alice in wonderland.

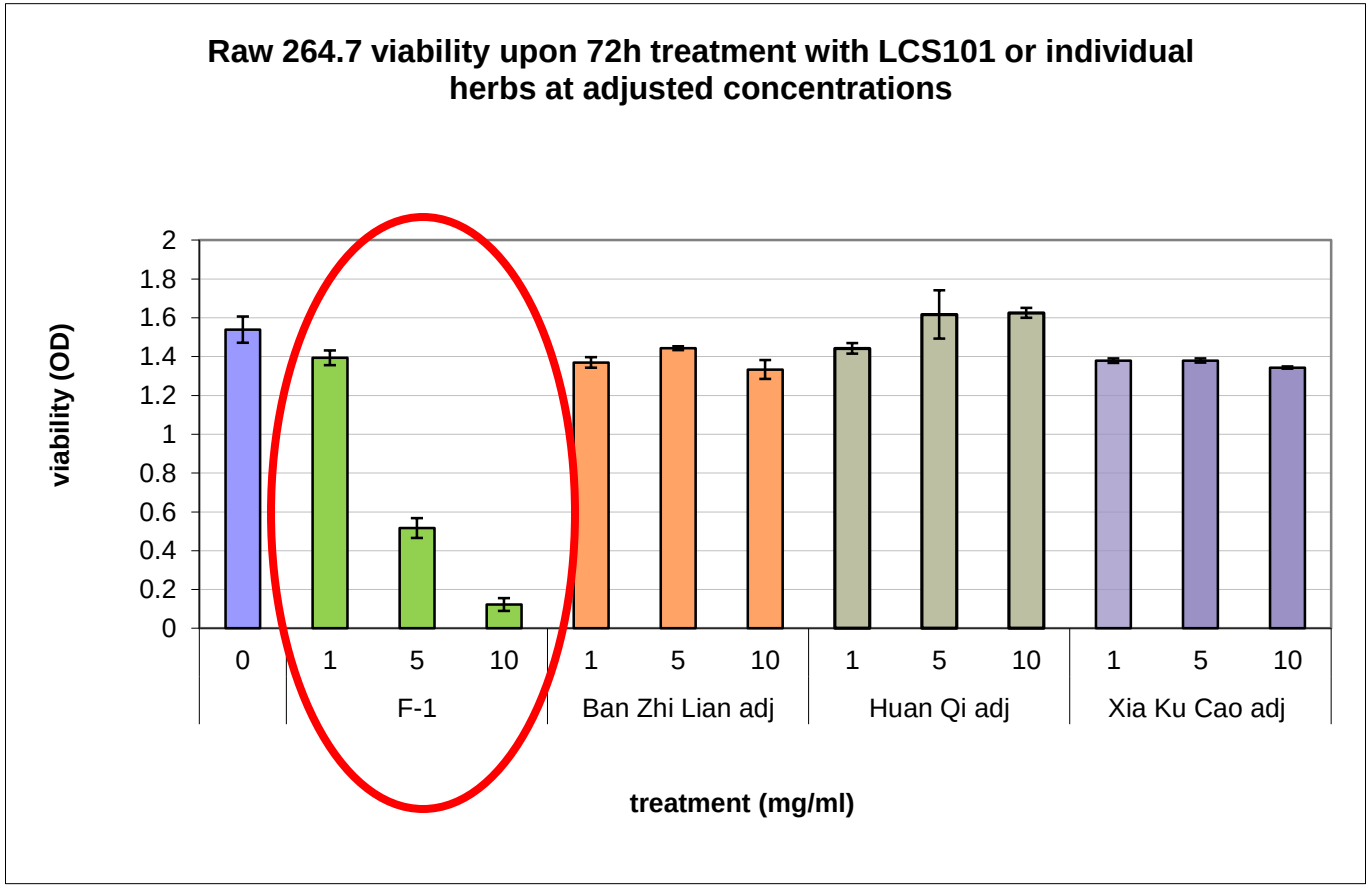
THANK YOU

Any questions:

Yair@tcm.org.il


LCS101
preparation
Each herb/part compering to whole
Batch to Batch consistency

Influence of LCS101 and single herbs



oncology laboratories of Sheba medical center

Other TCM cancer Research

- **PHY906 (4 herbs- *huang Qin tang*:**

Scutellaria **Huang qin** , Glycyrrhiz- **gan cao**, Ziziphus- **Suan Zao Ren** ,Paeonia- **Bai Shao)**

- **TJ-41(7 herbs- *Bu Zhong Yi Qi Tang*),**
- **BLZ101 (**Scutellaria Barbata- **Ban Zhi Lian**)

- **Astragals, Turmeric, Ginseng**
- **Dong Xia Cao-**Cordyceps**, Ling Zhi-**ganoderma**.**
- **Huachansu** injection**, and Kanglaite** injection

Questions? Yair@TCM.ORG.IL

Tal Center for Integrative Oncology

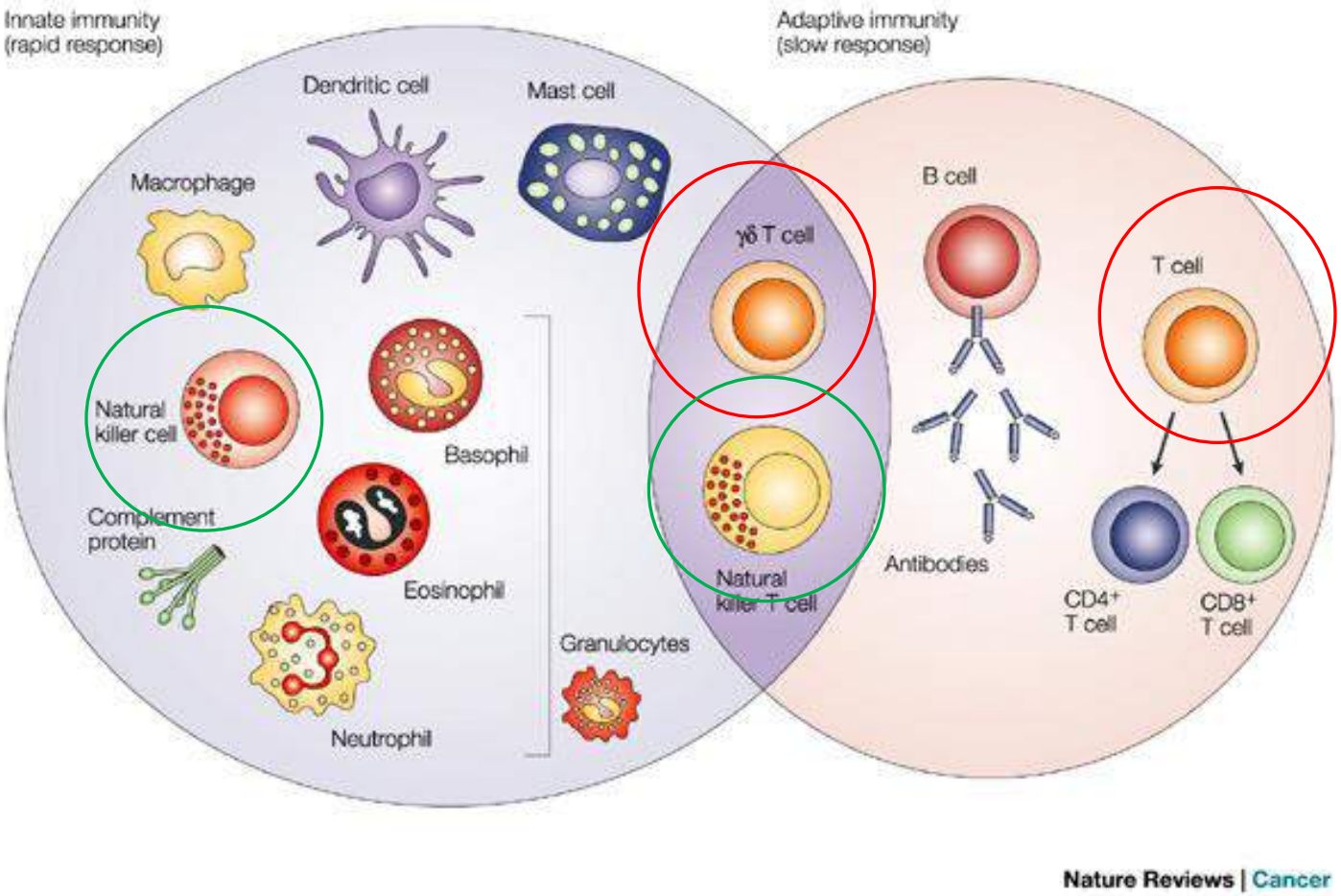
Providing Faith and Hope to Cancer Patients

Table 7.2 Constituent herbs in PC-SPES

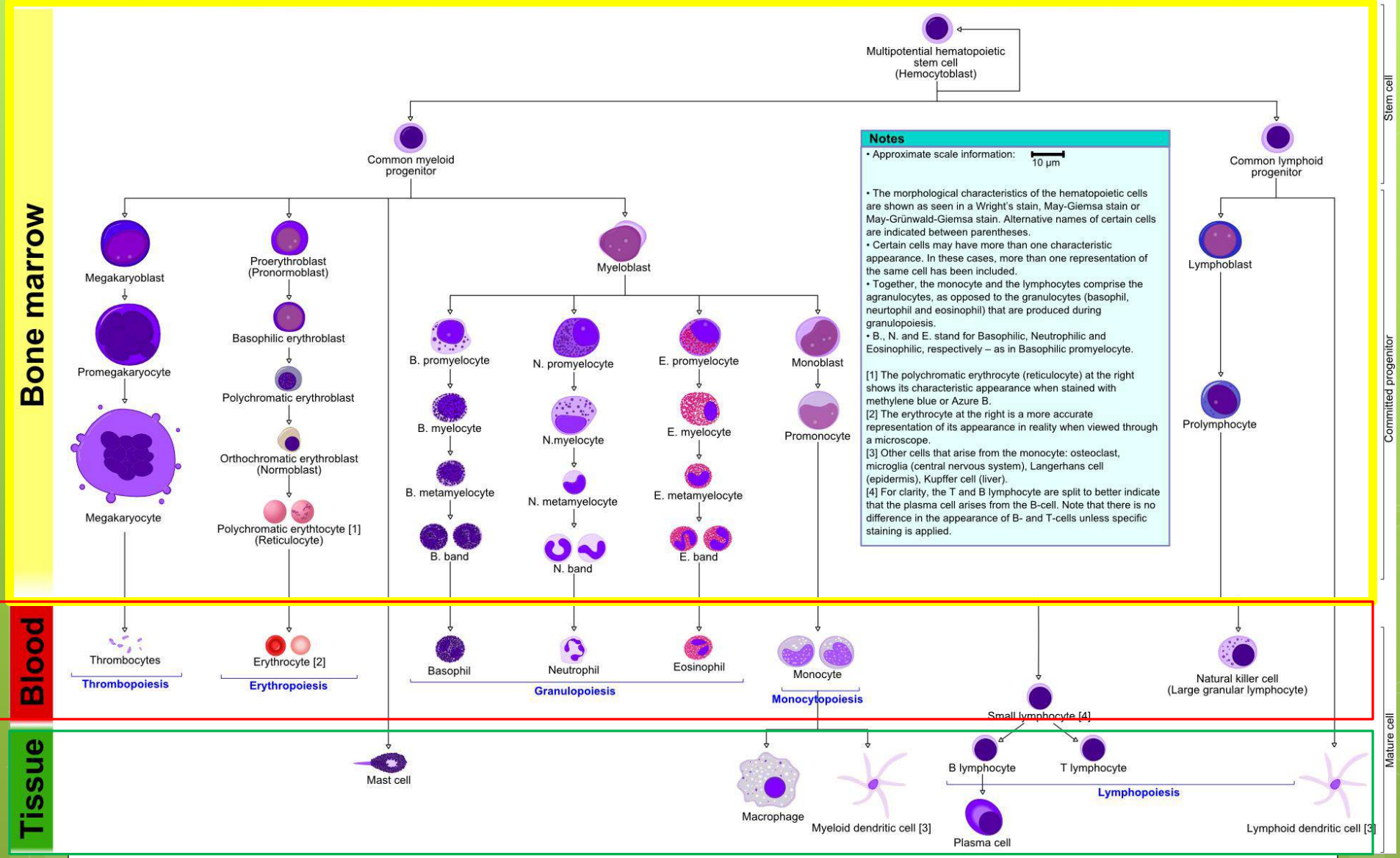
Scientific name	Common name	Chinese pinyin
Chrysanthemum morifolium	Chrysanthemum flower	Juhua
Isatis tinctoria	Indigowoad root	Banlangen
Glycyrrhiza uralensis	Licorice root	Gancao
Ganoderma lucidum	Lucid ganoderma	Lingzhi
Panax notoginseng	Notoginseng	Sanqi
Rabdosia rubescens	Blushred rabdosia	Donglingcao
Serenoa repens	Saw palmetto	Juzonglu
Scutellaria baicalensis	Baikal skullcap root	Huangqin

Innate immunity
(rapid response)

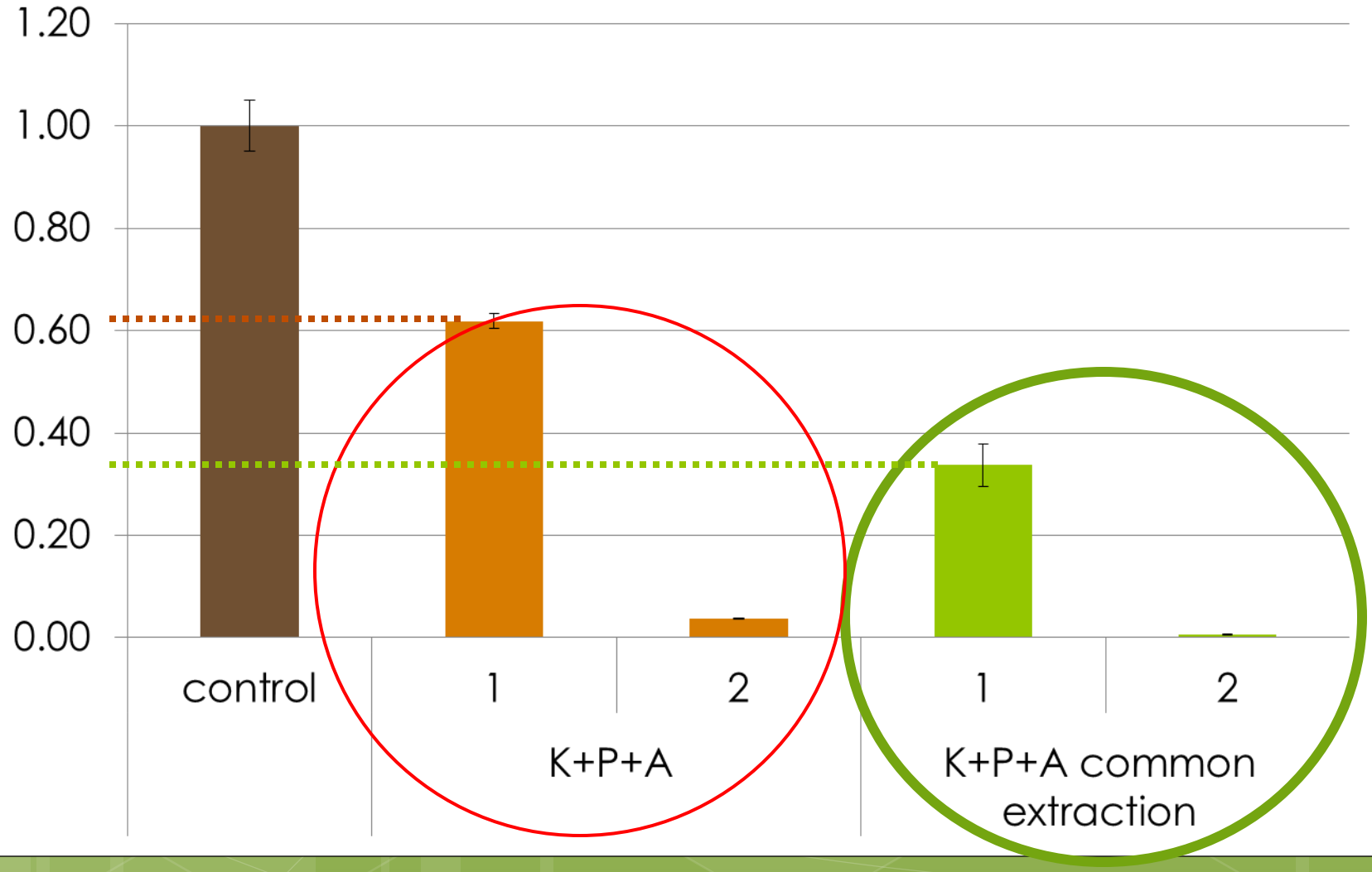
adaptive immunity
(slow response)



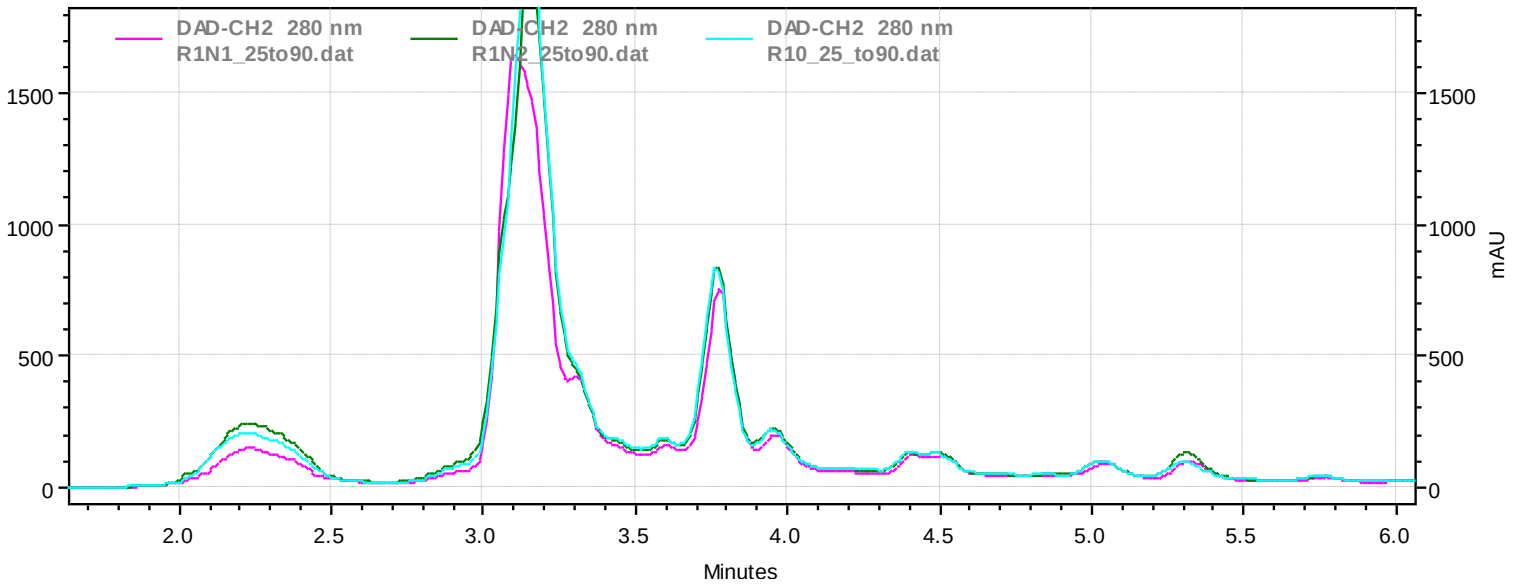
Hematopoiesis in humans

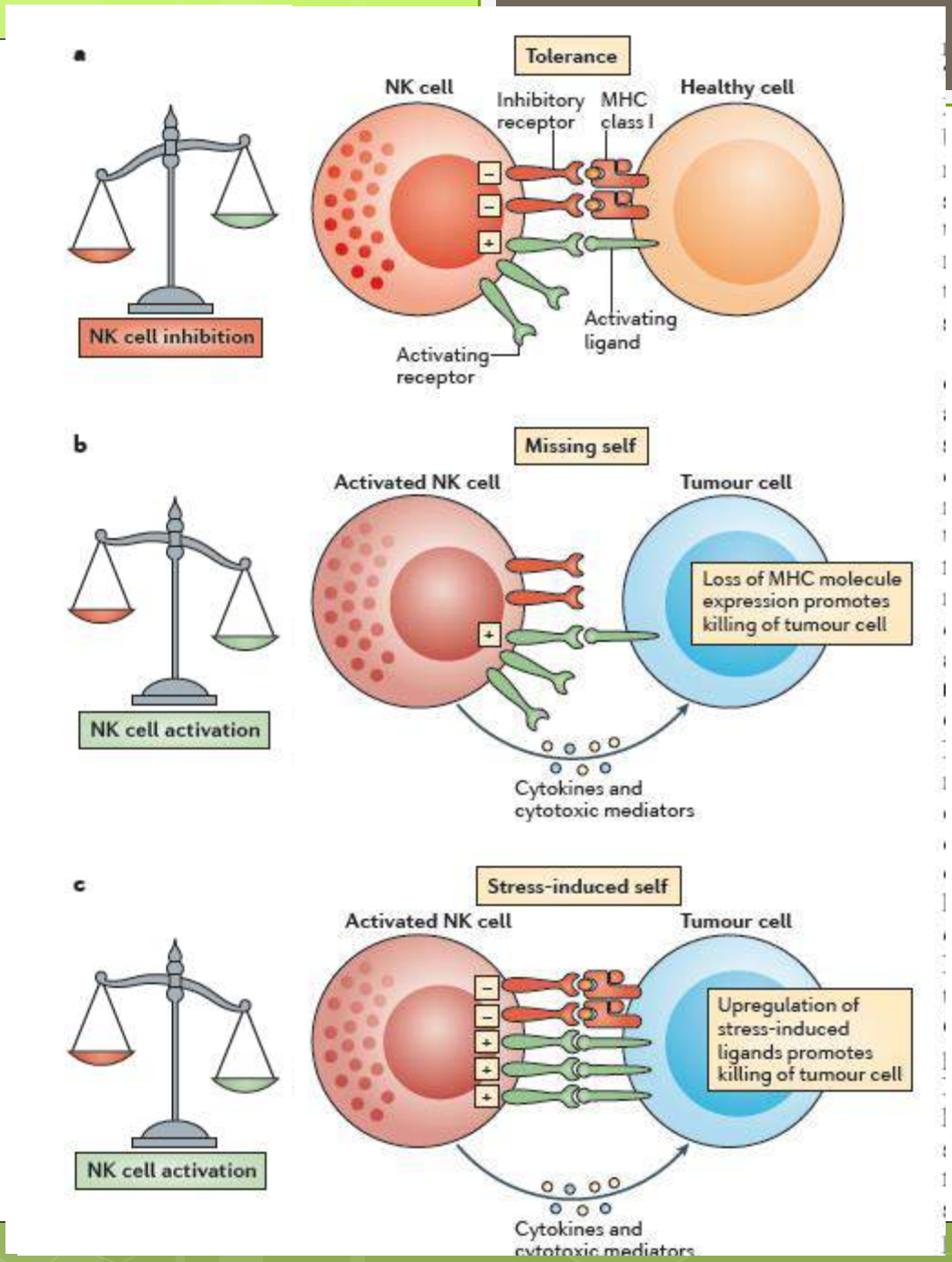


Individual herbal groups from LCS101 formula - anti-cancer effect (MDA-MB-231 cells, 72h)



Analysis of 4 different LCS101 by **HPLC** for batches for batch to batch consistency




a
Tolerance
NK cell
Inhibitory receptor
MHC class I
Healthy cell
NK cell inhibition
Activating ligand
Activating receptor
b
Missing self
Activated NK cell
Tumour cell
Loss of MHC molecule expression promotes killing of tumour cell
NK cell activation
Cytokines and cytotoxic mediators
c
Stress-induced self
Activated NK cell
Tumour cell
Upregulation of stress-induced ligands promotes killing of tumour cell
NK cell activation
Cytokines and cytotoxic mediators

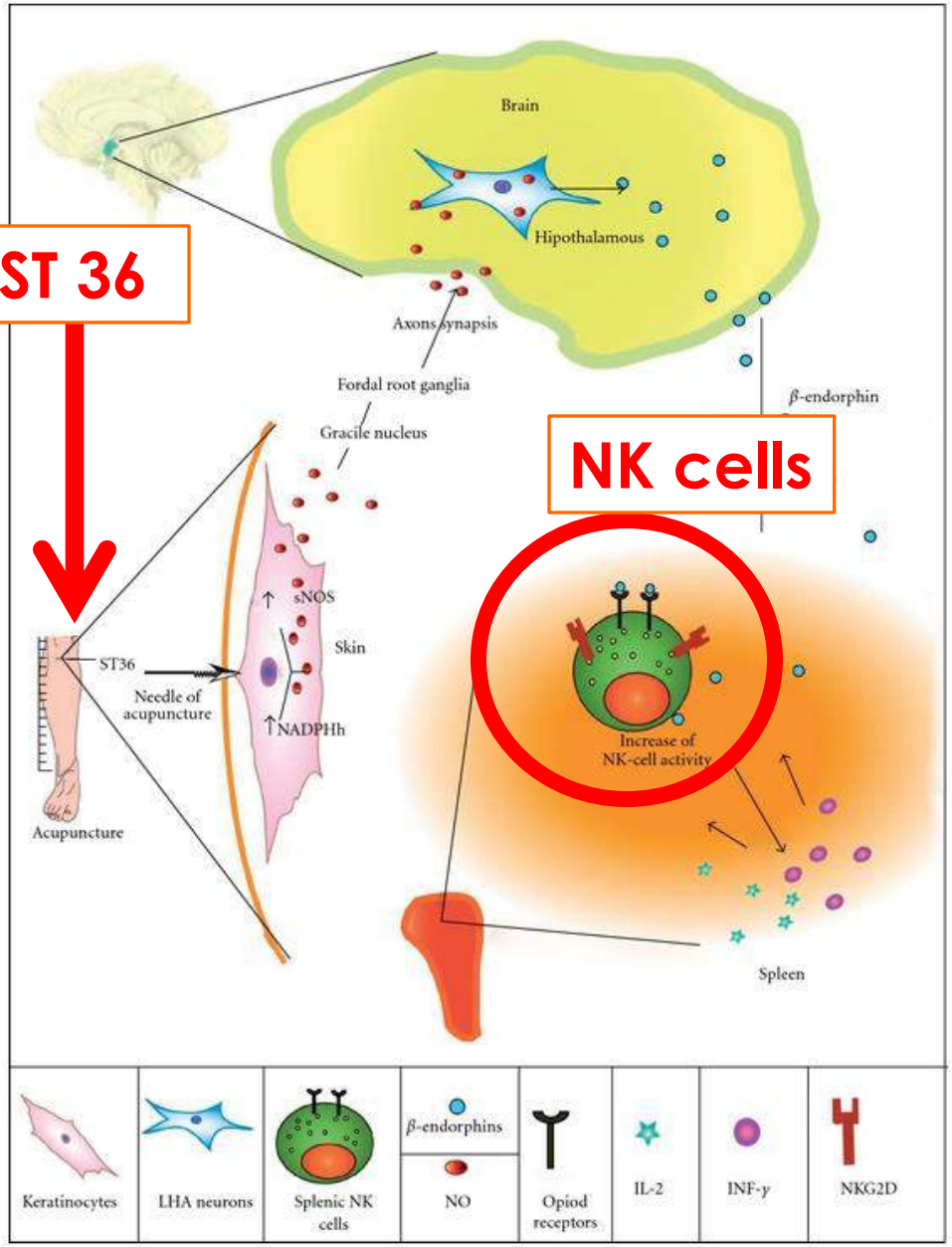
Acupuncture May Stimulate Anticancer Immunity via Activation of Natural Killer Cells.

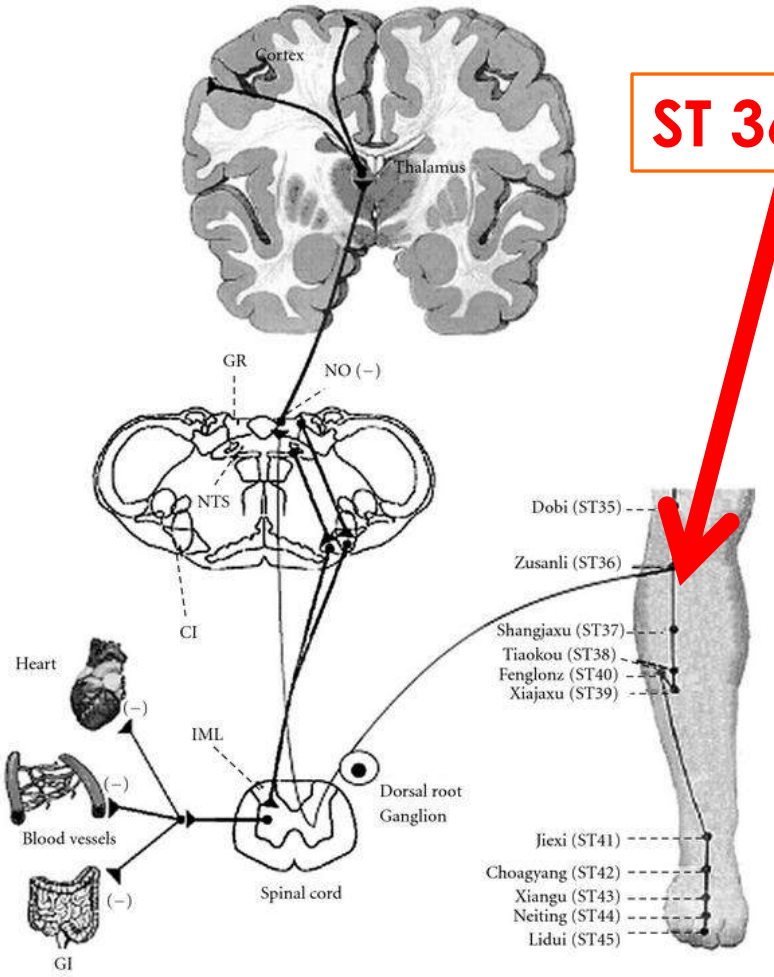
Johnston MF, Ortiz Sánchez E, Vujanovic NL, Li W.
Department of Medicine, University of California, USA.

- presents the hypothesis that acupuncture enhances anticancer immune functions by stimulating natural killer (NK) cells.

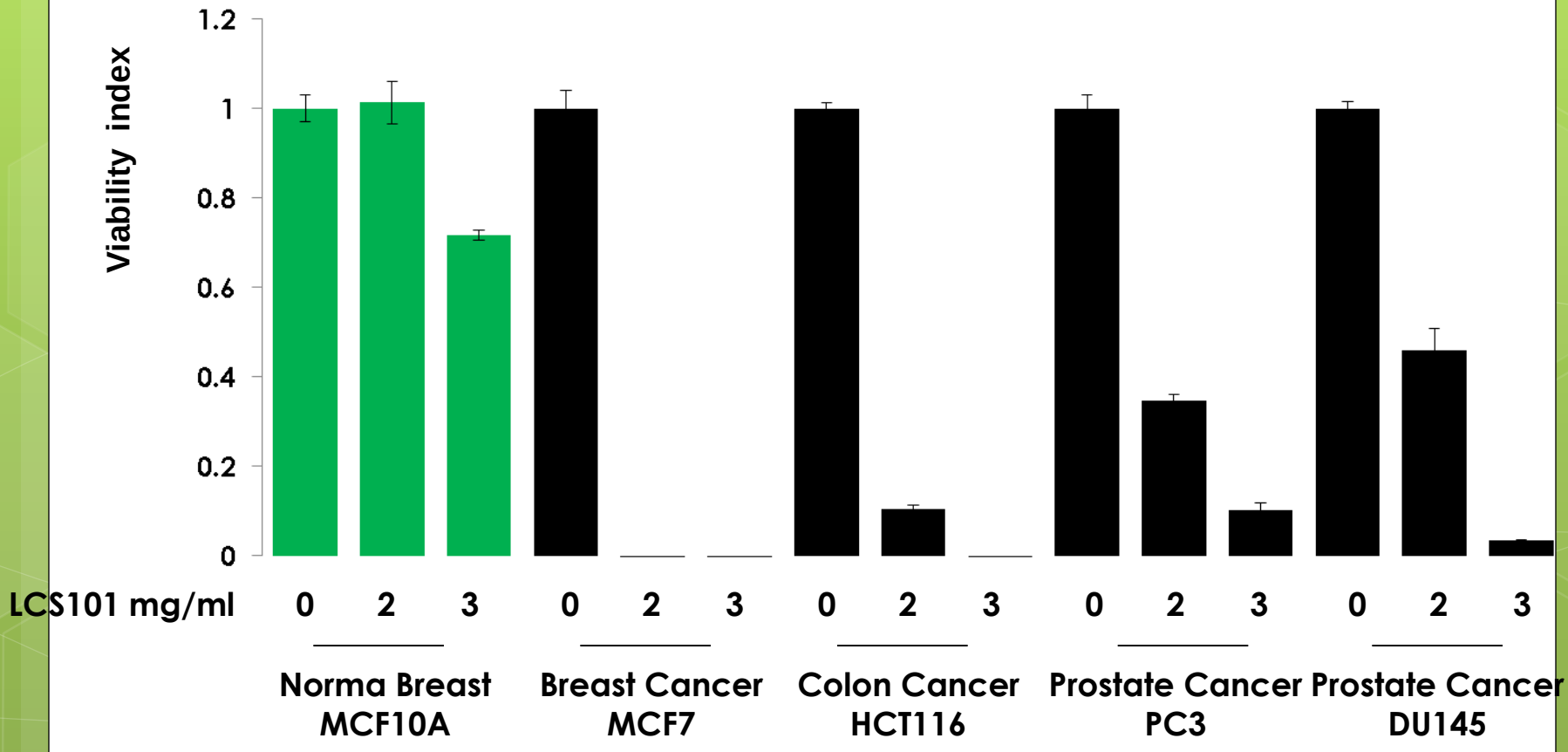
- **'acupuncture immuno-enhancement hypothesis'**

Evid Based Complement Alternat Med. 2011;2011:481625. Epub 2011 Mar 10.

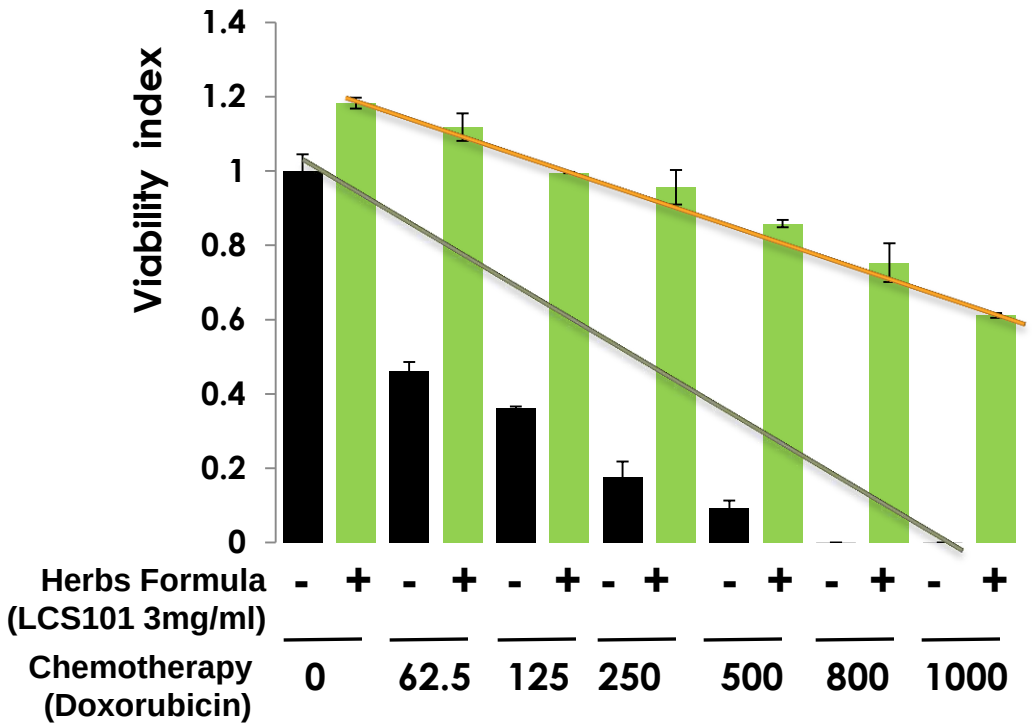

ST 36
Brain
Hipothalamous
Axons synapsis
Fordal root ganglia
Gracile nucleus
β-endorphin
NK cells
sNOS
Skin
ST36
Needle of acupuncture
NADPHh
Acupuncture
Increase of NK-cell activity
Spleen
Keratinocytes
LHA neurons
Splenic NK cells
β-endorphins
NO
Opiod receptors
IL-2
INF-γ
NKG2D


ST 36
Cortex
Thalamus
GR
NO (–)
NTS
CI
Heart
IML
Blood vessels
Dorsal root Ganglion
Spinal cord
GI
Dobi (ST35)
Zusanli (ST36)
Shangjaxu (ST37)
Tiaokou (ST38)
Fenglonz (ST40)
Xiajaxu (ST39)
Jiexi (ST41)
Choagyang (ST42)
Xiangu (ST43)
Neiting (ST44)
Lidui (ST45)

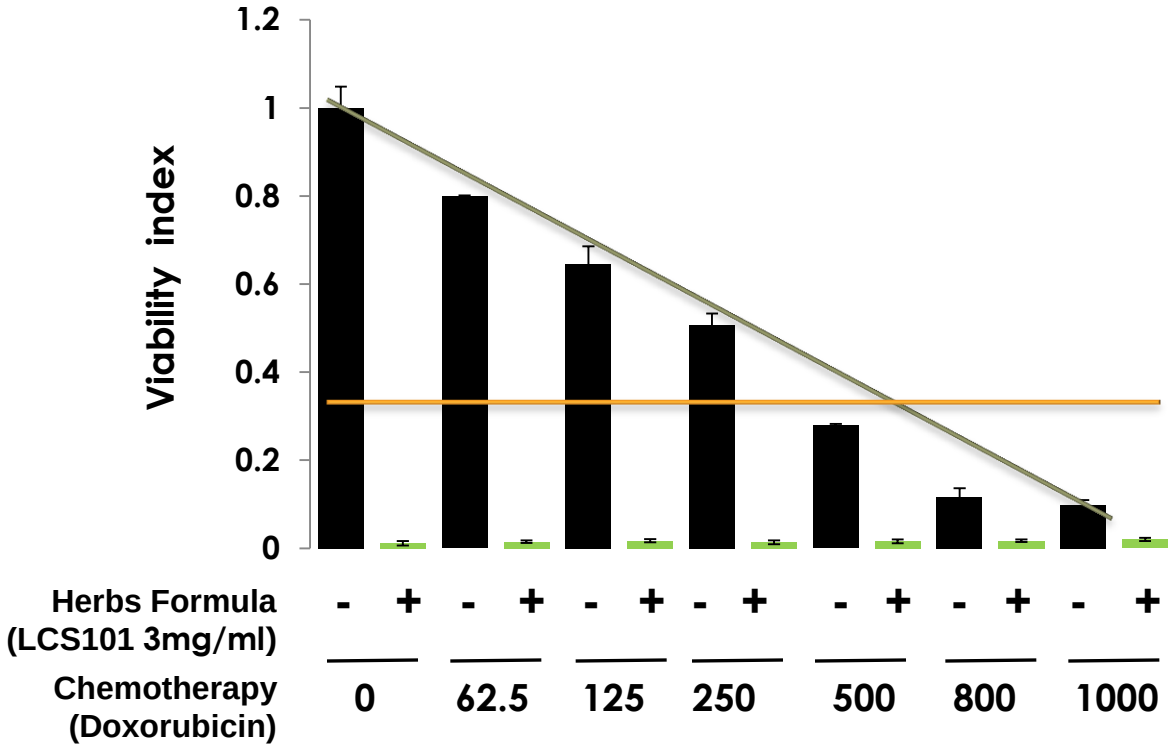
The Herbs Formula LCS101 Induces selective Cell Death in Cancer Cells

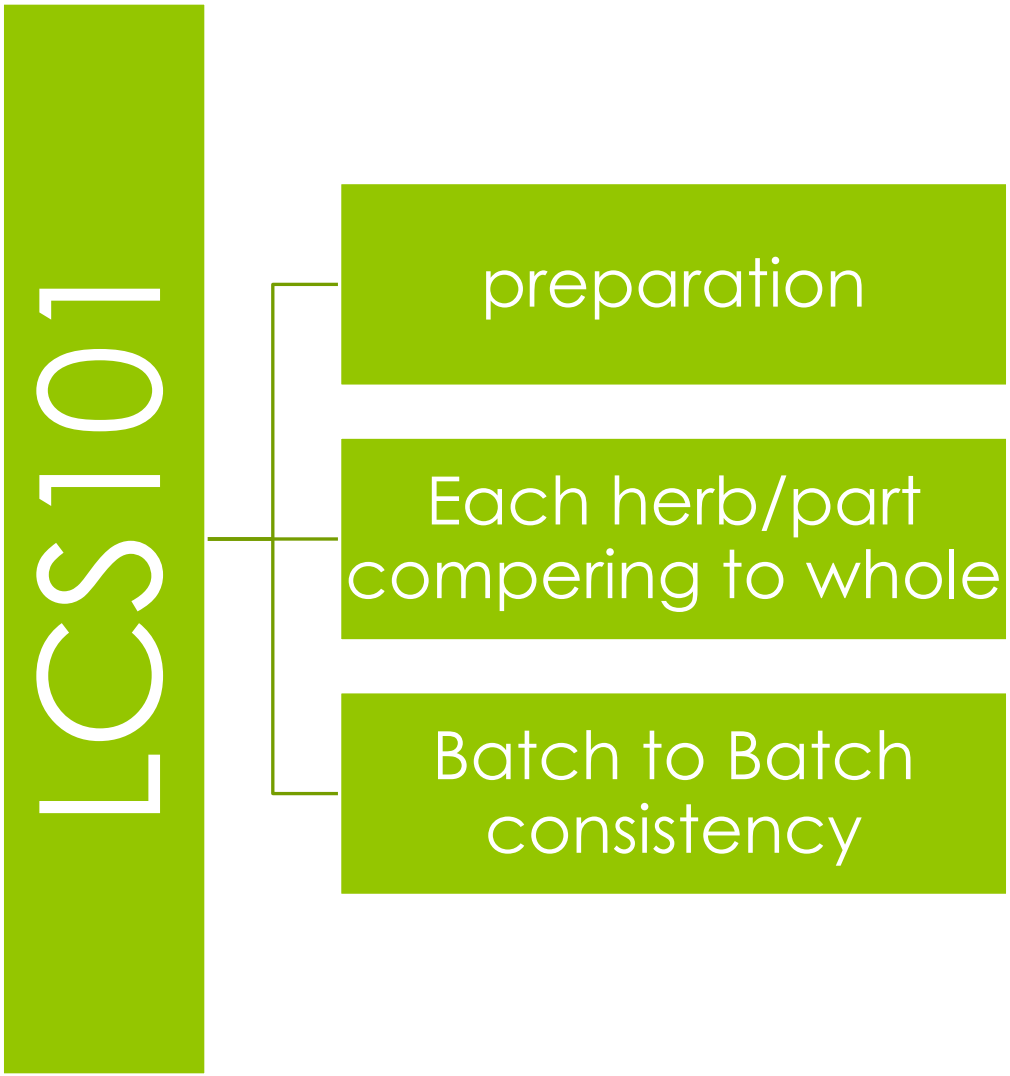


The Herbs Formula (LSC101) Protects Normal Breast Cells From Cell Death Induced by Chemotherapy.



The Herbs Formula and Chemotherapy Induce Cell Death in Brest Cancer Cells (MCF7)

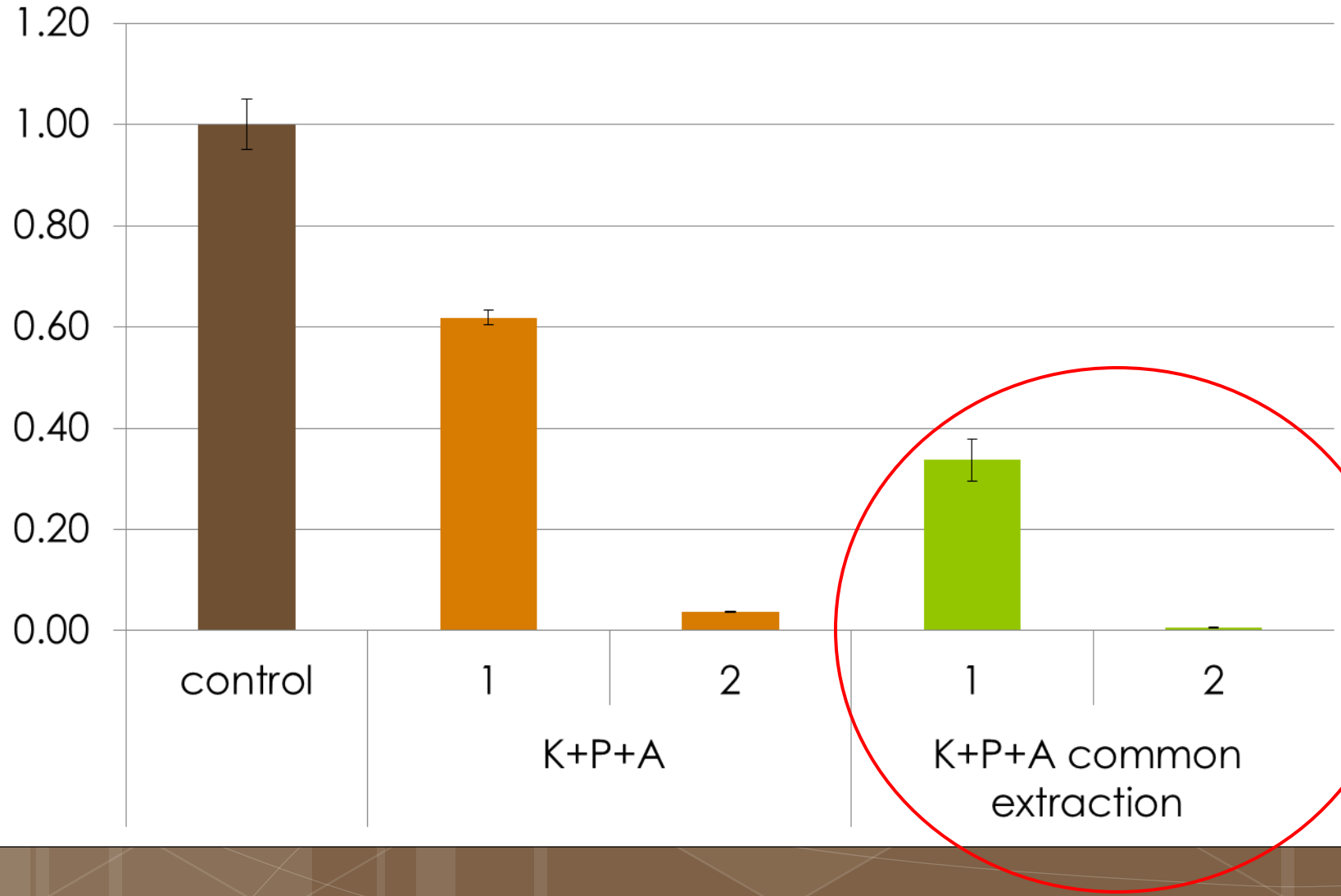



LCS101
preparation
Each herb/part compering to whole
Batch to Batch consistency

More about the formula

Special preparation

Individual herbal groups from LCS101 formula - anti-cancer effect (MDA-MB-231 cells, 72h)

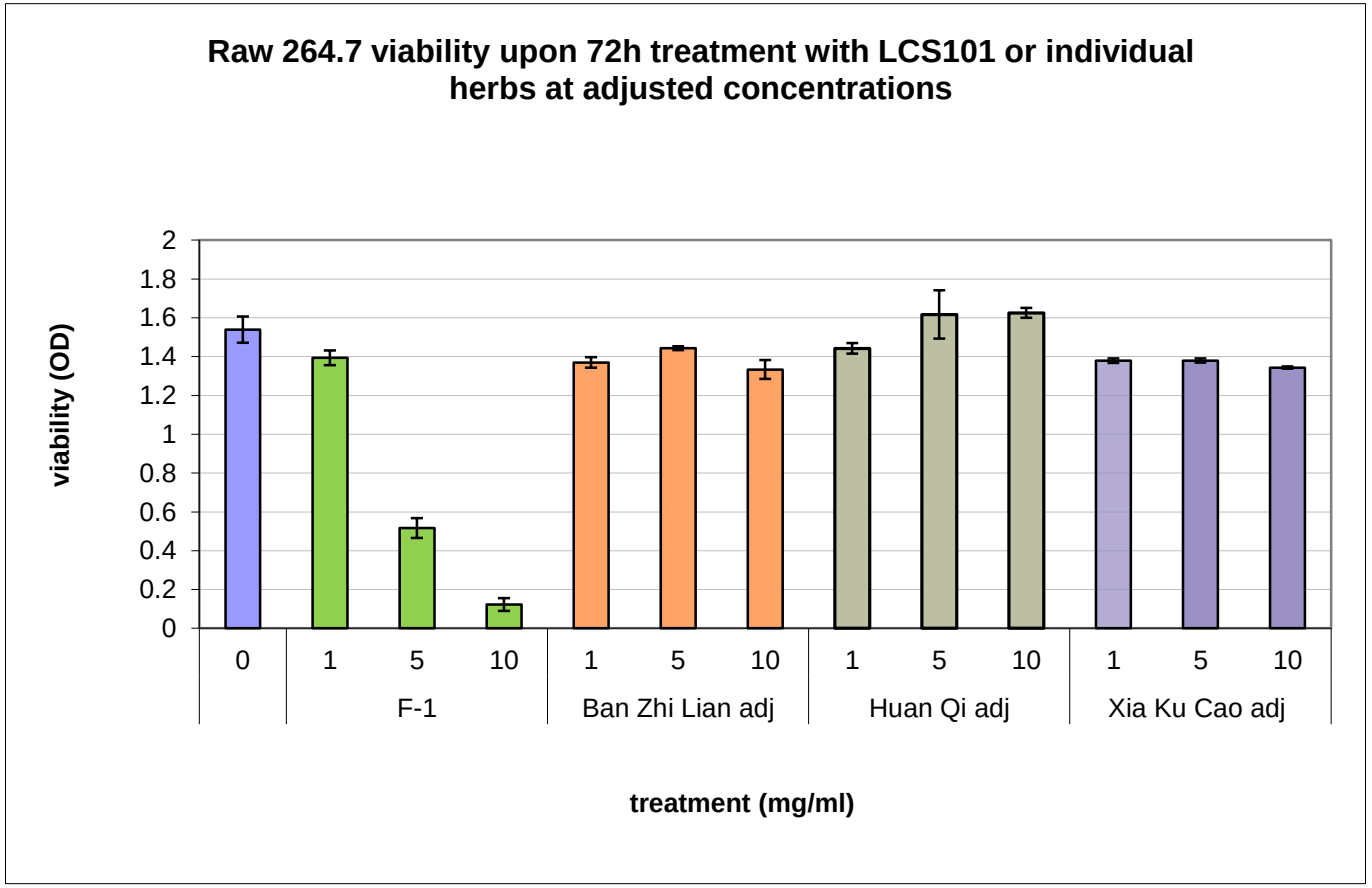


More about the formula

Each of the herb is not effective as the whole formula

Example of research (there are many more).

Influence of LCS101 and single herbs on viability of Raw cells



oncology laboratories of Sheba medical center

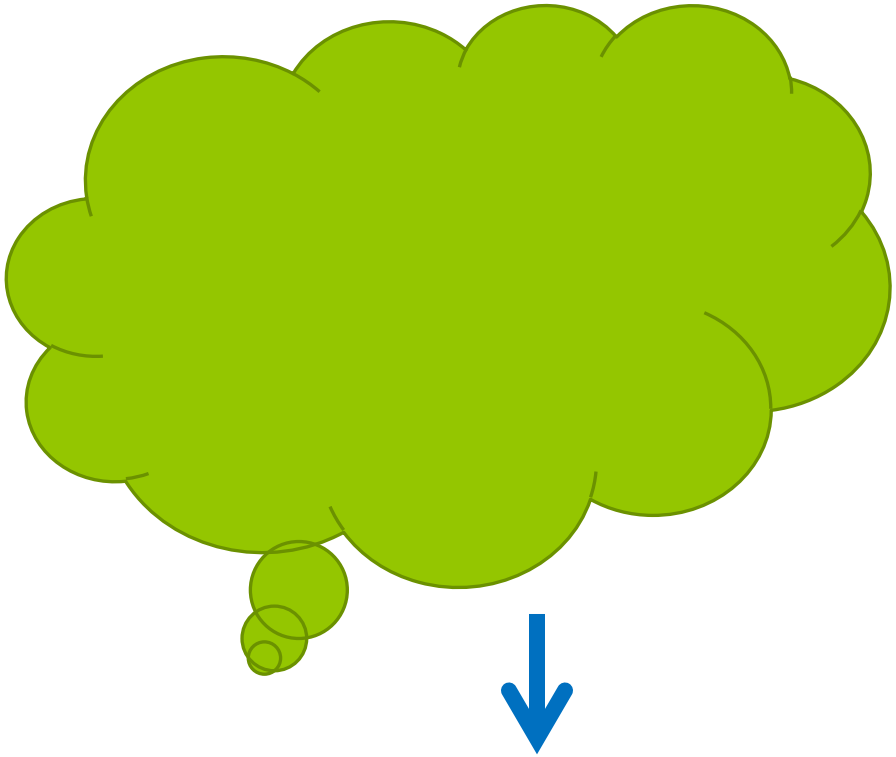
Communication

TCM

Sounds like Chinese????

WM

Communication



TCM

Complexity

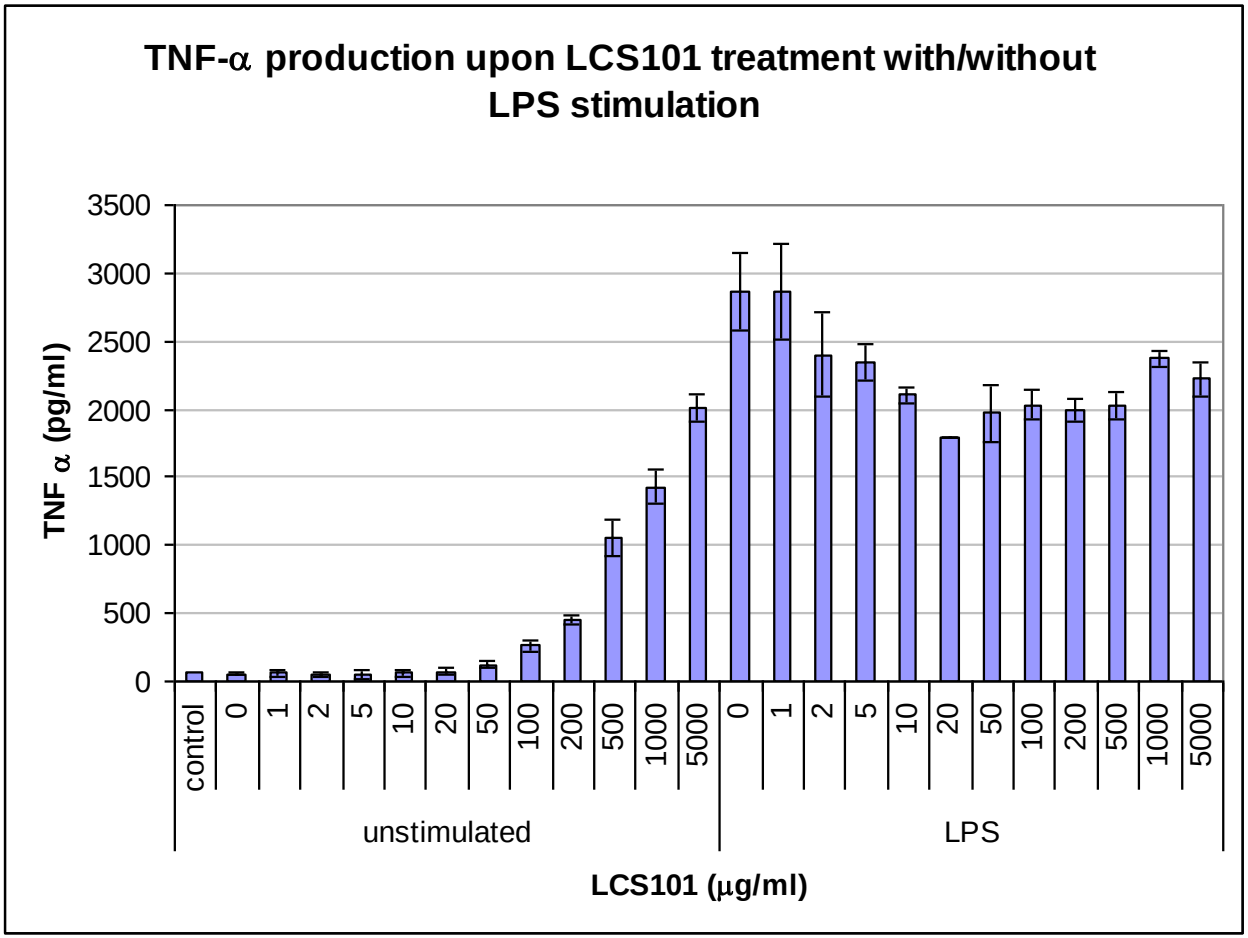
WM

- Thinking in formulas rather than molecule and even single herbs can be compered to team work where you have synergistic effect. This is the core of Chinese medical rational for many years.

- Nature works in this way also sociality ; this laws also govern medicine. System biology is acknowledging this fact.

- Bioavailability: the formula is build in the way that it has an inherent high bioavailability

Immunomodulatory function of LCS101 **adaptogenic**



Result: buffer-like action on TNF production

- **Protection**: of non-cancer cell lines from chemotherapy-induced damage
- **Synergy** : Synergy with chemotherapy in anti cancer activity
- **Selectivity** : promotion of immune cells , Growth inhibition and apoptosis induction in cancer cell lines

Acupuncture

- Nk cells activation

Reductionism

Complexity

The future

Reductionism Complexity

In the fight for prevention and treatment of cancer

Sheba is the Leading Hospital in the Middle East

- 64 medical departments
- 75 laboratories
- 110 outpatient clinics
- 1,200 doctors
- 1,500 paramedic professionals
- 1,700 technicians and support staff
- 1,700 beds
- 2,300 nurses
- 6,700 healthcare professionals and scientists on campus
- 31,000 operations conducted annually
- 1.5 million patient visits annually

ISRAEL'S FOREMOST MEDICAL RESEARCH CENTER

Conducting 25 percent of all Israeli medical research

- *מרכז טל הוא אחד המרכזים הבודדים בעולם המשלב מחקר מדעי במעבדה עם מחקר קליני במטופלים.*
- *שילוב כזה מאפשר פריצות דרך ברמה של פיתוח תרופות ופרוטוקולי טיפול חדשניים. פריצות דרך אלו ישפיעו על הדרך שבה מתמודדים ומרפאים סרטן.*

Sheba is the Leading Hospital in the Middle East

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ISRAEL'S FOREMOST MEDICAL RESEARCH CENTER

Conducting 25 percent of all Israeli medical research

Acknowledgment and thanks

- Yaal-Hahoshen N,
- Siegelmann-Danieli N,
- Lev-Ari S,
- Ron I,
- Sperber F,
- Samuels N,
- Shoham J,
- Merimsky O.
- Rachmut Isaac
- Sahrabi yeddida
- Burger Raanan
- Steve Melnick
- Zoya Cohen
- Merav Lerner

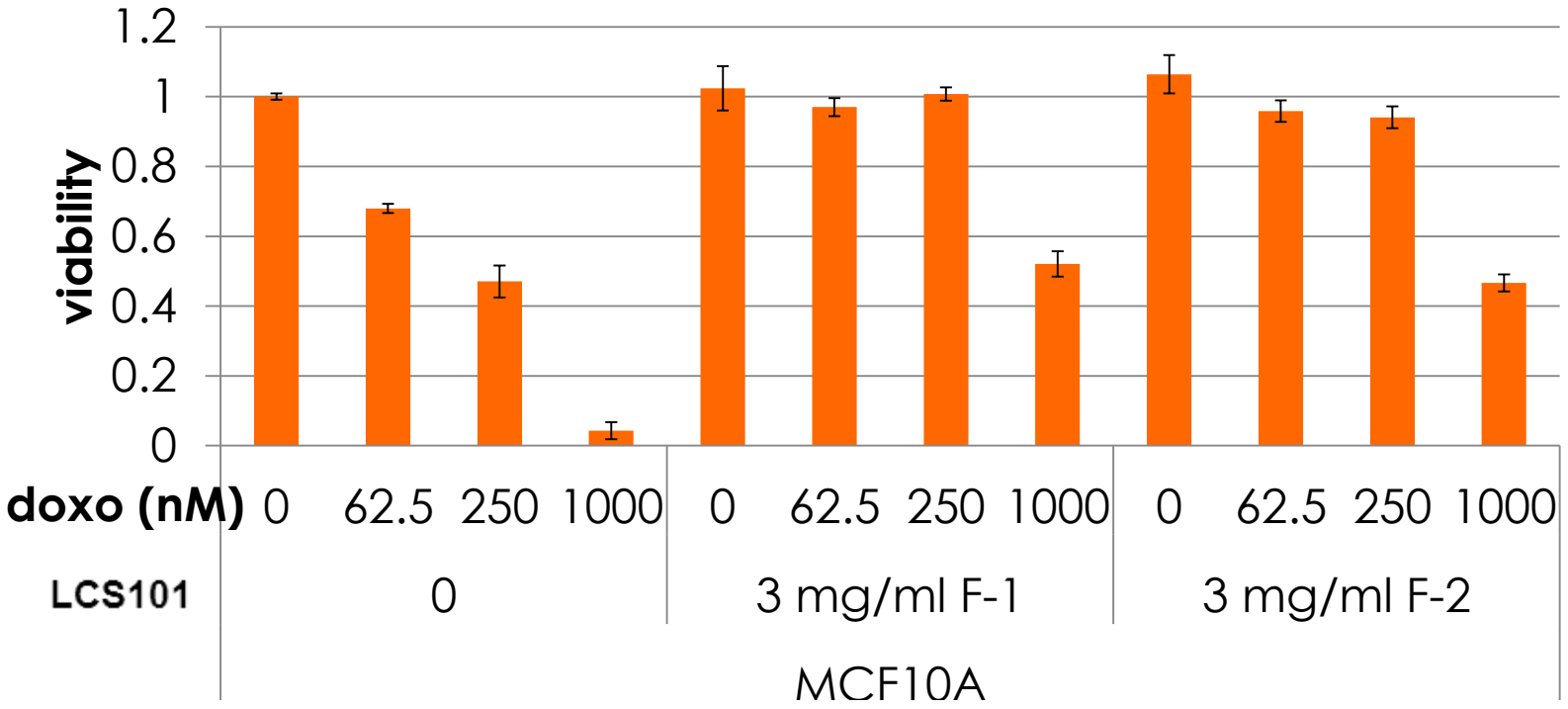
Compereing the whole formula to groups within the formula

- L = LCS101
- K = killing: Bai Hua She She Cao, Ban Zhi Lian, Xia Ku Cao
- P = protection: Huang Qi, Gou Qi Zi, Fu Ling, Bai Zhu, Nu Zhen Zi, Mai Men Dong, Ji Xue Teng
- A = additional: Bei Sha Shen, Chen Pi, Chi Shao, Bai Shao
- K+P+A = all the herbs, mixed after extraction
- K+P+A = all the herbs, mixed before extraction (LCS101 reconstitution)

For Batch to batch consistency

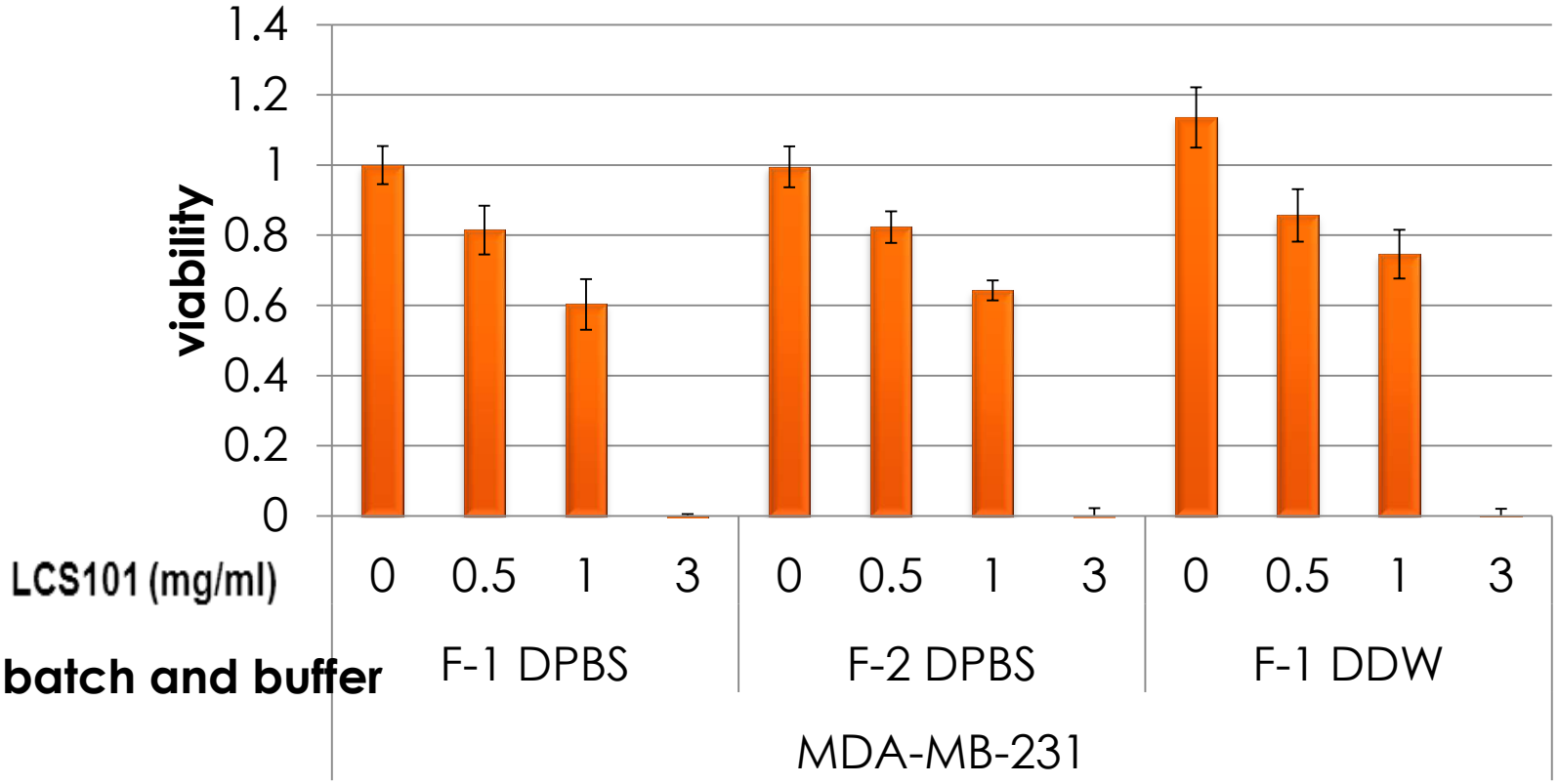
- **Anti cancer** (phenol)
- **Protection from chemotherapy** (antioxidant)
- **Immune activity** (polysaccharides)

Batch to batch consistence assay- doxorubicin protection test



Exp 32

Batch to batch consistence assay- anti-cancer activity test

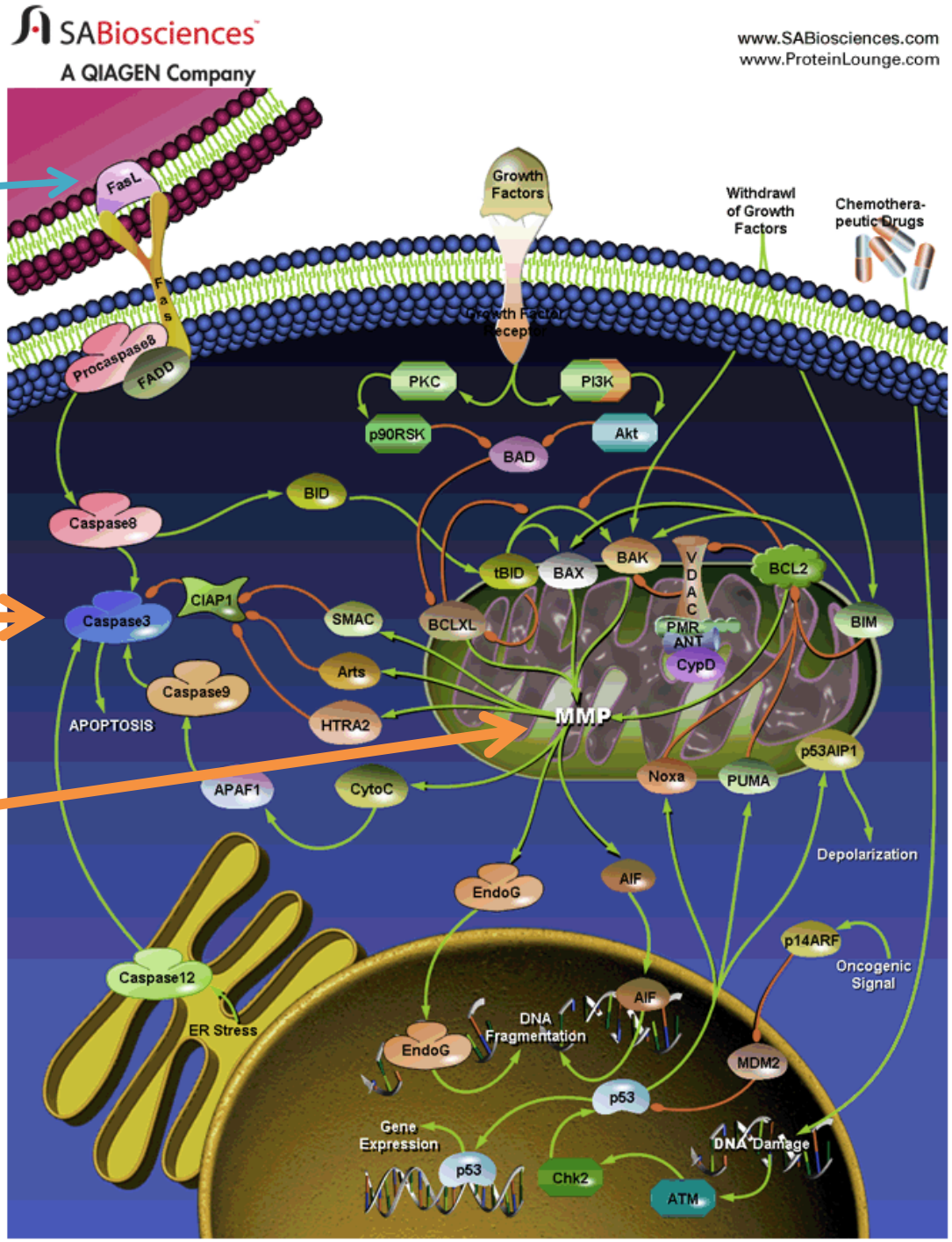


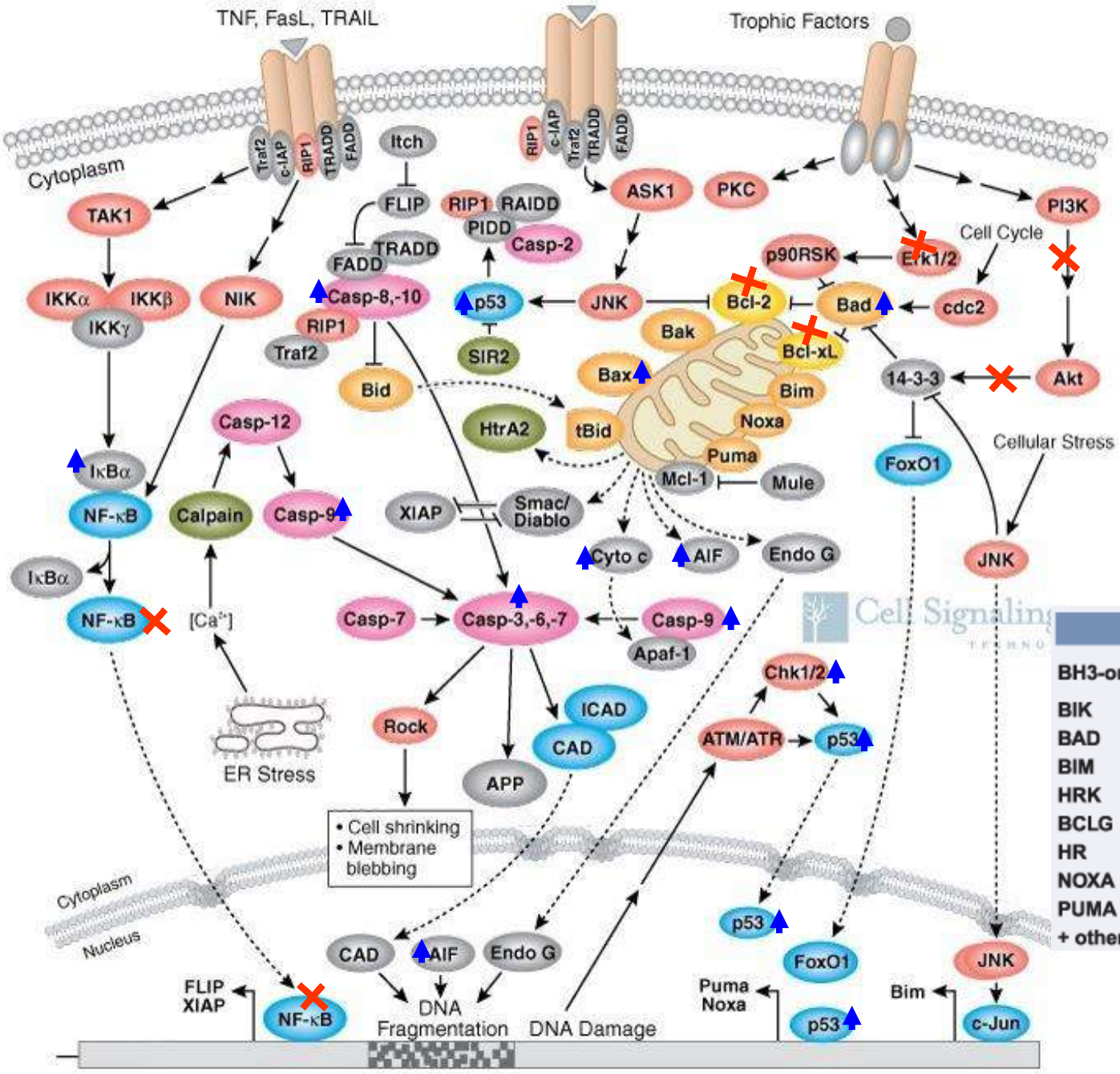
Exp 32

Apoptosis

Extra-cellular

Intra-cellular





Bai Zhu
Fu Ling
Xia Ku Cao
Nu Zhen Zi
Ji Xue Teng
Bai Hua She
She Cao
Bai Shao
Bei Sha Shen

Anti-apoptotic
BCL-2
BCL-X_L
BCLW
MCL1
BCLB

Pro-apoptotic	
BH3-only proteins	Multidomain (Bl
BIK	BAX
BAD	BAK
BIM	BOK
HRK	BOO
BCLG	BCLG
HR	BCLB
NOXA	BCL-RAMBO
PUMA	
+ others	

Acupuncture May Stimulate Anticancer Immunity via Activation of Natural Killer Cells.

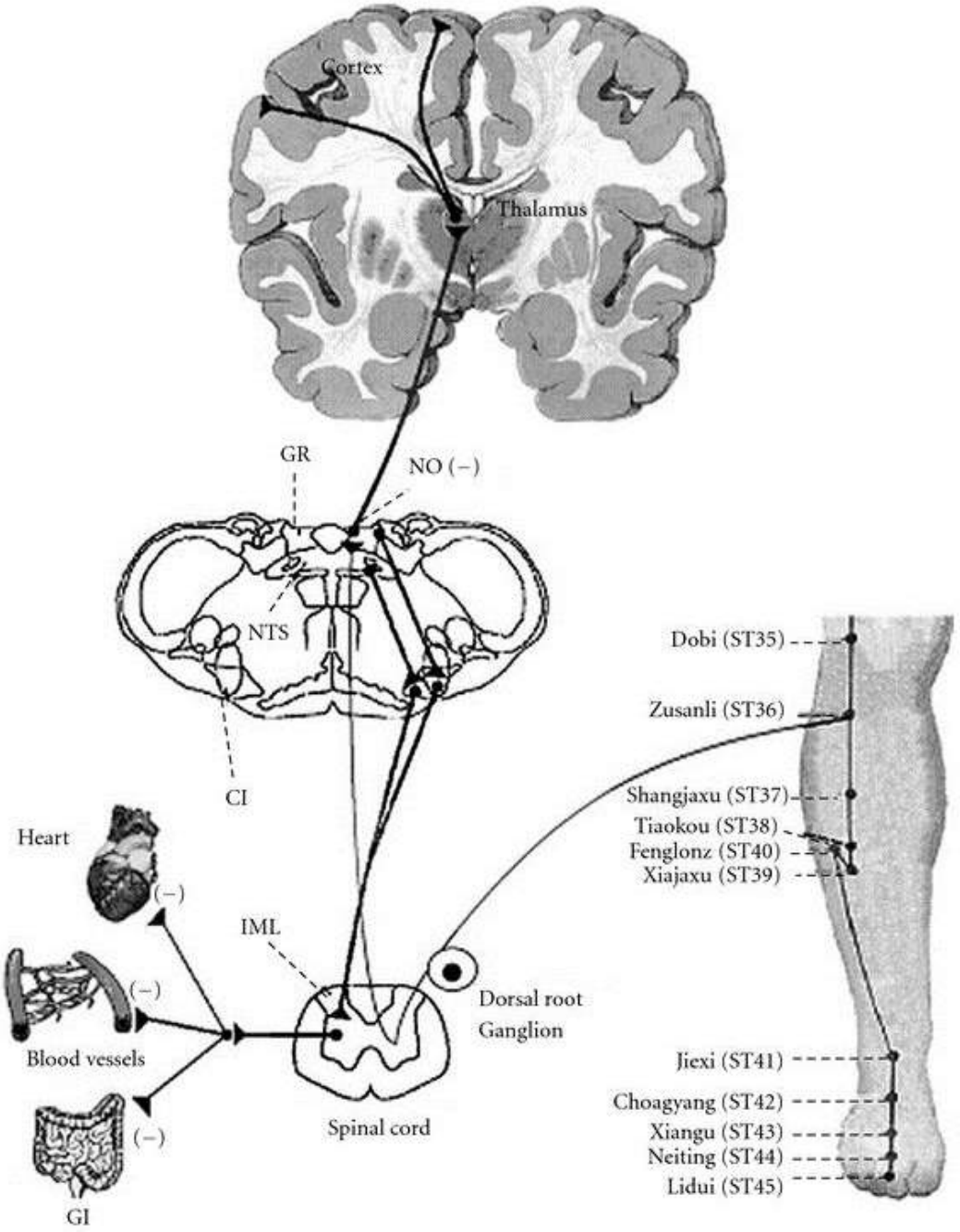
Johnston MF, Ortiz Sánchez E, Vujanovic NL, Li W.
Department of Medicine, University of California, USA.

- presents the hypothesis that acupuncture enhances anticancer immune functions by stimulating natural killer (NK) cells.

- summarizes the current scientific understanding of the mechanisms through which NK cells act to eliminate cancer cells.

- **'acupuncture immuno-enhancement hypothesis'**

Evid Based Complement Alternat Med. 2011;2011:481625. Epub 2011 Mar 10.


Cortex
Thalamus
GR
NO (−)
NTS
CI
Heart
(−)
IML
(−)
Blood vessels
(−)
GI
Spinal cord
Dorsal root
Ganglion
Dobi (ST35)
Zusanli (ST36)
Shangjaxu (ST37)
Tiaokou (ST38)
Fenglonz (ST40)
Xiajaxu (ST39)
Jiexi (ST41)
Choagyang (ST42)
Xiangu (ST43)
Neiting (ST44)
Lidui (ST45)

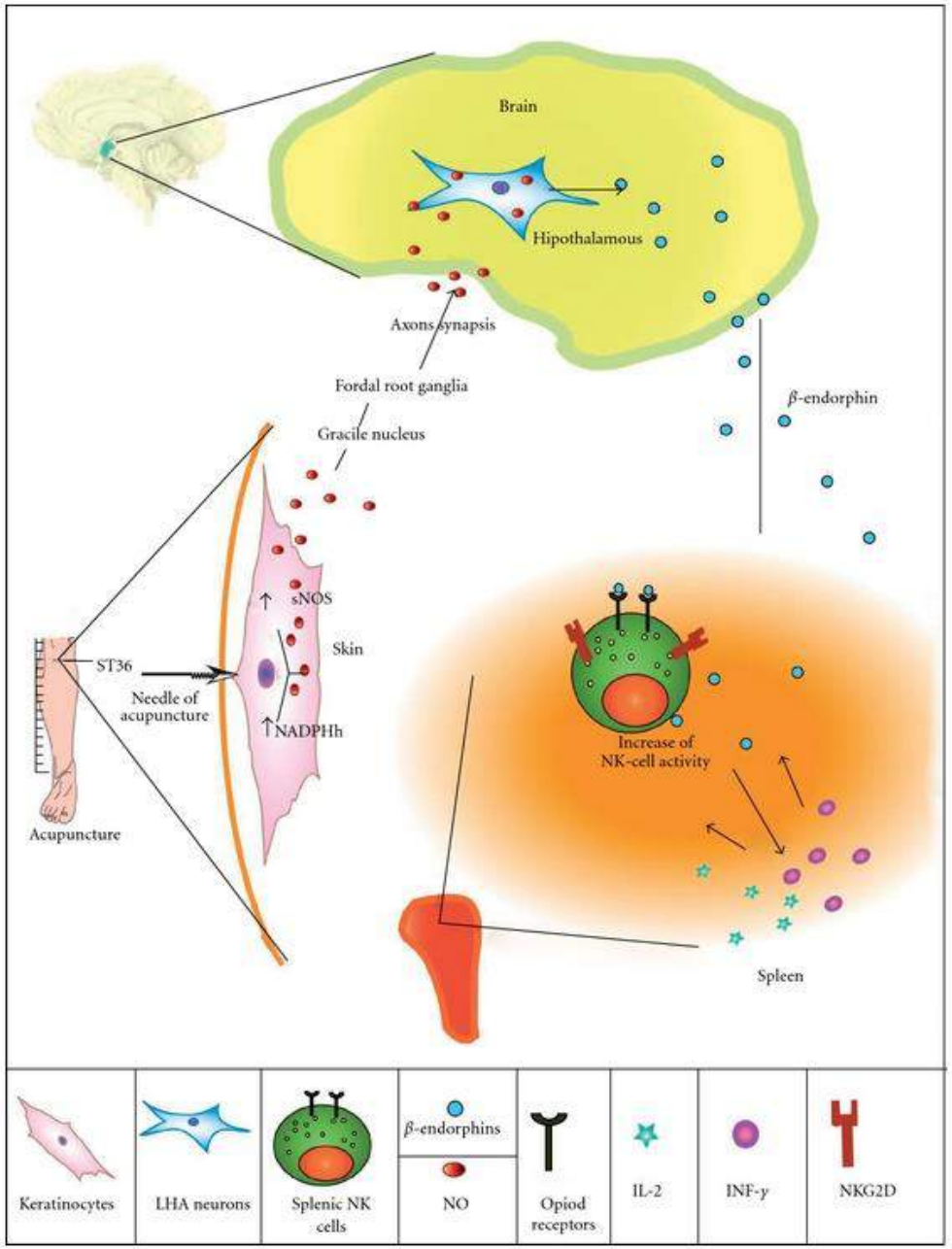


Figure 3

Hypothetic model of the mechanisms how acupuncture stimulates the immune system. Acupuncture stimulation of ST36 acupoint induces release of nitric oxide (NO). NO, a neurotransmiter, stimulates via the sensory nerves, spinal cord and medulla oblongata Gracile nuclceus the lateral hypothalamic area (LHA), where it promotes secretion of opiod peptides such as *β*-endorphin. *β*-endorphin travels via blood circulation to the spleen and other body locations containing immune cells where it binds to opiod receptors expressed on the surface of NK cells and stimulates NK cells to amplify their expression of cytotoxic molecules and consequently tumoricidal activity, and production of IFN-*γ*. This cytokine induces the expression of NK cell receptors and cytokine receptors on NK cells and perhaps cytokine secretion by other immune cells, thereby orchestrating and further amplifying anticancer immune

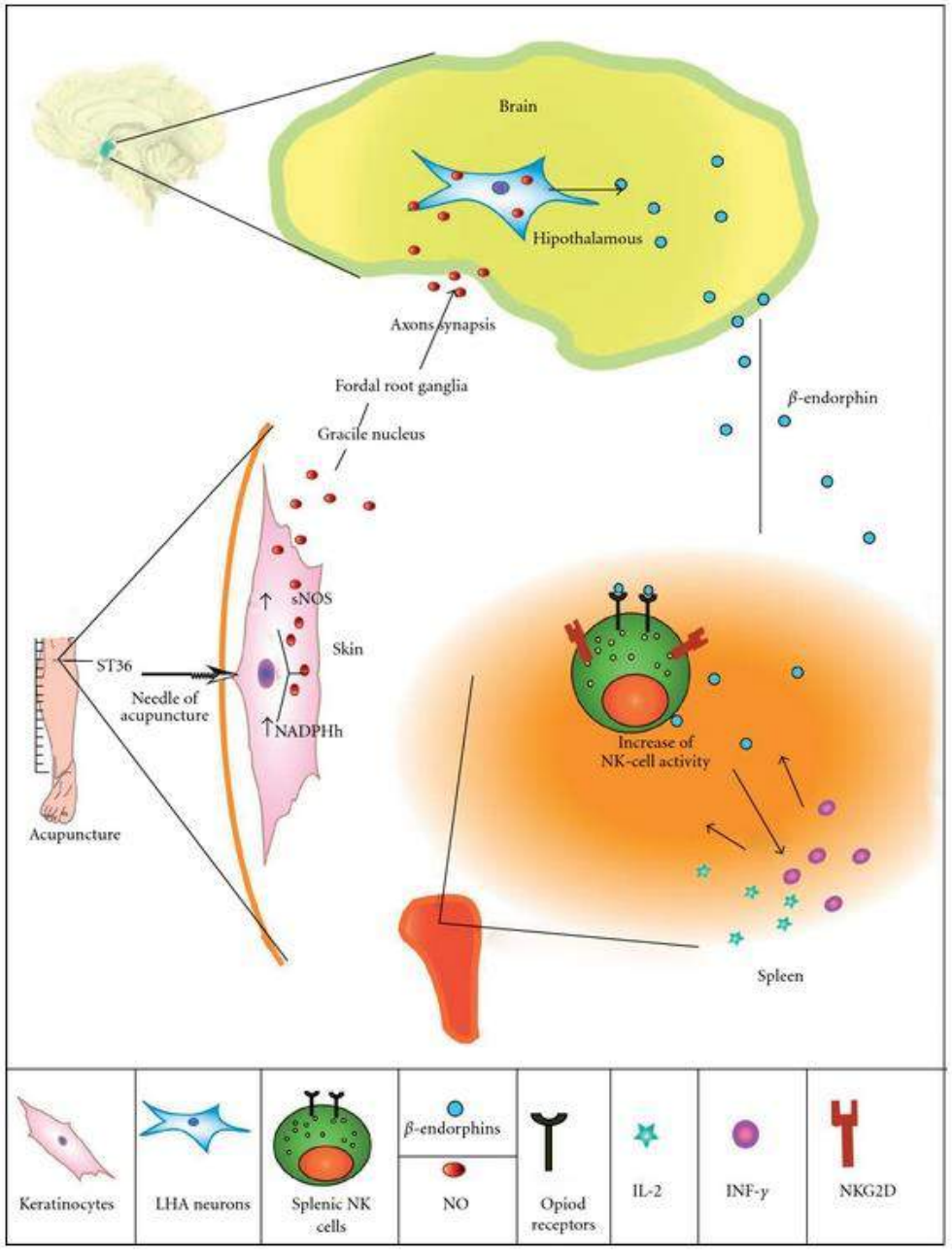


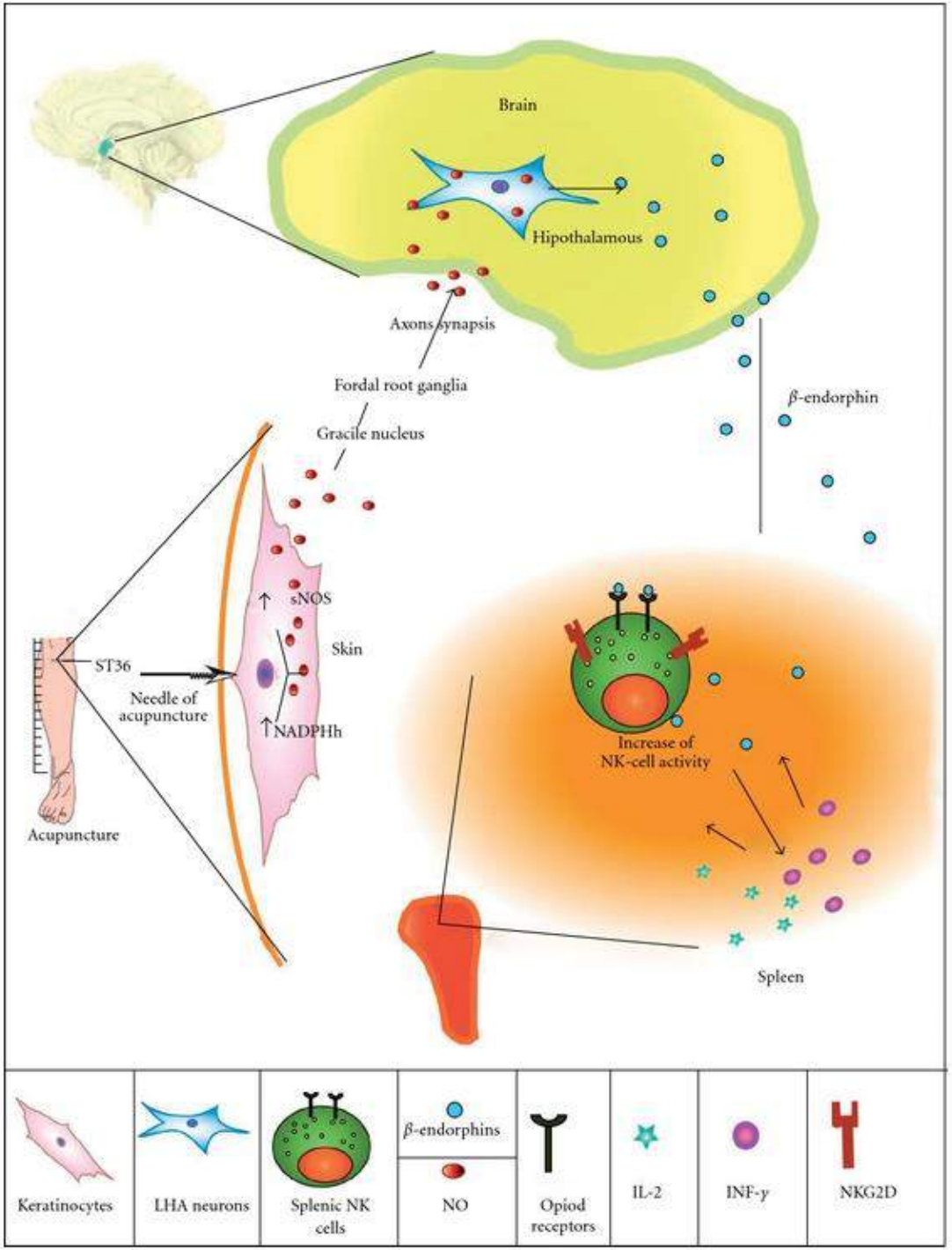
Figure 3

stimulation of ST36 acupoint induces release of nitric oxide (NO).

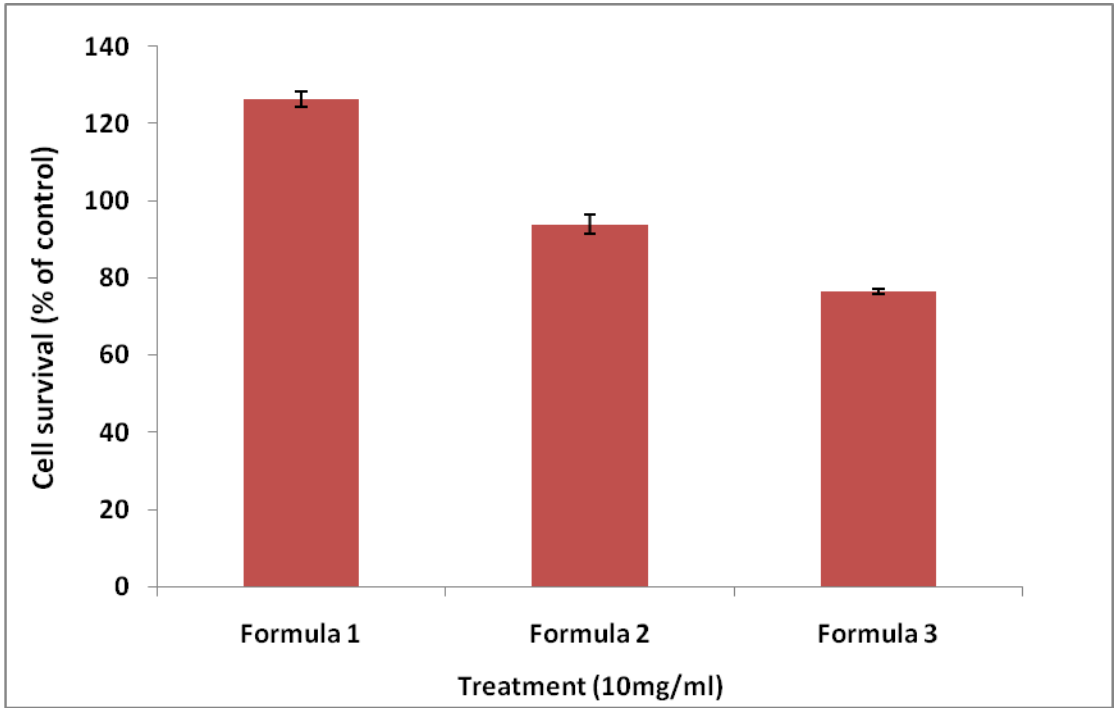
NO, a neurotransmiter, stimulates via the sensory nerves, spinal cord *β*-endorphin.

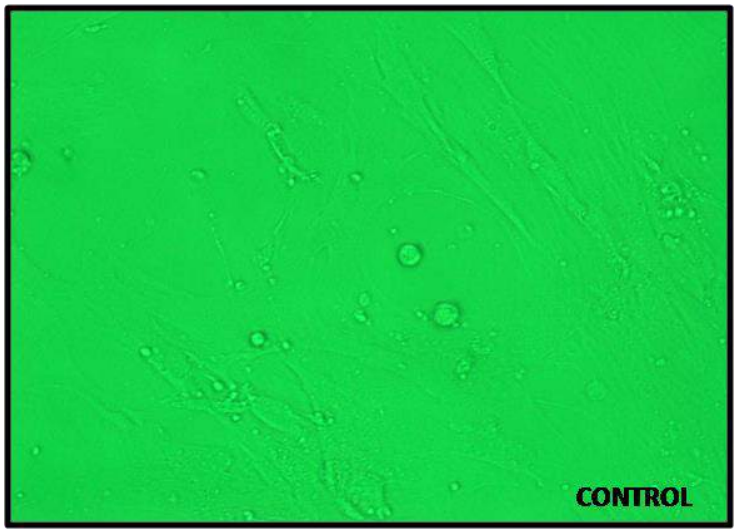
binds to opiod receptors expressed on the surface of NK cells

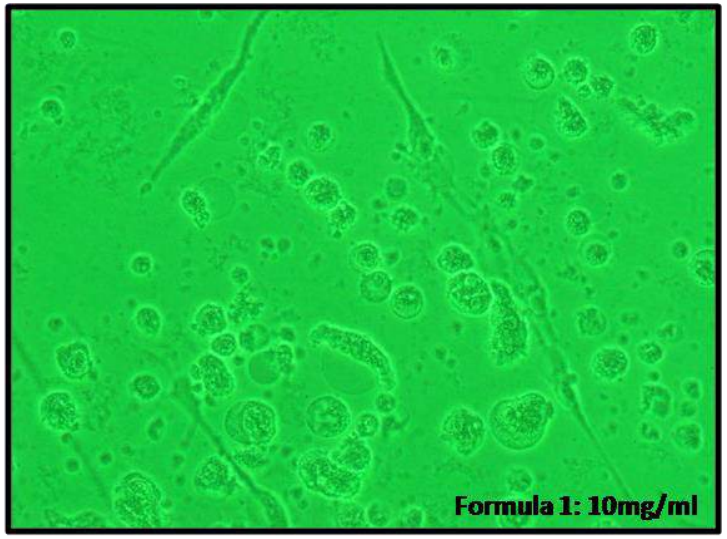
and further amplifying anticancer immune functions

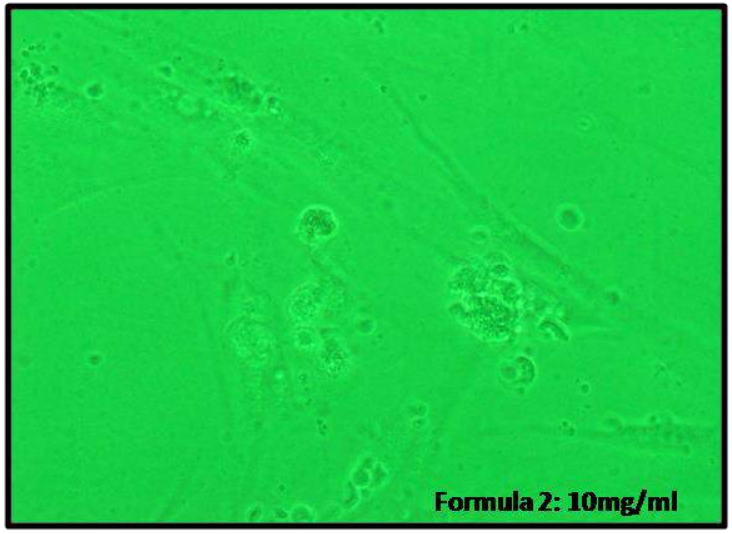

Brain
Hipothalamous
Axons synapsis
Fordal root ganglia
Gracile nucleus
β-endorphin
sNOS
Skin
ST36
Needle of acupuncture
NADPHh
Acupuncture
Increase of NK-cell activity
Spleen
Keratinocytes
LHA neurons
Splenic NK cells
β-endorphins
NO
Opiod receptors
IL-2
INF-y
NKG2D

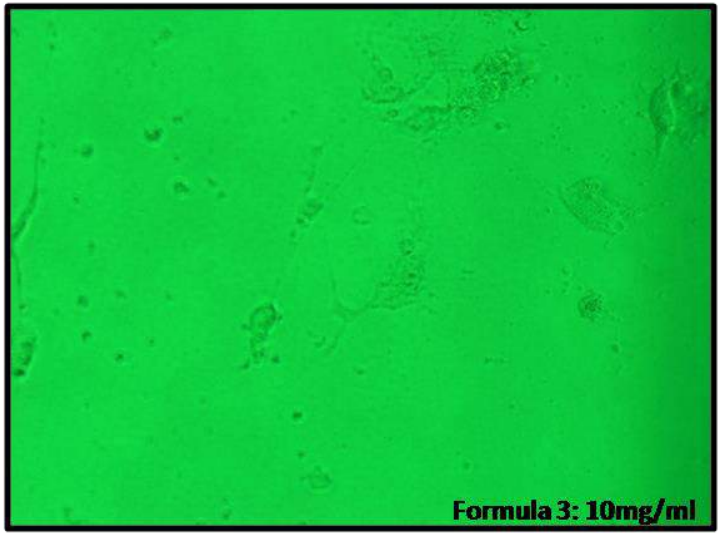

BENCH TO
BEDSIDE


140
120
100
80
60
40
20
0
Cell survival (% of control)
Formula 1
Formula 2
Formula 3
Treatment (10mg/ml)


CONTROL

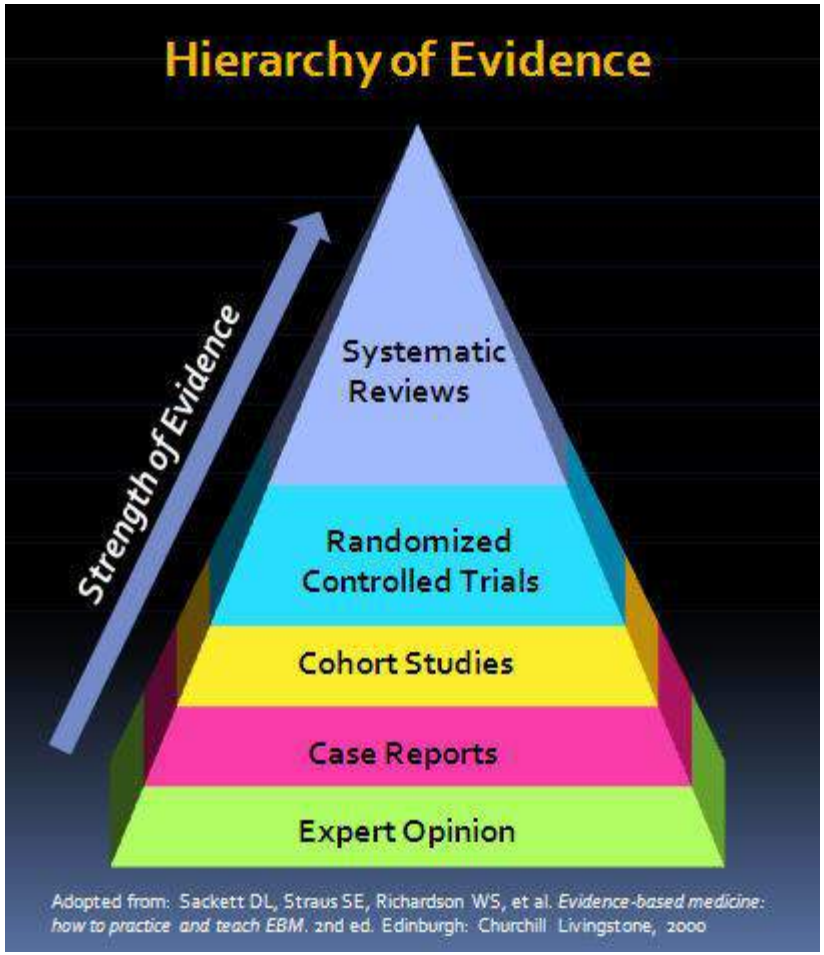

Formula 1: 10mg/ml


Formula 2: 10mg/ml

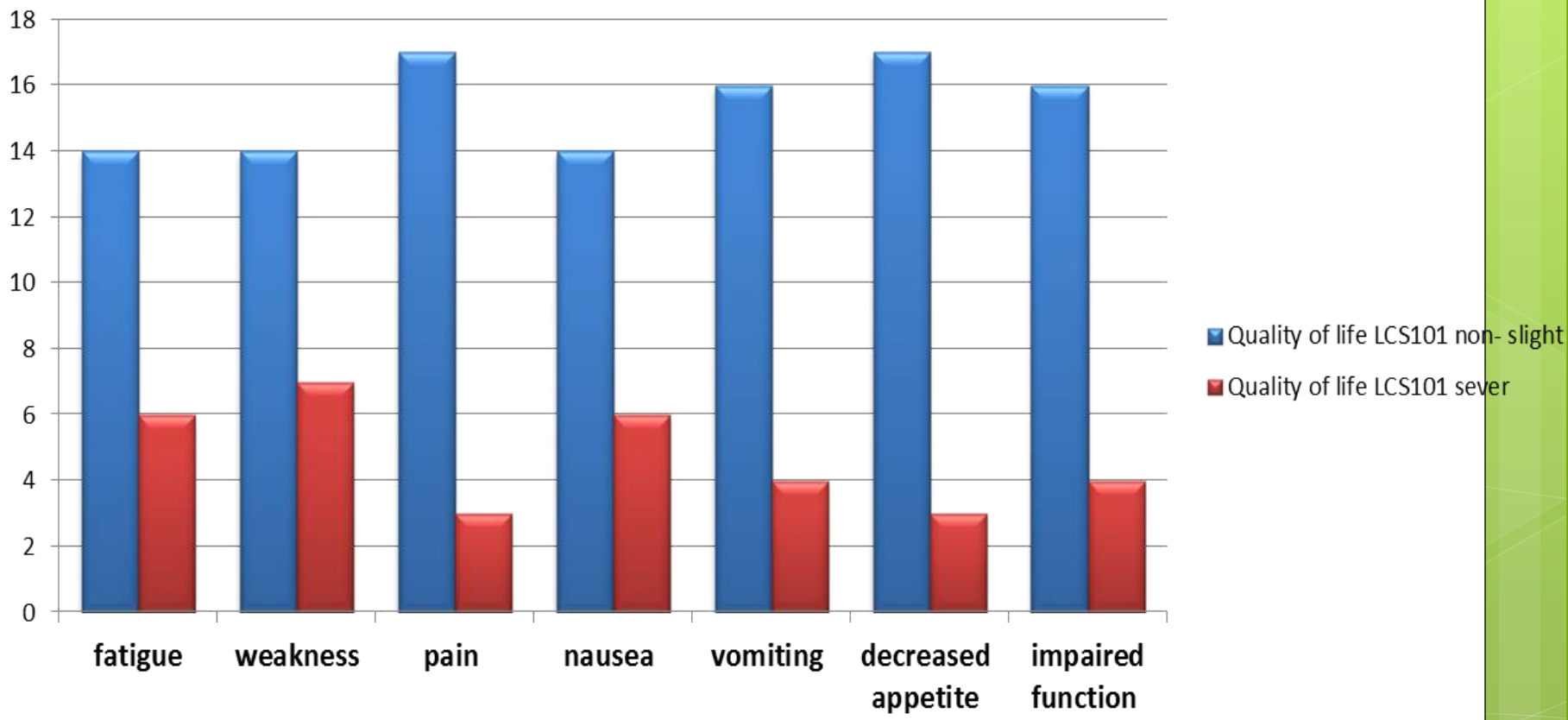

Formula 3: 10mg/ml

- **Validity** *Reliability Unbiased and objective*
- research questions.
- methodology
- Random assignment - treatment or control group.
- Double blind -neither the subject nor the experimenter knows whether the subject is in the treatment of the control condition
- Collecting the Data
- Analysis of Data

Pyramid of Evidence (hierarchy (level) of evidence)


Hierarchy of Evidence
Strength of Evidence
Systematic Reviews
Randomized Controlled Trials
Cohort Studies
Case Reports
Expert Opinion
Adopted from: Sackett DL, Straus SE, Richardson WS, et al. Evidence-based medicine: how to practice and teach EBM. 2nd ed. Edinburgh: Churchill Livingstone, 2000

Effect of botanical compound LCS 101 on chemotherapy-induced symptoms in breast cancer patients: an observational study



Retrospective study on 20 patients at Refout Integrative medical center
Status: before publication

סיכום ביניים

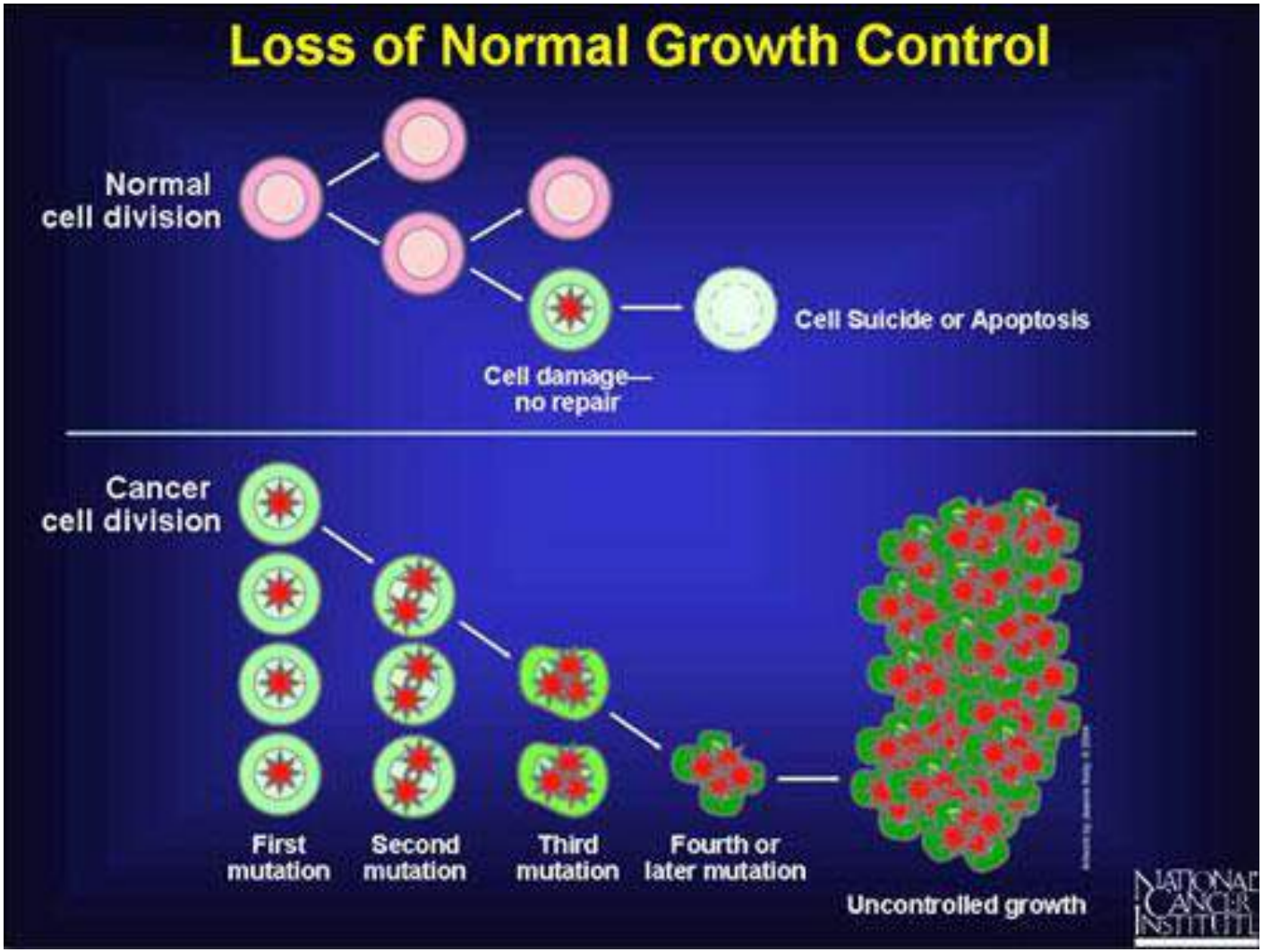
- פורמולה יעילה ובטוחה למתן בזמן כימותרפיה
- **יעילה להפחתת תופעות הלוואי (המטולוגים):**

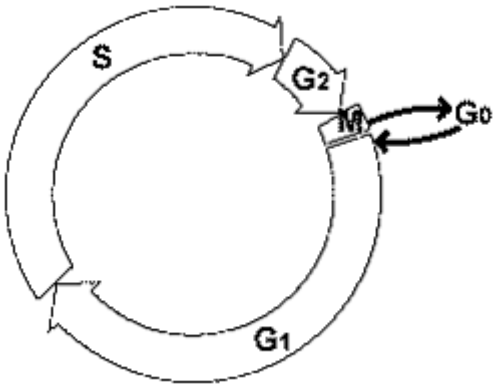
ירידה בספירות דם אדומות ולבנות –מאשפרת לסיום הטיפול.

מחזקת מערכת חיסון- מפחיתה סכנה להדבקות במחלות

- **יעילה להפחתת תופעות לוואי (איכות חיים).**

עייפות, חולשה, בחילות, ירידה בתיאבון, כאב


Loss of Normal Growth Control
Normal cell division
Cell Suicide or Apoptosis
Cell damage—no repair
Cancer cell division
First mutation
Second mutation
Third mutation
Fourth or later mutation
Uncontrolled growth
NATIONAL CANCER INSTITUTE



The Cell Cycle

G0 phase (resting stage): The cell has not yet started to divide. Cells spend much of their lives in this phase. Depending on the type of cell, G0 can last from a few hours to a few years. When the cell gets a signal to reproduce, it moves into the G1 phase.

G1 phase: During this phase, the cell starts making more proteins and growing larger, so the new cells will be of normal size. This phase lasts about 18 to 30 hours.

S phase: In the S phase, the chromosomes containing the genetic code (DNA) are copied so that both of the new cells formed will have matching strands of DNA. The S phase lasts about 18 to 20 hours.

G2 phase: In the G2 phase, the cell checks the DNA and gets ready to start splitting into 2 cells. This phase lasts from 2 to 10 hours.

M phase (mitosis): In this phase, which lasts only 30 to 60 minutes, the cell actually splits into 2 new cells.

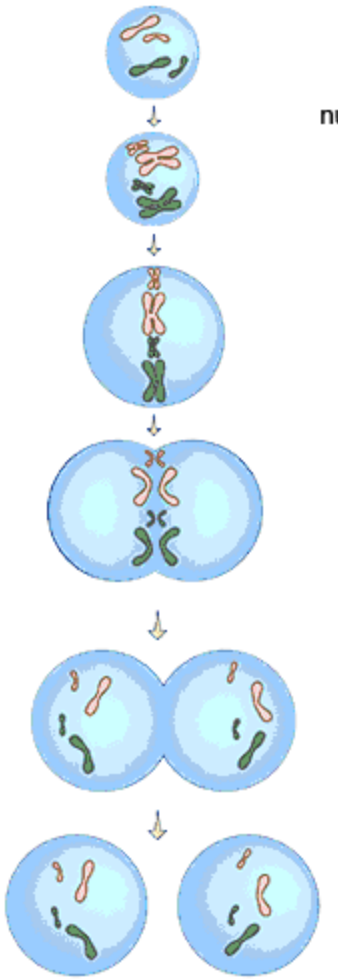
What is chemotherapy and how does it work?

Chemotherapy is used to describe medications that treat cancer. In order to understand how these medications work, we need to understand a bit about tumor cells. Tumors are made up of cells that are reproducing at abnormally high rates. Normal cells know to stop reproducing (or dividing) when they come into contact with other cells. In the case of a tumor, this stop mechanism is missing, causing cells to continue to divide over and over. The RNA or DNA of a cell tell it how to replicate itself, and classic chemotherapy (which excludes immunotherpeutics and biological response modifiers) works by destroying this RNA or DNA. The more rapidly the tumor cells are replicating, the better chemotherapy is able to kill the cells.

Some chemotherapy agents are able to kill a cell during any phase of the cycle (these are called cell-cycle nonspecific), others are only able to kill during a specific phase and are unable to work in the resting phase (called cell-cycle specific). By giving cell-cycle specific agents at multiple time points, they are able to reach the maximum number of cells in the particular phase they affect. Therefore, these are most effective when given in divided doses (over multiple days or time points, for example: once a day for 5 days or every three hours for 4 doses) or by continuous infusion. Cell-cycle nonspecific drugs act against cancer cells at any phase of the cell cycle, including the resting phase. Cell-cycle nonspecific drugs are most effective when given in bolus doses (for example, over 20 minutes once). Cell death may not take place at the exact time the chemotherapy is given. Often a cell must undergo several divisions before it ultimately dies. Because not all the cancer cells die after a chemotherapy treatment, repeated doses are used to continue to reduce the number of cells.

Side effect

- Although chemotherapy is given to kill cancer cells, it also can damage normal cells. The normal cells most likely to be damaged are those that divide rapidly, for instance:
- Bone marrow/blood cells
- Cells of hair follicles
- Cells lining the digestive tract
- Cells lining the reproductive tract

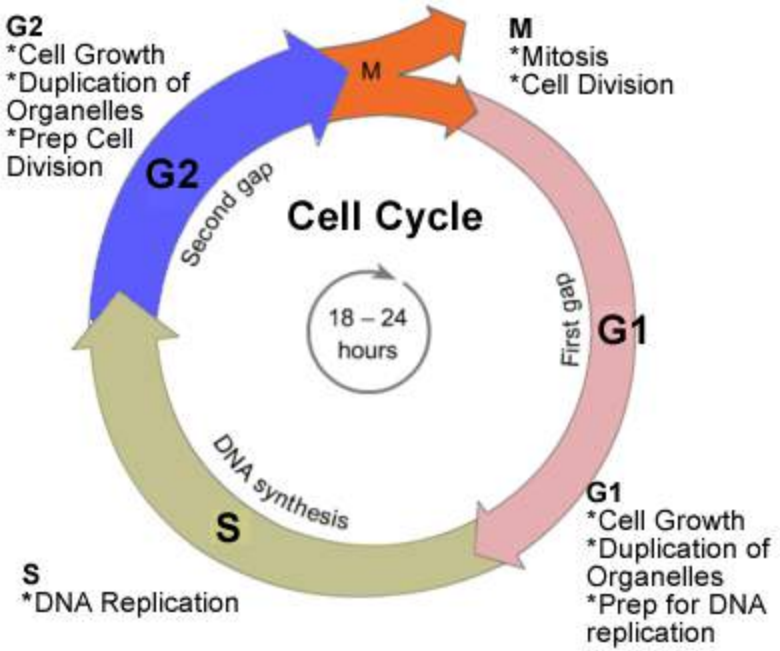


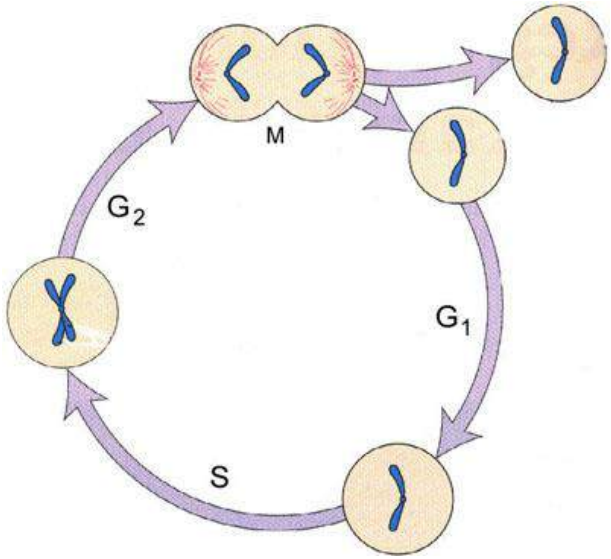
Chromosomes in nucleus are copied

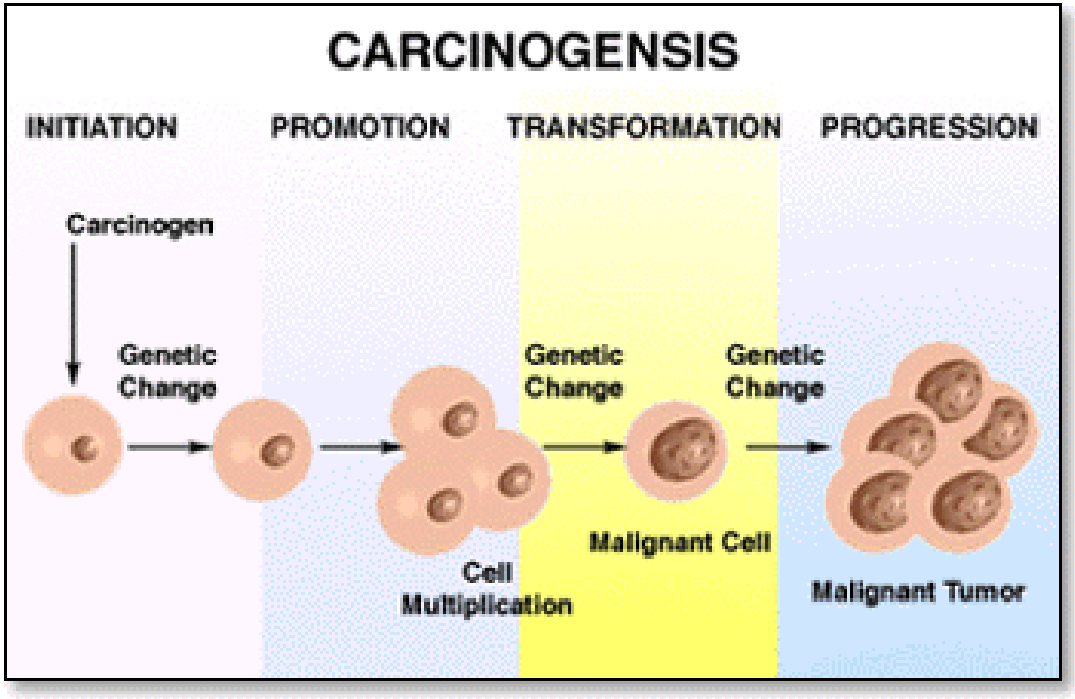
Chromatids pulled apart and moved towards poles

Chromosomes separate

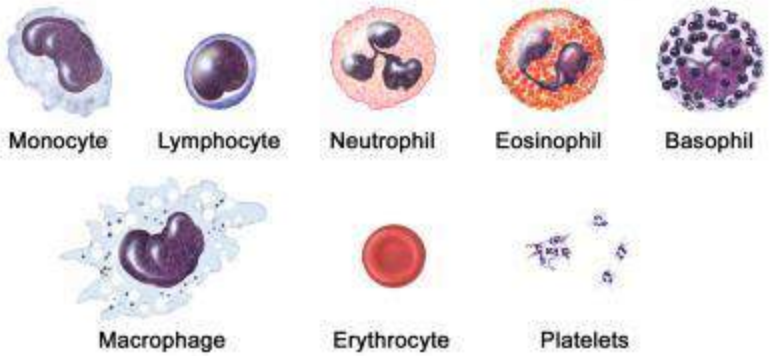
Cell divides






CARCINOGENSIS
INITIATION
PROMOTION
TRANSFORMATION
PROGRESSION
Carcinogen
Genetic Change
Genetic Change
Genetic Change
Cell Multiplication
Malignant Cell
Malignant Tumor

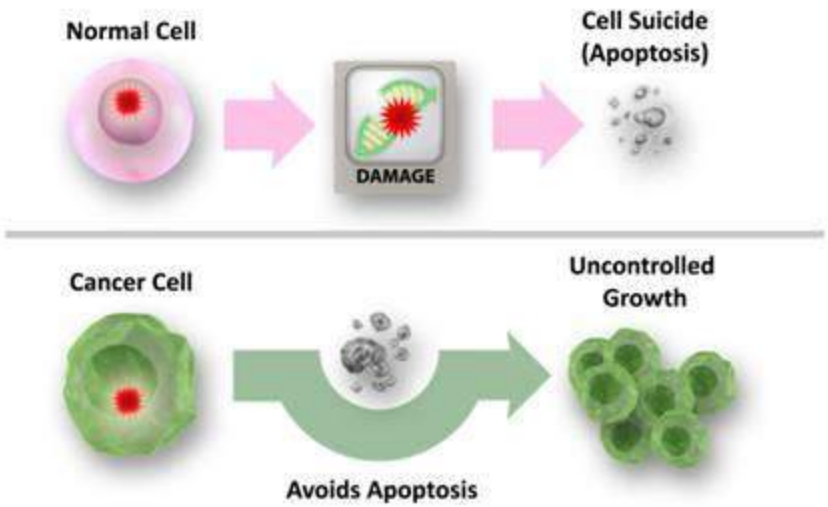
Blood Cells



Some common side effects from chemotherapy are
fatigue, nausea, vomiting, decreased blood cell counts, hair loss, mouth sores, and pain.

What causes side effects?

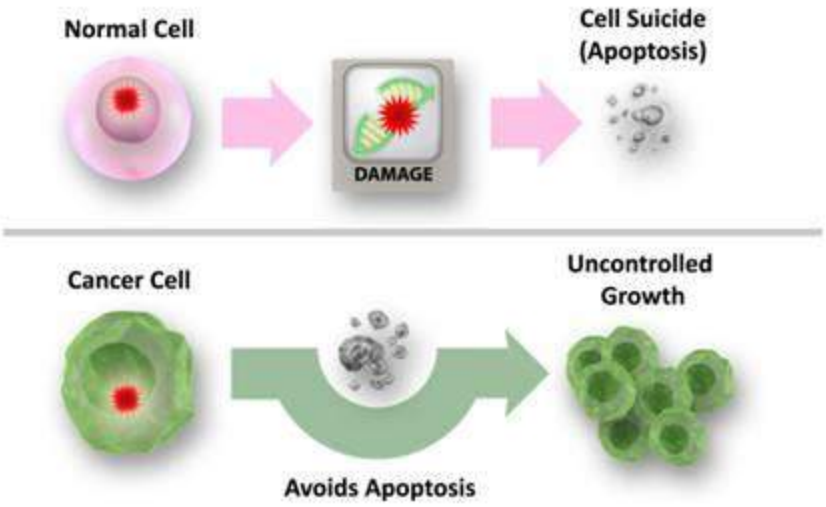
Chemotherapy is designed to kill fast-growing cancer cells. But it can also affect healthy cells that grow quickly. These include cells that line your mouth and intestines, cells in your bone marrow that make blood cells, and cells that make your hair grow. Chemotherapy causes side effects when it harms these healthy cells.

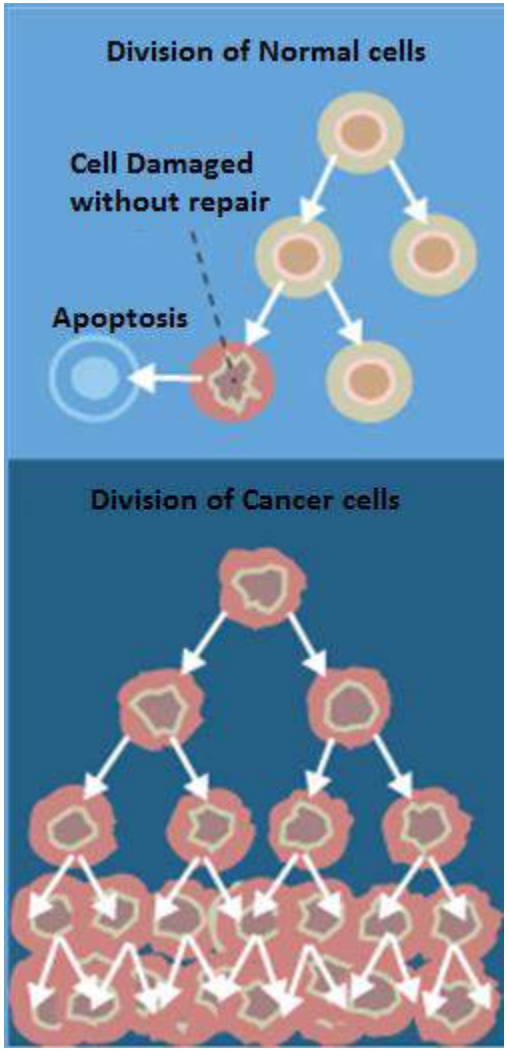

Normal Cell
DAMAGE
Cell Suicide
(Apoptosis)
Cancer Cell
Avoids Apoptosis
Uncontrolled
Growth

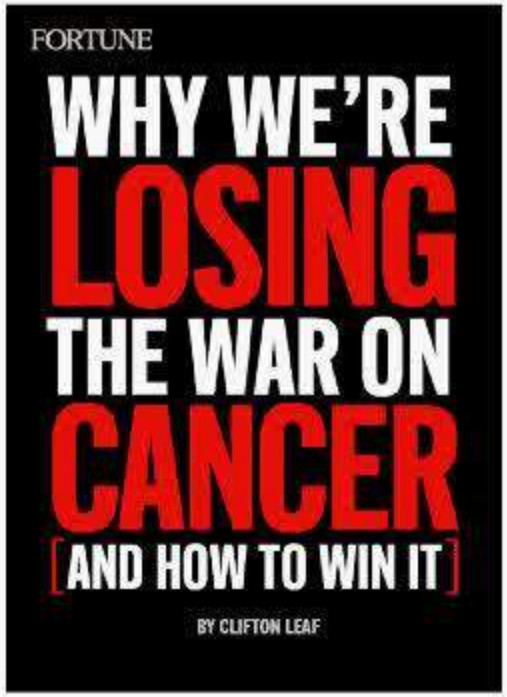
Normal cell

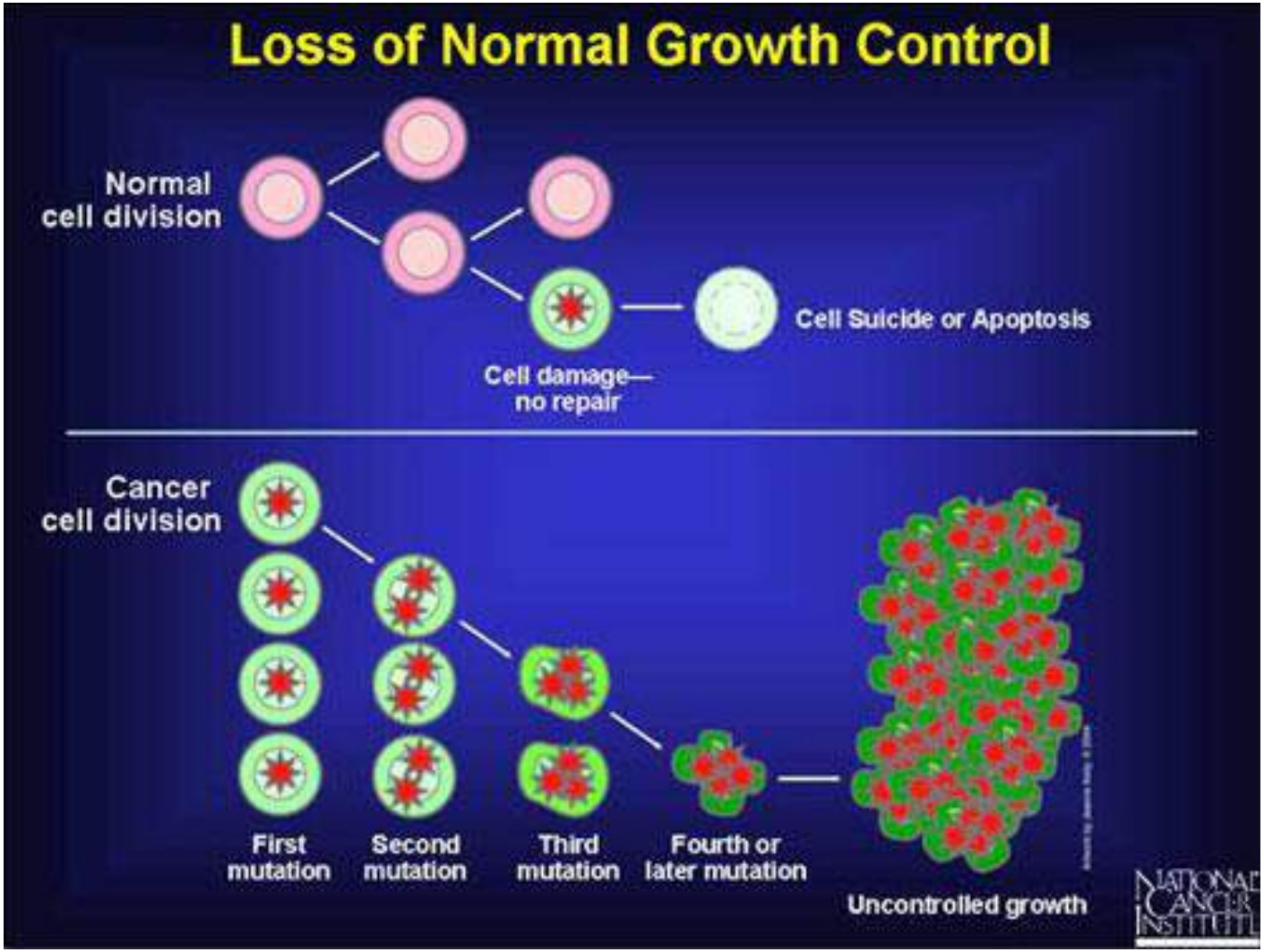
Example of one type of abnormal or cancerous cell

Cancer cell

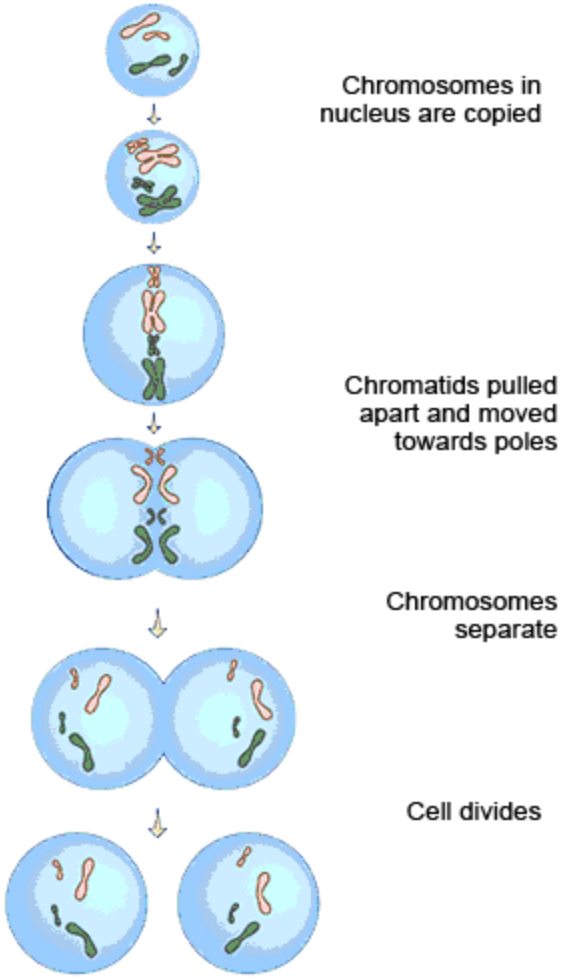

Normal Cell
DAMAGE
Cell Suicide
(Apoptosis)
Cancer Cell
Avoids Apoptosis
Uncontrolled
Growth


Division of Normal cells
Cell Damaged
without repair
Apoptosis
Division of Cancer cells


FORTUNE
WHY WE'RE
LOSING
THE WAR ON
CANCER
[AND HOW TO WIN IT]
BY CLIFTON LEAF


Loss of Normal Growth Control
Normal cell division
Cell Suicide or Apoptosis
Cell damage—no repair
Cancer cell division
First mutation
Second mutation
Third mutation
Fourth or later mutation
Uncontrolled growth
NATIONAL CANCER INSTITUTE

Chemotherapy how it works



PHY906

- PHY906 is based on the ancient Chinese herbal formula Scutellaria Decoction (Huang Qin Tang)
- Detoxifying since 220 AD. Huang Qin Tang (Scutellaria Decoction) is a simple modification of the #1 formula in Shang Han Lun style Chinese herbalism

- *Scutelleria baicalensis Georgi (*Huang Qin :黄芩)
- *Glycyrrhiza uralensis Fisch (*Gan Cao :甘草)
- *Paeonia lactiflora Pall (*Bai Shao :白芍
- *Ziziphus jujuba Mill* (Da Zao :大棗)

at a ratio of 3:2:2:2

First-in-human phase II trial of the botanical formulation PHY906 with capecitabine as second-line therapy in patients with advanced pancreatic cancer.

http://www.ncbi.nlm.nih.gov/pubmed/24297682