

A scenic view of a Japanese garden. In the foreground, a wooden railing with a dark metal post and cap runs along a paved walkway. Beyond the railing is a calm pond reflecting the sky and surrounding trees. The garden is filled with various trees, including a large weeping willow on the left and several cherry blossom trees in full bloom, displaying shades of pink and white. The background shows more lush greenery and a hillside under a bright, slightly overcast sky.

# Mechanisms of MRN-100 Against Gastric Cancer

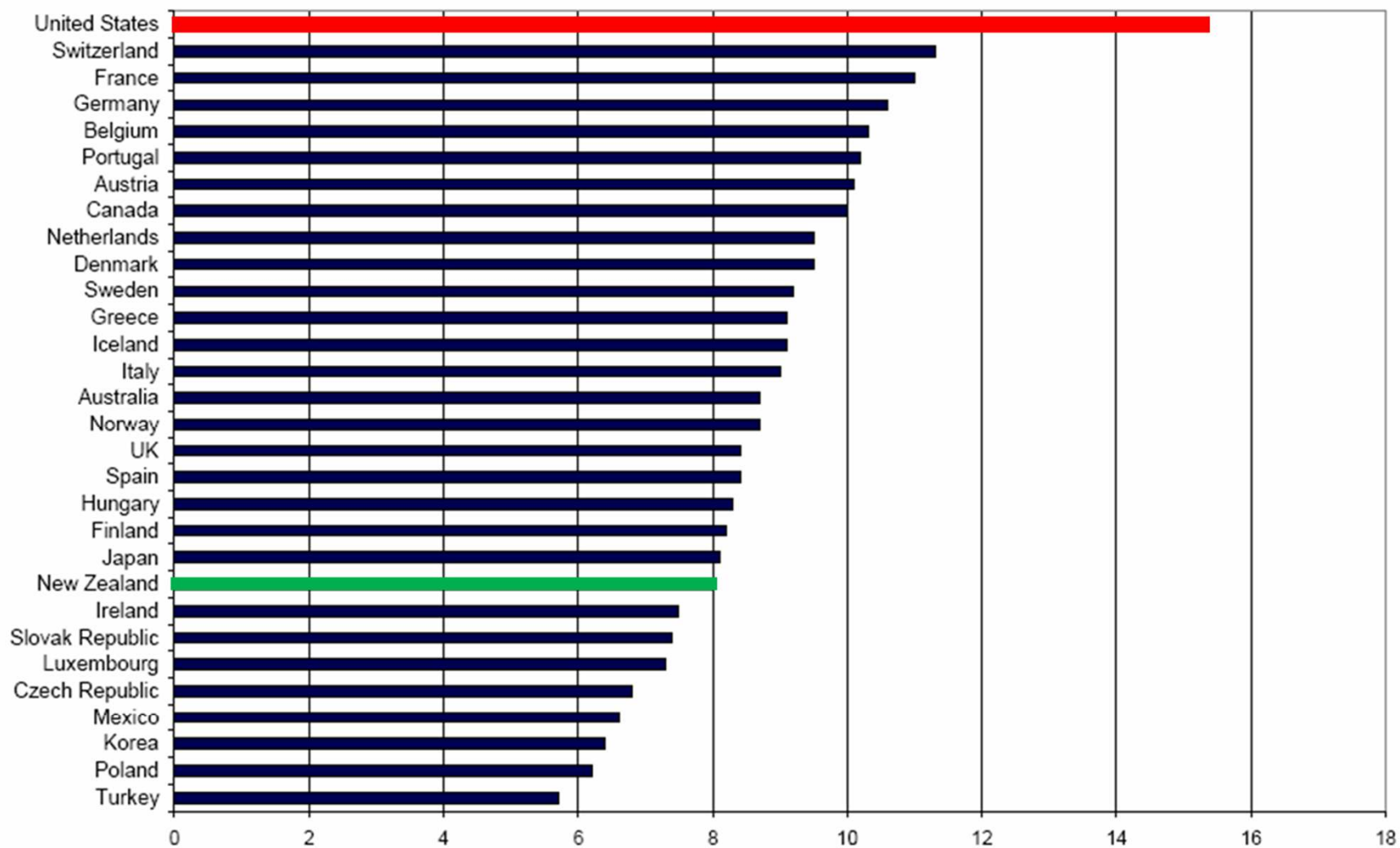
**MAMDOOH GHONEUM, Ph.D.**

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UCLA, Department of Neurobiology*

# Outline

- 1. Healthcare Systems Worldwide**
- 2. Cancer History and Statistics**
- 3. Esophageal Cancer**
  - A) Histopathology
  - B) Number of cancer cell foci
- 4. Gastric Cancer**
  - A) Histopathology
  - B) Number of cancer cell foci
- 5. Mechanisms of protection against cancer**
  - A) Antioxidant Activity
  - B) Immunomodulatory Effect

## Healthcare Spending as % GDP (Gross Domestic Product)



Source: Organization for Economic Cooperation and Development, OECD Health Data, 2008 (Paris: OECD, 2008).

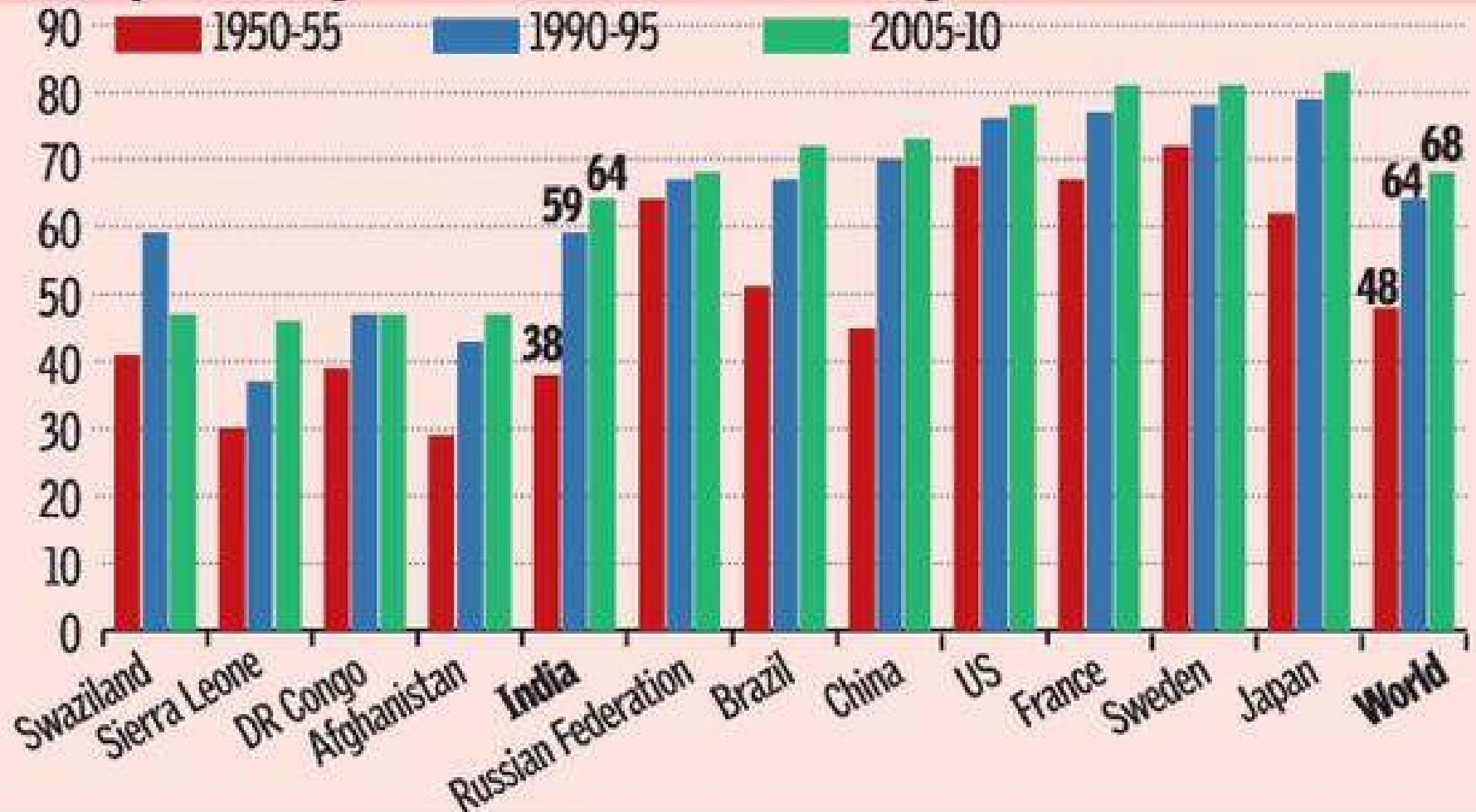
Note: For countries not reporting 2006 data, data from previous years is substituted.

**Gross domestic product (GDP) is the market value of all officially recognized final goods and services produced within a country in a year, or over a given period of time. GDP per capita is often used as an indicator of a country's material standard of living.**

# Infant Mortality 2009 (Per 1,000 Live Births)

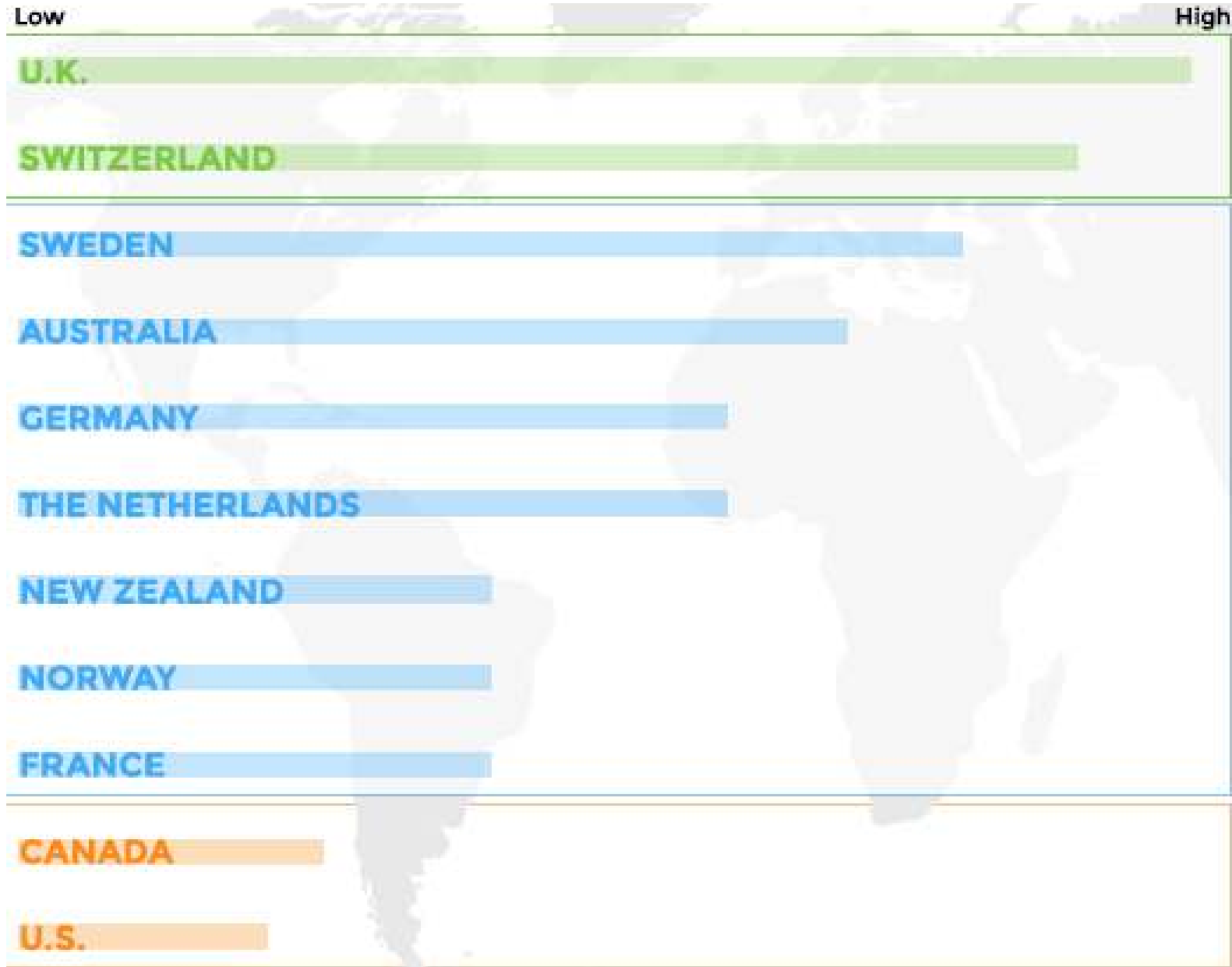


## Life expectancy in selected countries, years



Life expectancy in the US slowly increases, while in Japan the life expectancy steadily increases, and is the highest in the world at the moment

# Overall Satisfaction of Health Care (2013)



# Commonwealth Fund Study

- **The main way the U.S. differs from other industrialized countries is the absence of universal health insurance coverage**

# The U.S. Health System is “challenged” on many fronts.....

- Compared to other industrialized countries the U.S. health care system .....
- Is more expensive: >\$2.0 trillion/year, 18% GDP
- Has the highest inflation (> 8%/yr)
- Does not produce the best outcomes
- Is not rated highly by its citizens or doctors
- Does not cover all of its citizens.... ~15% uninsured (~46 Million)



## Preventive Care

**We should think of  
new therapies for  
the purpose of  
preventive care**

# **MRN-100:**

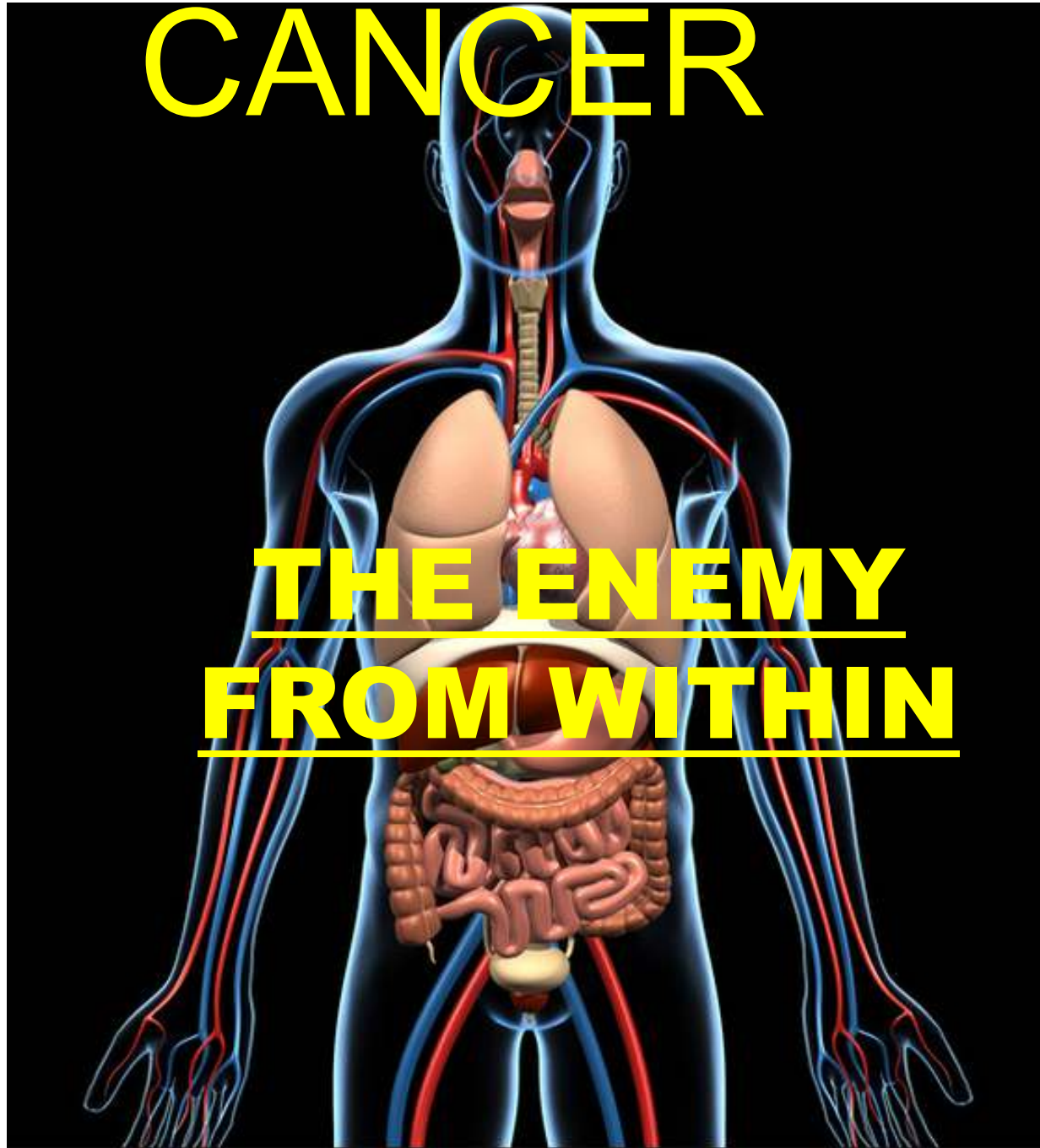
**MRN-100 may be a novel adjuvant for the treatment of gastric or esophageal cancers.**

**It is characterized as:**

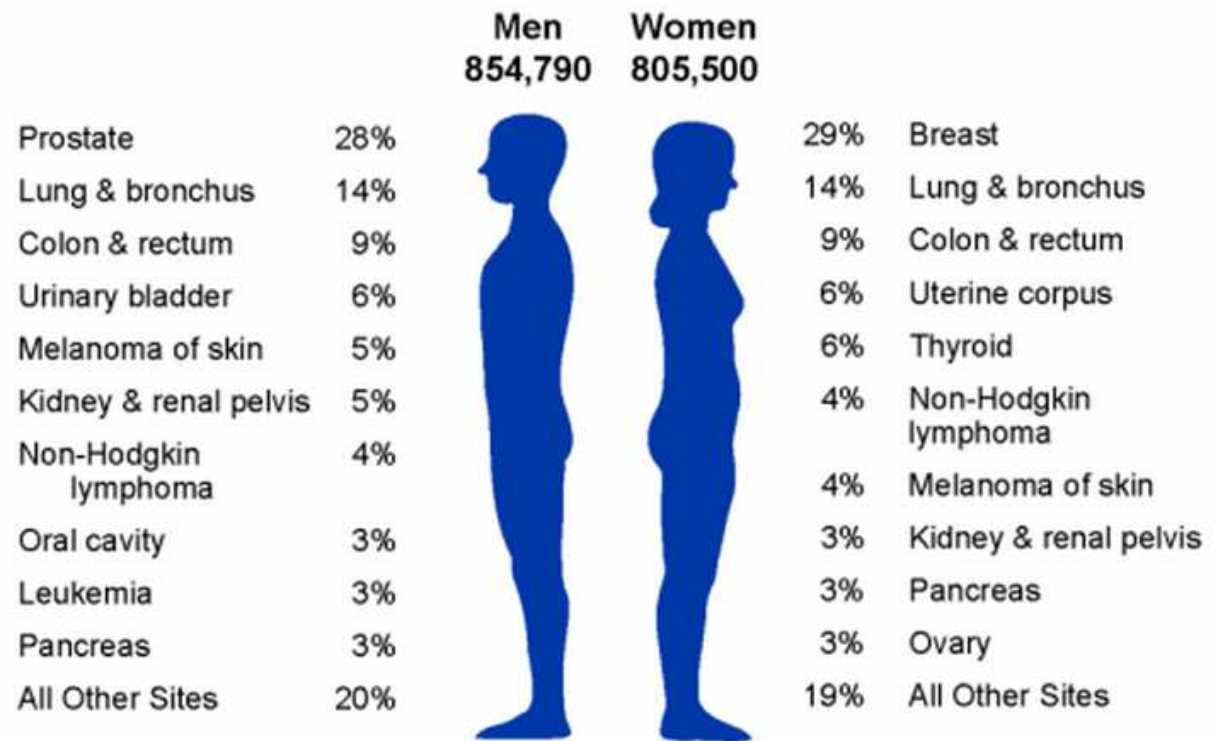
- 1- Highly effective**
- 2- Safe**
- 3- Low cost**

# CANCER

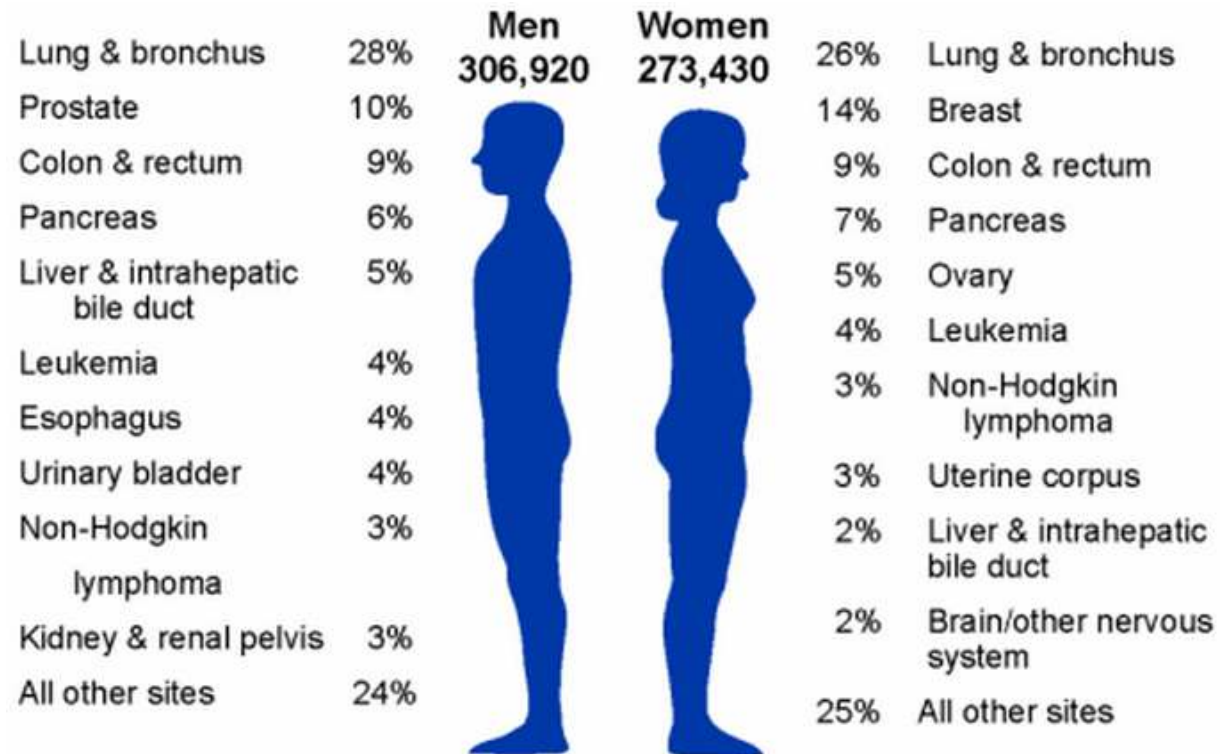
THE ENEMY  
FROM WITHIN



## Estimated New Cancer Cases in the US in 2013



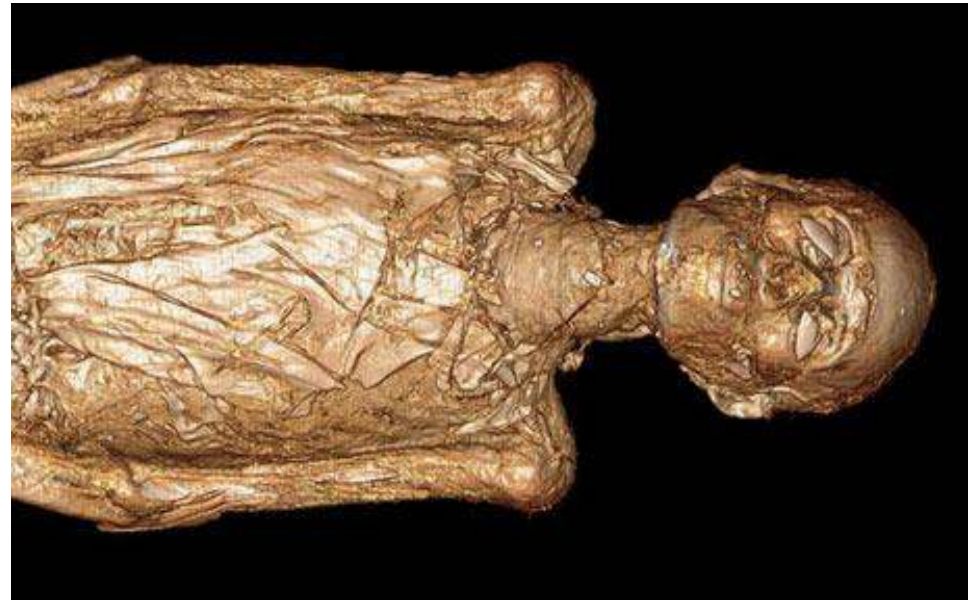
## Estimated Cancer Deaths in the US in 2013



# Reasons

1. Smoking
2. Diet
3. Stress
4. Genetic
5. Hepatitis C Virus
6. Pollution

# Lack of Effective Cancer Treatment Since 1500 BC



- The world's oldest recorded case of breast cancer hails from ancient Egypt in 1500 BC.
- It was recorded that there was no treatment for the cancer, only palliative treatment.



# U.S. Cancer Deaths

	2005	2013
Daily		1600
Yearly	570,280	580,350

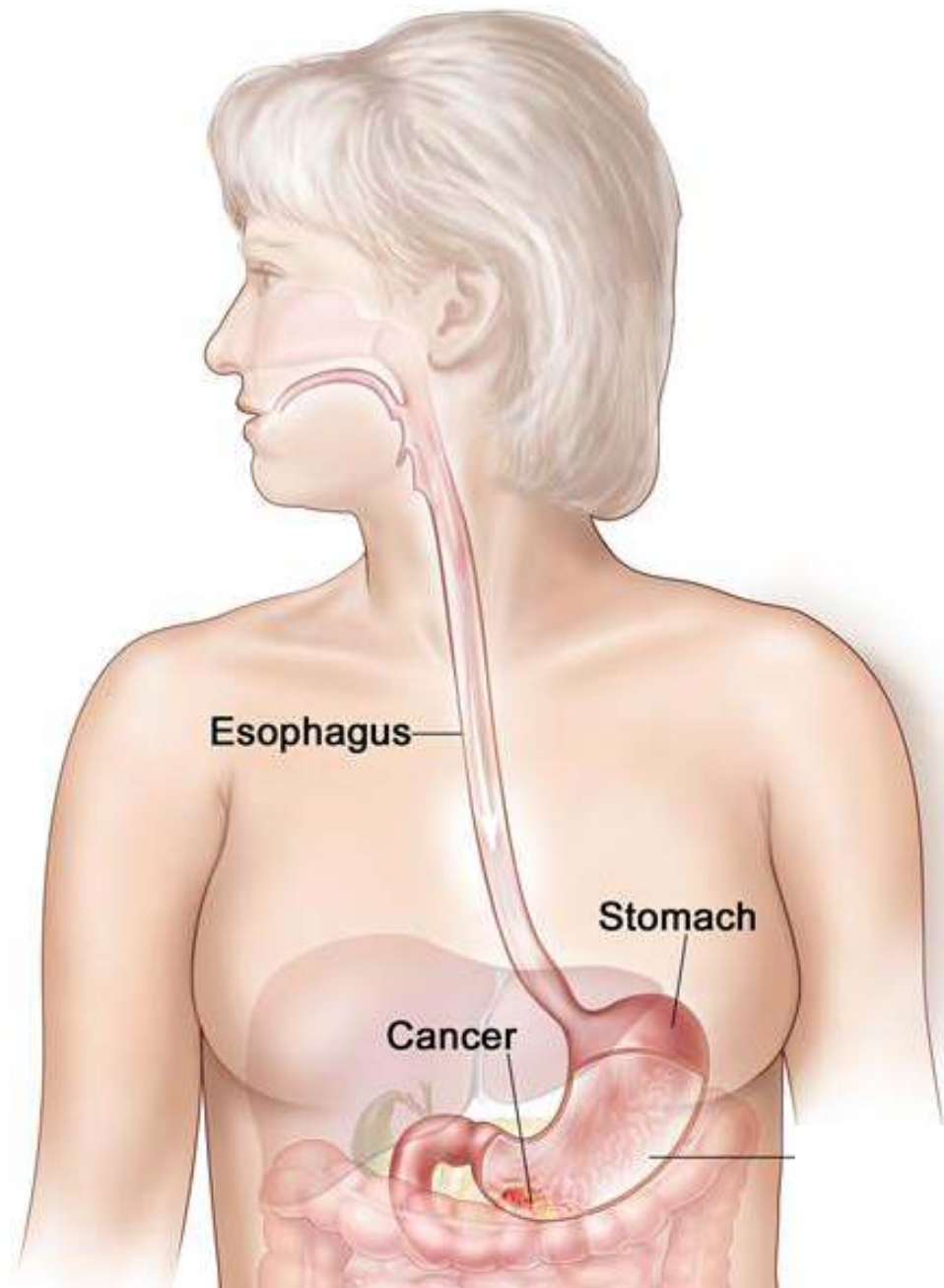


# 2008

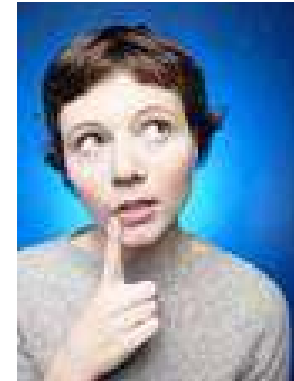
## NIH Estimation of Annual Cost of Cancer

- **Total cost: \$228.1 billion**
  - **Direct medical costs (total of all health expenditures): \$ 93.2 billion**
  - **Indirect morbidity costs (cost of lost productivity due to illness): \$ 18.8 billion**
  - **Indirect mortality costs (cost of lost productivity due to premature death): \$116.1 billion**

American Cancer Society. *Cancer Facts & Figures 2009*. Atlanta, GA. 2009.



# Do You Know ?



1. Gastric and esophageal cancers are two leading causes of cancer-related deaths throughout the world
2. The 5-year survival rates are 17% for esophageal cancer and 27% for gastric cancer (Howlader et al, 2013, de Martel et al, 2013).
3. In Japan in 2013, approximately 60,000 total people had gastric cancer and 17,500 new cases of esophageal cancer were diagnosed
4. In the United States in 2013, approximately 40,000 people were diagnosed with esophagus or stomach cancer

# Chemotherapy and Radiation Therapy

Exhibit an indiscriminate killing that involves cancer cells and many normal cells



**We should think  
of new therapies  
for the  
treatment of  
CANCER**

**Hydroferrate fluid, MRN-100,  
protects against chemical-induced  
gastric and esophageal cancer in  
Wistar rats.**

**Mamdooh Ghoneum<sup>1</sup>, Nariman K. Badr  
El-din<sup>2</sup>, Salma M. Abdel Fattah<sup>3</sup>, Deyu  
Pan<sup>1</sup>, and Lucilene Tolentino<sup>1</sup>**

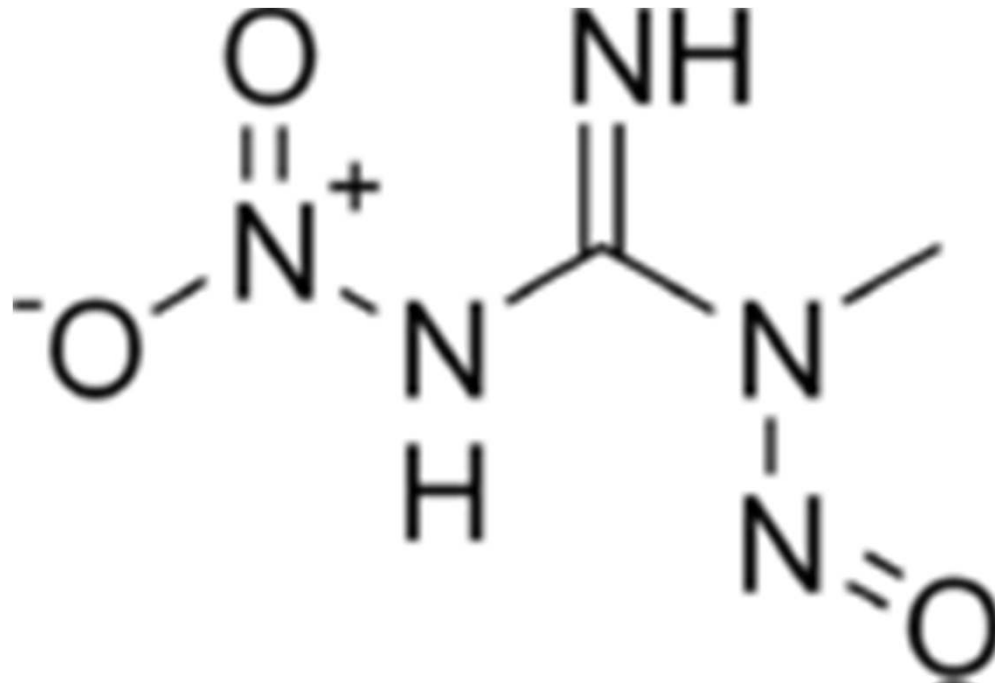
<sup>1</sup>Charles Drew University of Medicine and  
Science, Los Angeles, California, USA

<sup>2</sup>University of Mansoura, Mansoura, Egypt

<sup>3</sup>National Center for Radiation and Technology,  
Cairo, Egypt

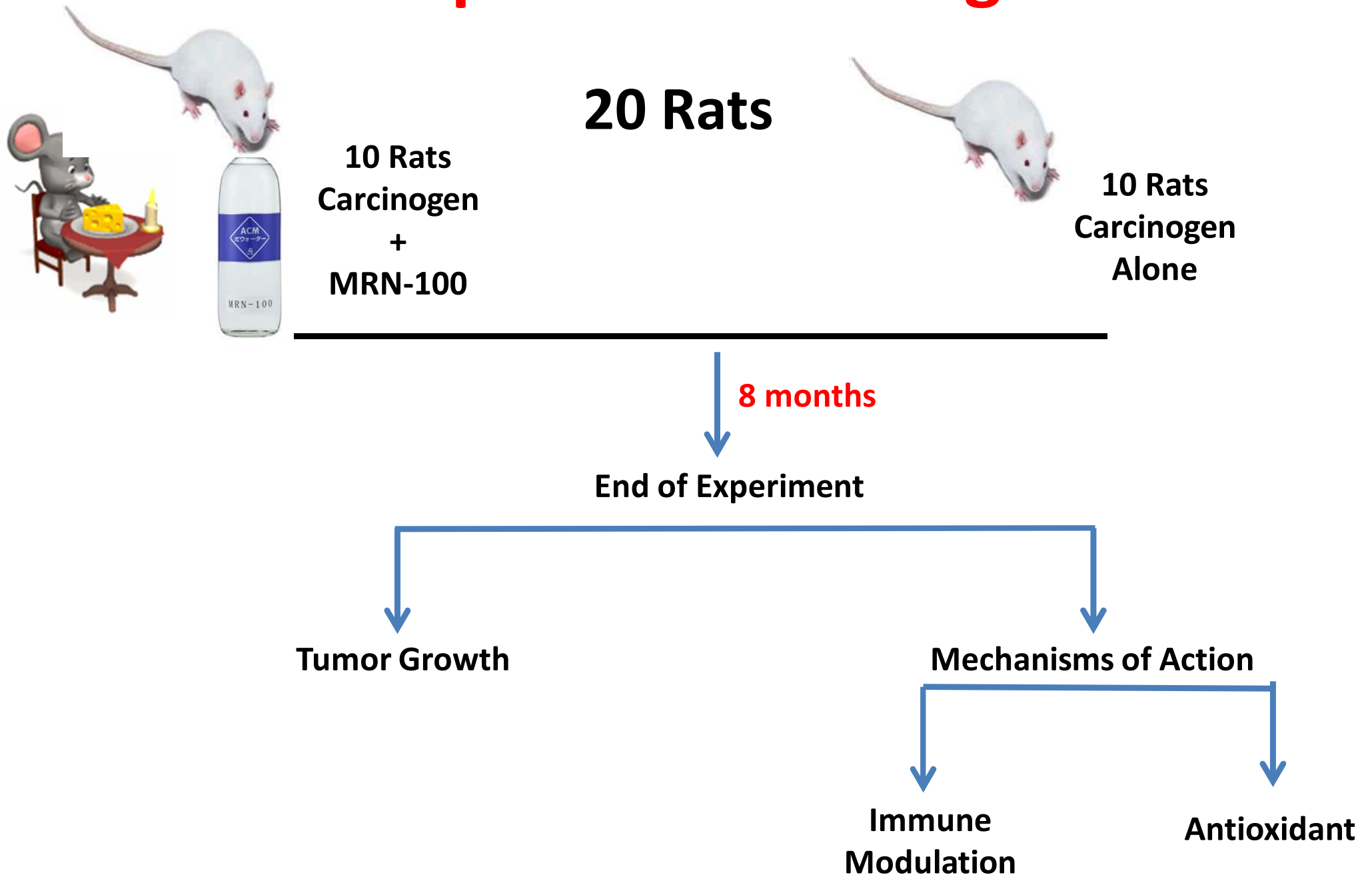
Carcinogen

**Methylnitrosoguanidine**  
**(MNNG)**





# Experimental Design



**14<sup>th</sup> Int. Conference of Functional Food Center (FFC)  
2<sup>nd</sup> Int. Academic Symposium for the Functional Food and  
Bioactive Compounds (ASFFBC)**

**14th International Conference of FFC - Second International Symposium of ASFFBC:  
Functional Foods and Bioactive Compounds in the Management of Chronic Inflammation:**

*Science and Practical Application*

**August 20-22, 2013,**

*University of California, Los Angeles (UCLA), USA*



# UCLA









**Hydroferrate fluid, MRN-100, provides protection against chemical-induced gastric and esophageal cancer in Wistar rats**

**RESULTS**

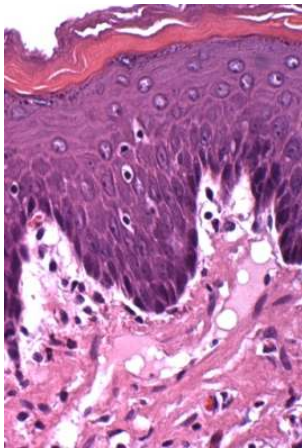
# Induction of Esophageal and Gastric Cancer



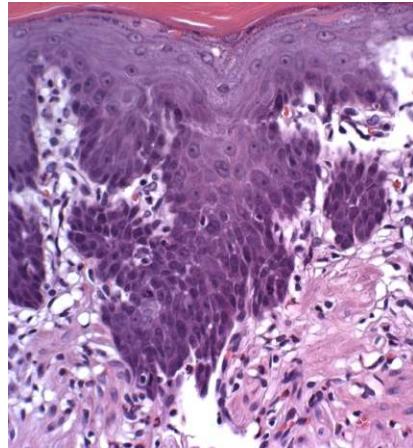


# Stages of esophageal cancer

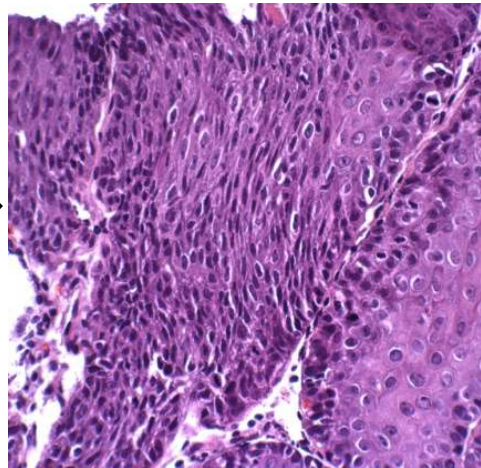
Normal



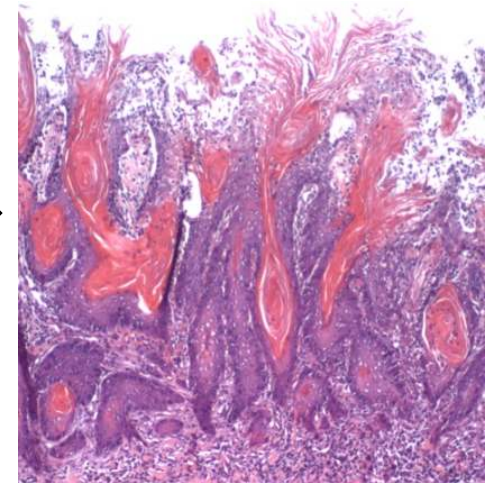
1



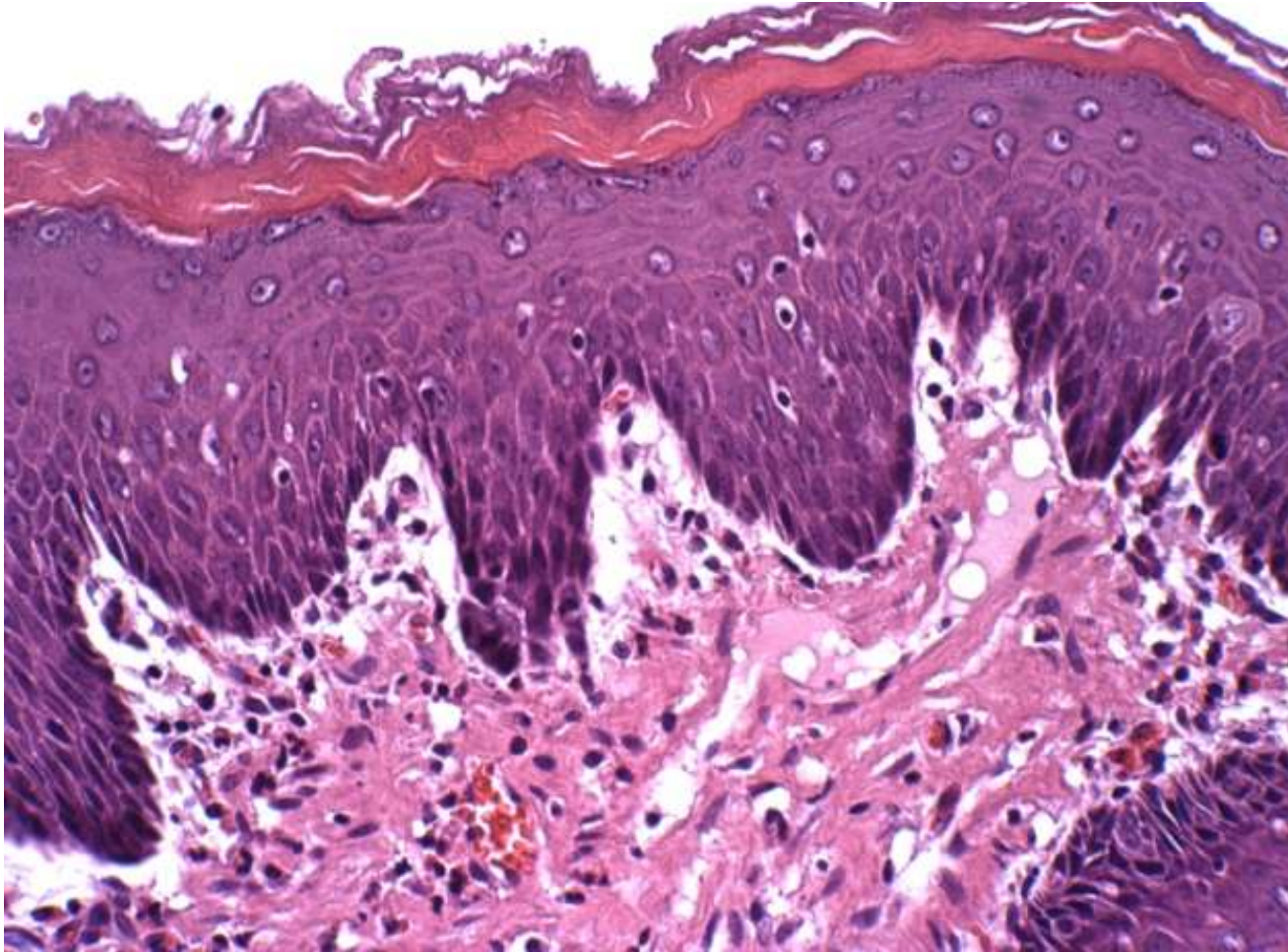
2



3

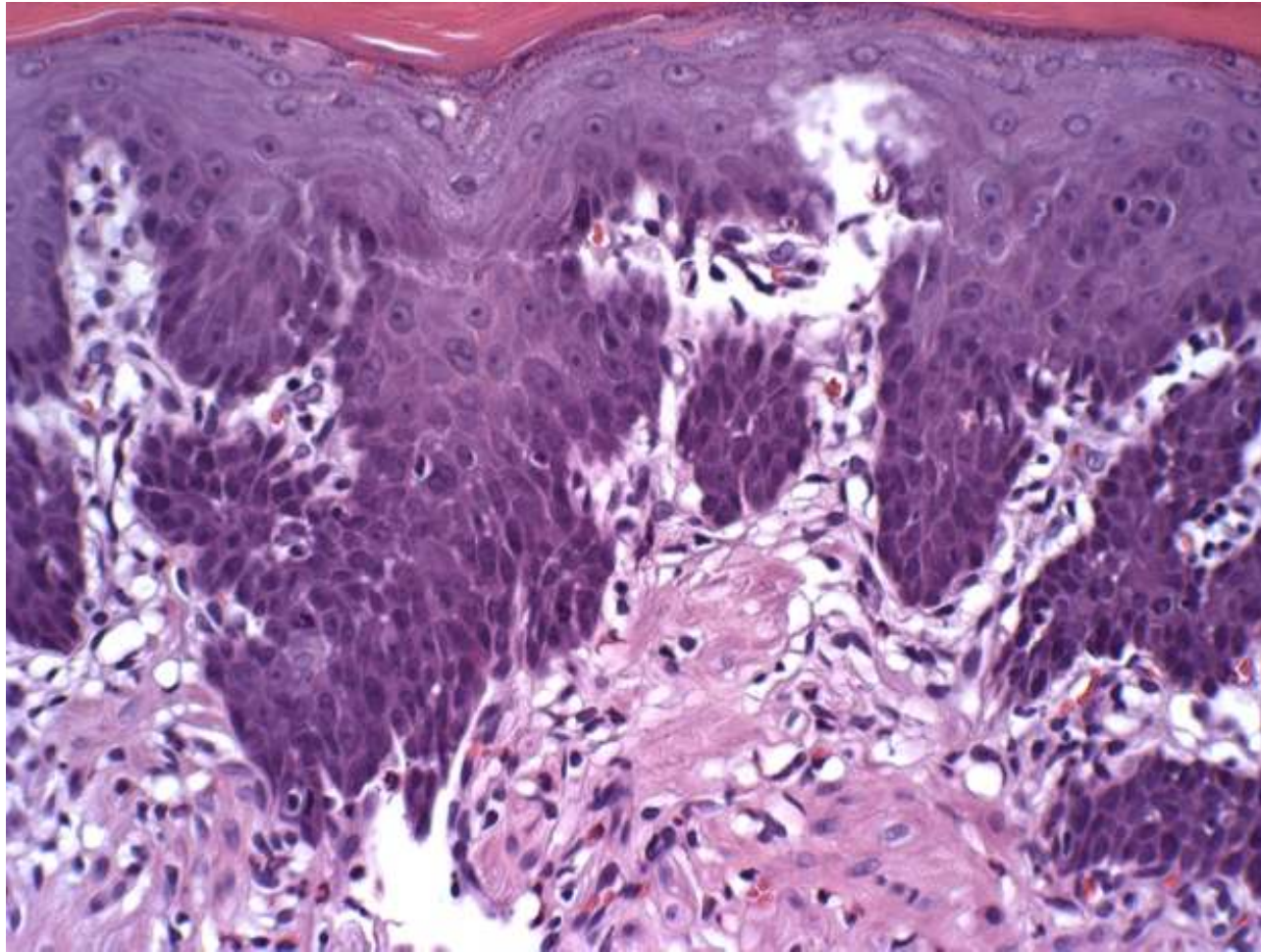


# Normal or healthy esophagus



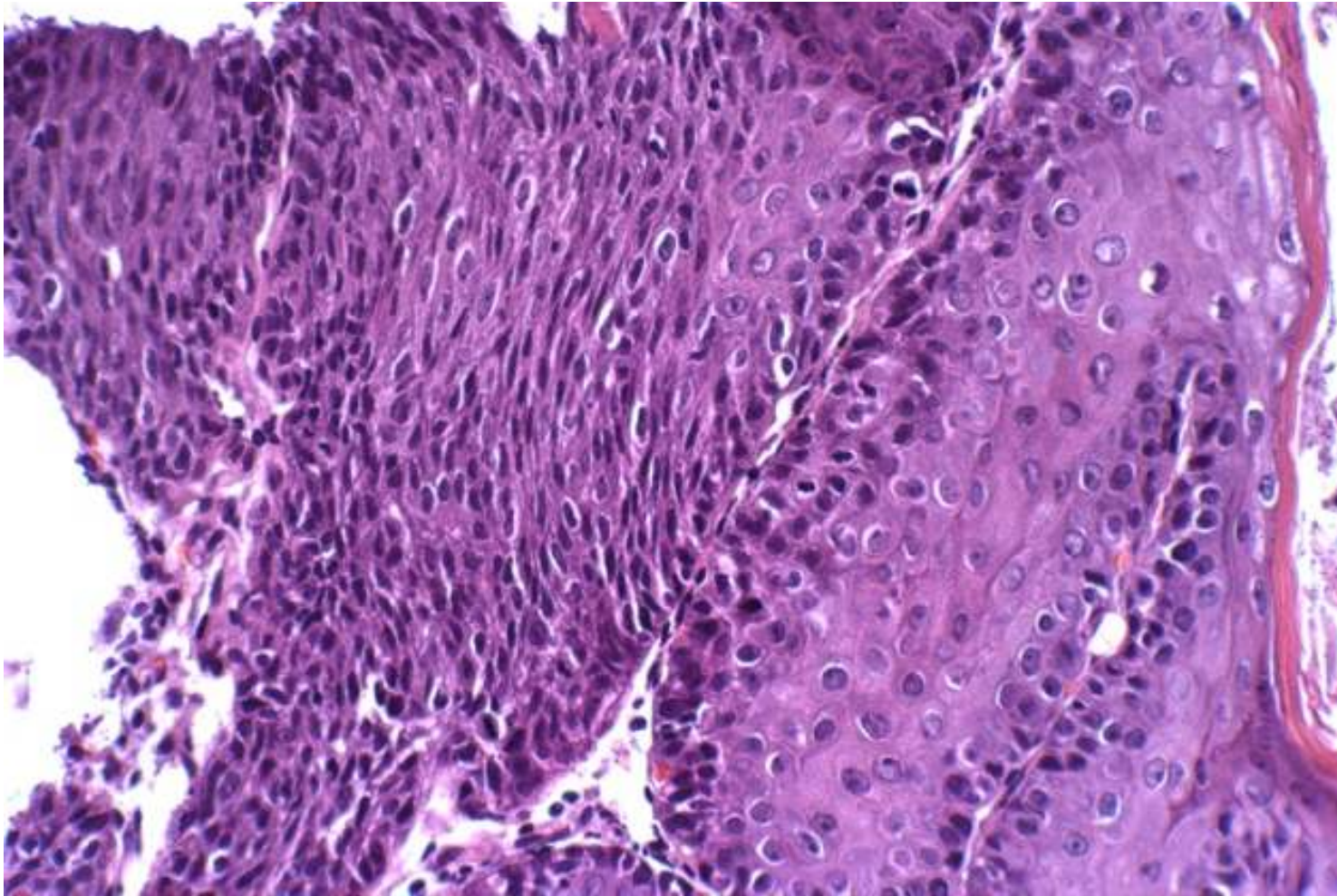
Esophageal mucosa (foregut) showing hyperkeratosis and squamous hyperplasia. Intraepithelial lymphocytes and stromal lymphocytes and eosinophils are present.

# 1-mild squamous dysplasia



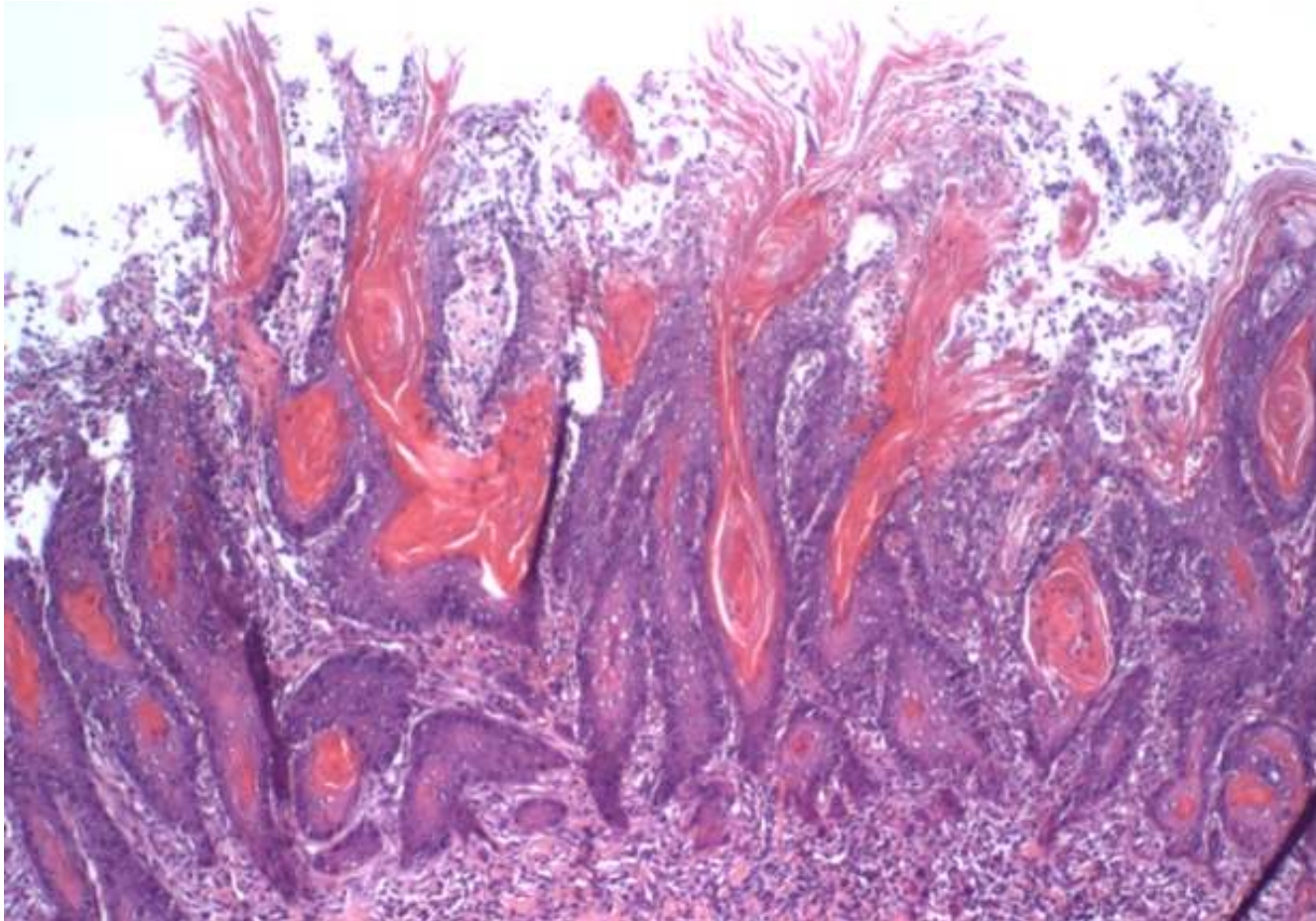
Esophageal mucosa showing hyperkeratosis, squamous hyperplasia and mild squamous dysplasia. Intraepithelial lymphocytes and stromal lymphocytes and eosinophils are present.

# 2-high grade squamous dysplasia



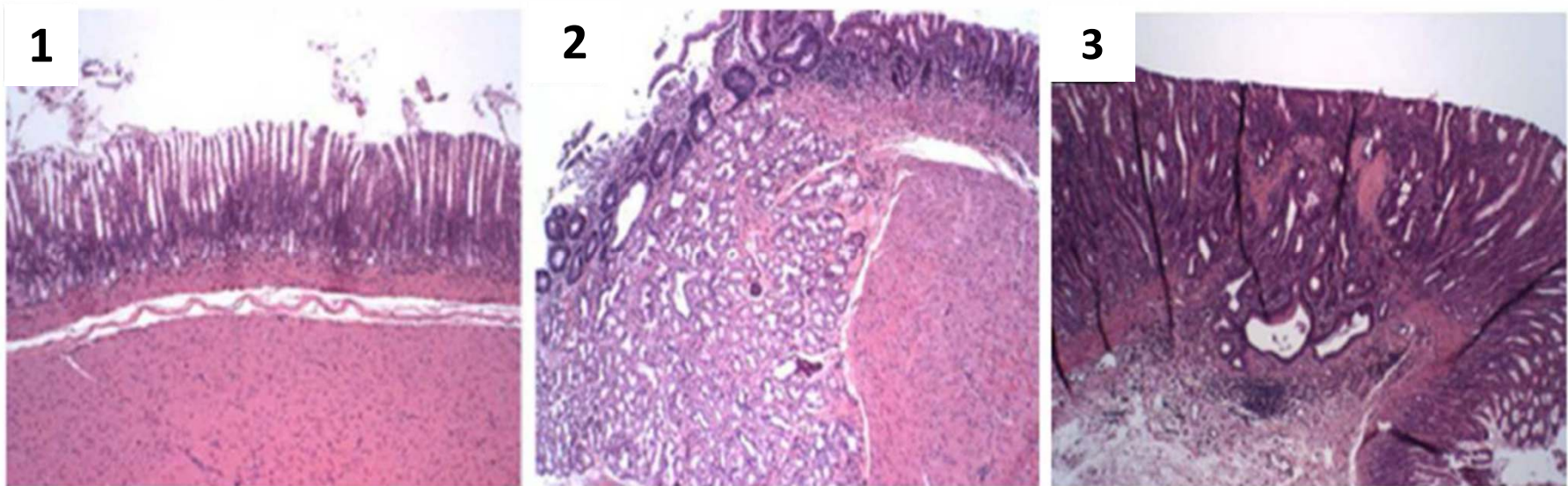
Esophageal mucosa showing hyperkeratosis, squamous hyperplasia, and high grade squamous dysplasia

# 3- squamous cell carcinoma.



Esophageal mucosa showing invasive well-differentiated keratinizing squamous cell carcinoma.

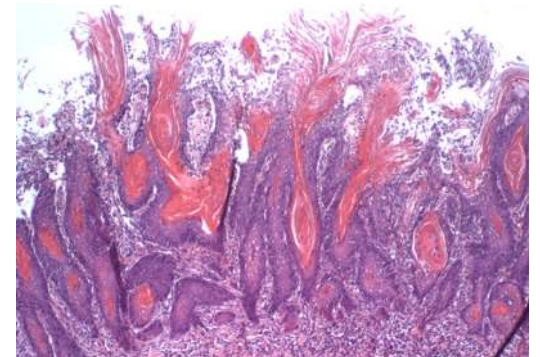
# Stages of Gastric cancer



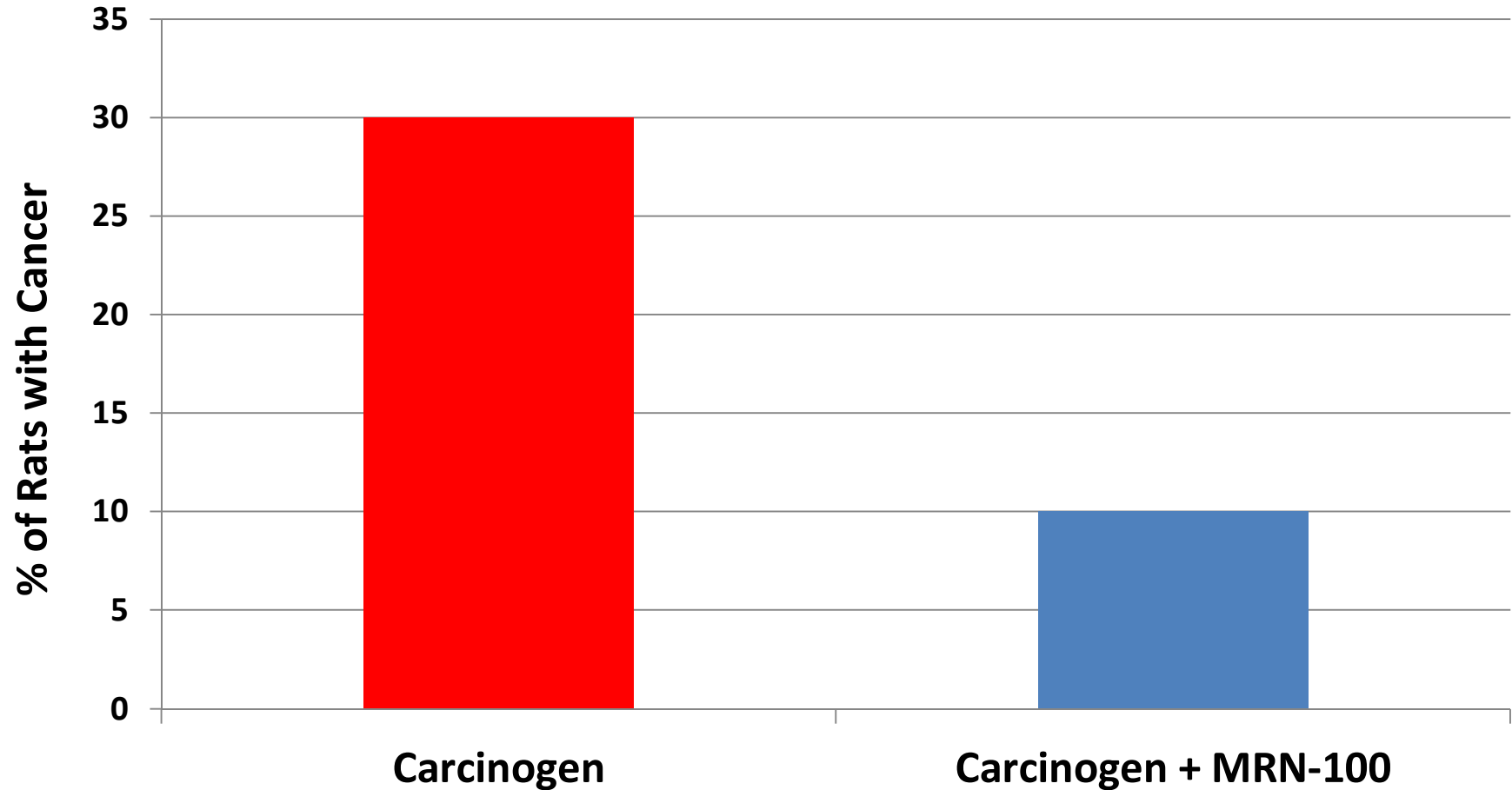
# MRN-100 Protects Against Gastroesophageal Cancer

**1:**

**Evidence from tumor tissues**



# % Gastroesophageal Cancer

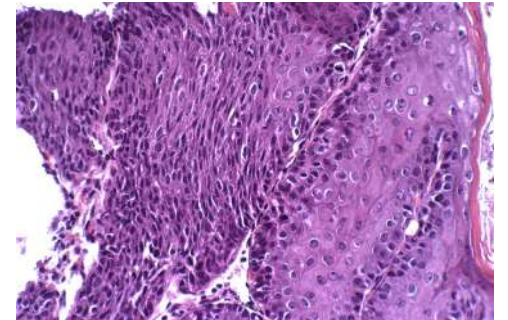




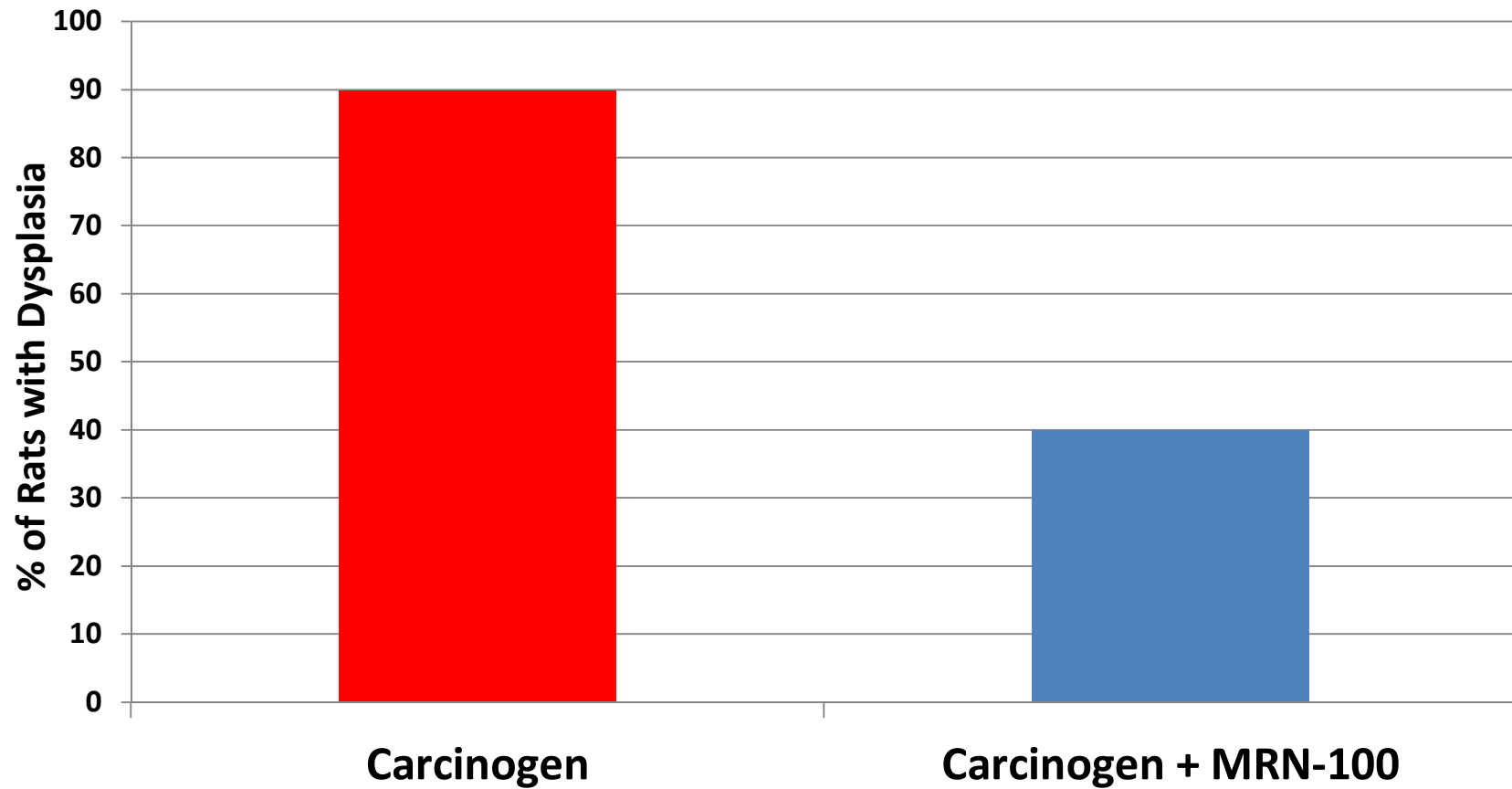
# MRN-100 Protects Against Gastroesophageal Cancer

**2:**

**Evidence from Tissue Dysplasia**



# % Gastroesophageal Dysplasia

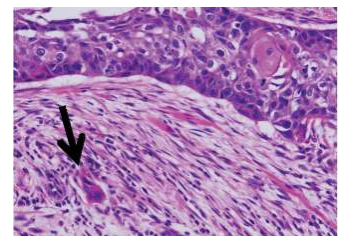


# MRN-100 Protects Against Gastroesophageal Cancer

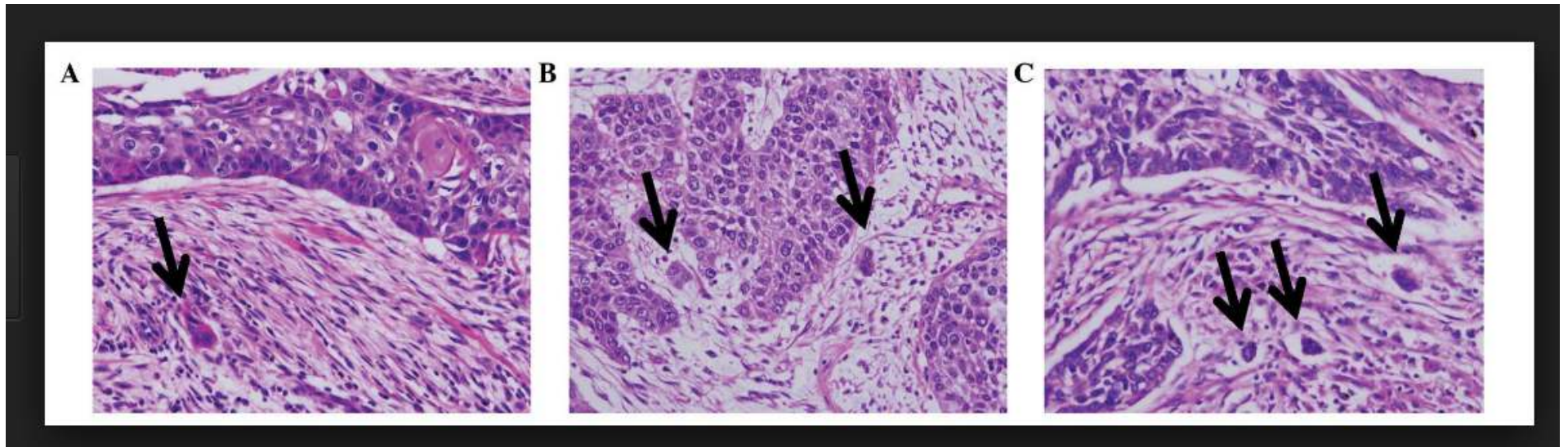
## 3- New Data

**Evidence from the cancer cell level  
(foci)**

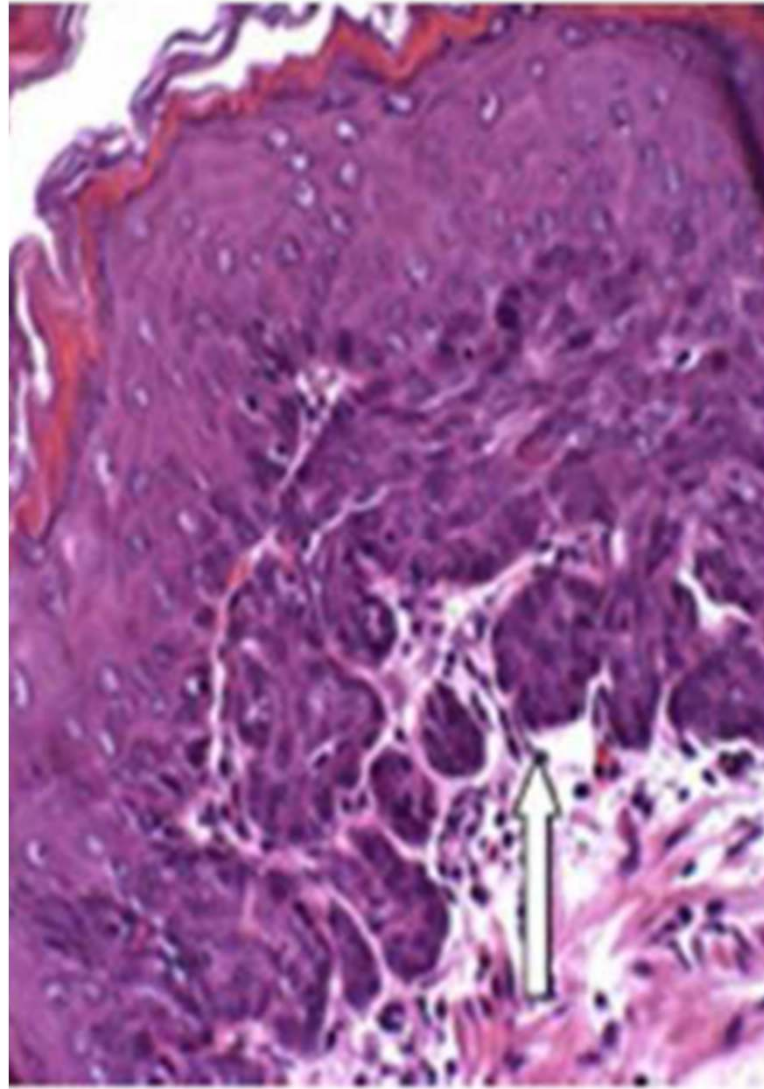
**\*The study of foci is very important because it is one of the prerequisites of developing cancer, such as family history\***

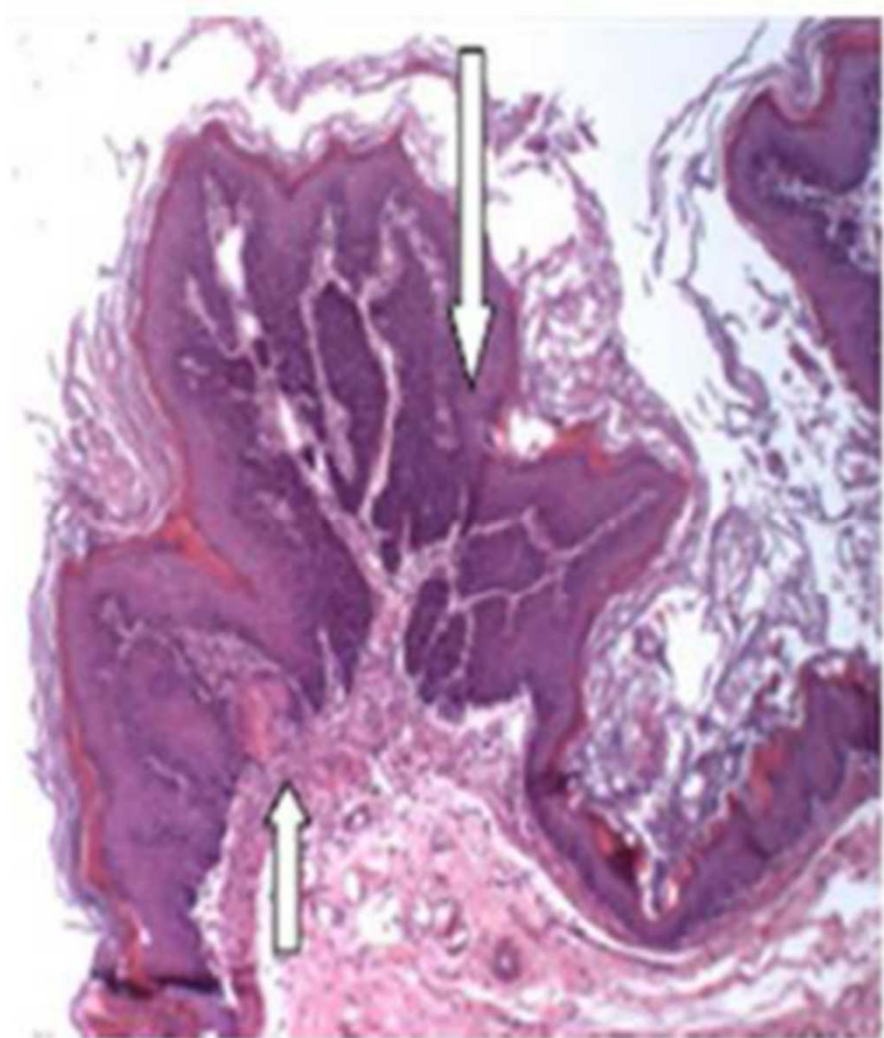


**(foci)**

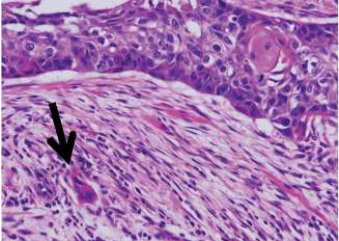
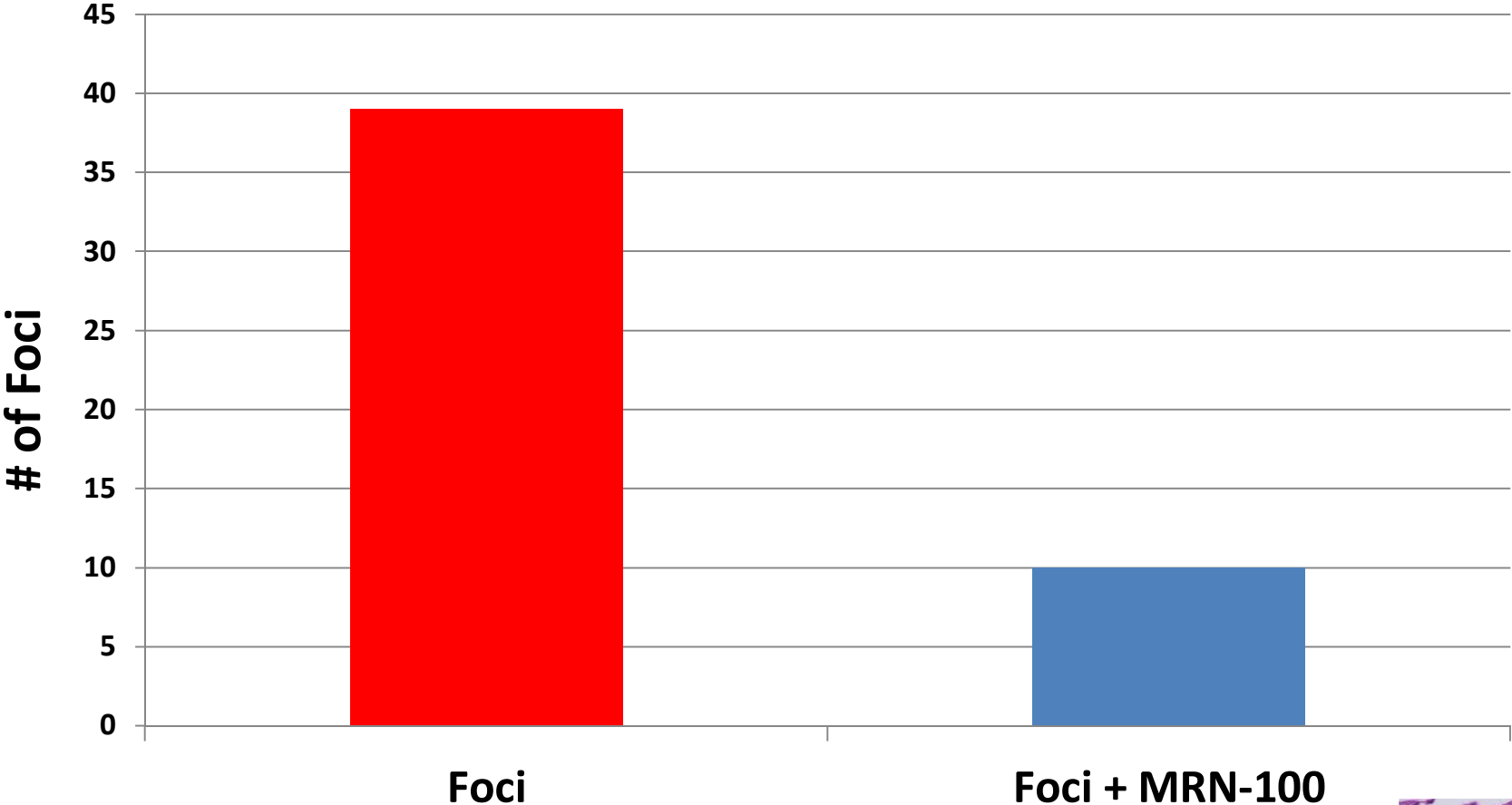


**Tumor budding is defined as single cancer cells and/or clusters composed of up to four cancer cells**





# MRN-100 Suppresses Number of Foci



# Extent of dysplasia and cancer (Number of Foci)

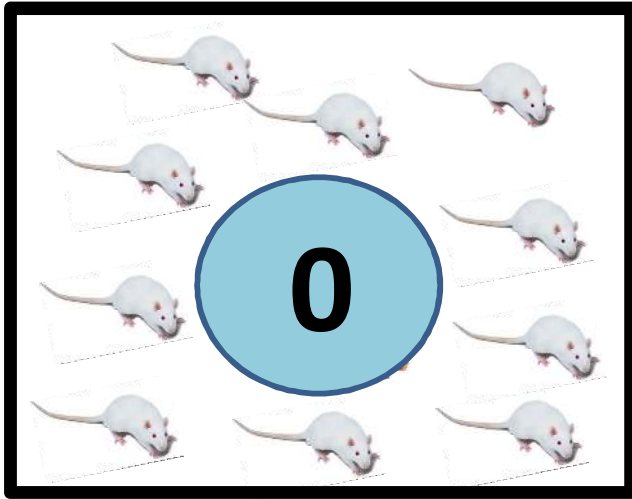
GROUP	NO. OF RATS	NO. OF TISSUES	NO. OF FOCI						
			ESOPHAGUS				GASTRIC		
			SQUAMOUS DYSPLASIA		SQUAMOUS CELL CARCINOMA	TOTAL RATS WITH FOCI	GLANDULAR DYSPLASIA	ADENO-CARCINOMA	TOTAL RATS WITH FOCI
			MILD	SEVERE					
<b>CONTROL</b>	7	14	0	0	0	0/7	0	0	0/7
<b>MRN-100</b>	9	18	0	0	0	0/9	0	0	0/9
<b>CARCINOGEN</b>	10	20				9/10			2/10
Rat #3			10	2	3		1	1	
Rat #4			8	5	0		1	1	
Rats #2, 5-10			1	0	0		0	0	
Rat #1			0	0	0		0	0	
<b>CARCINOGEN + MRN-100</b>	10	20				4/10			0/10
Rat #5			2	6	1		0	0	
Rats #1, 2, 4			1	0	0		0	0	
Rats #3, 6-10			0	0	0		0	0	

**Table I.** Number of rats in each group with variable degree and extent of dysplasia and cancer.

Fishers exact test shows significant difference between carcinogen group and carcinogen plus MRN-100 group ( $p < 0.01$ ).



# Esophogus: Total Rats with Foci

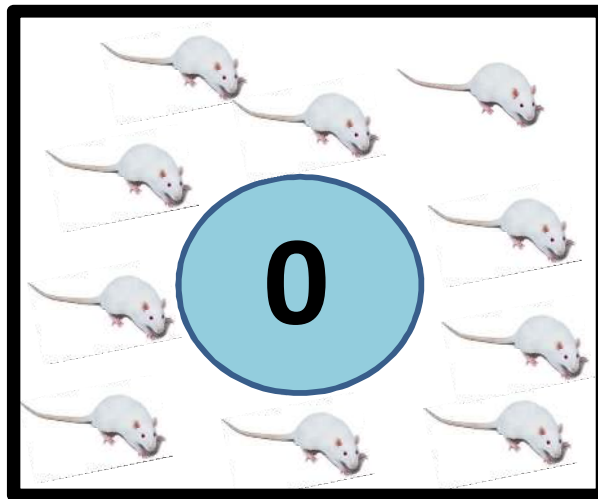
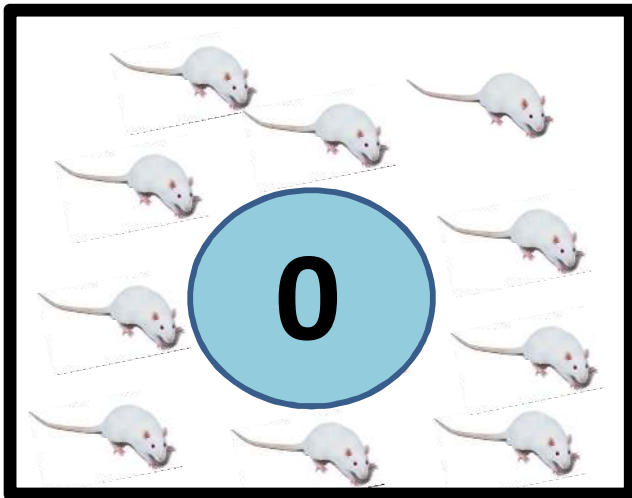


**CONTROL**



**8 month**

□8□□□□

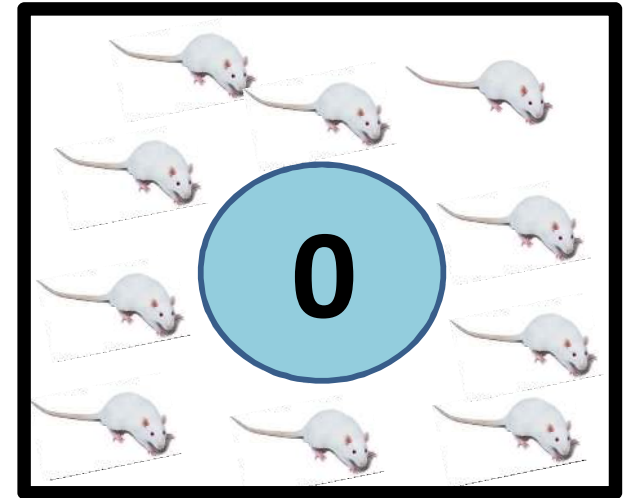
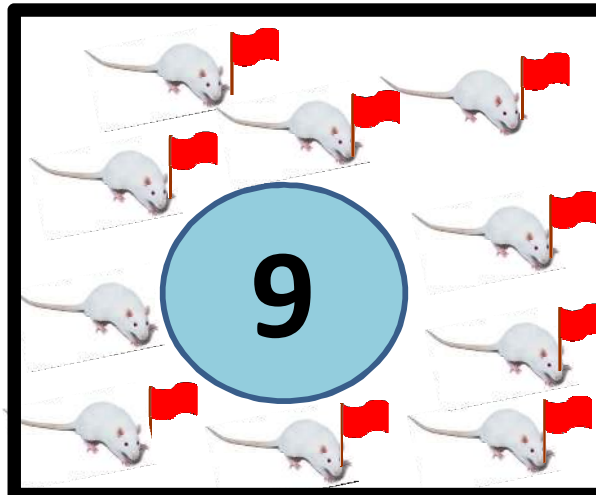


**Carcinogen**



**8 month**

□8□□□□

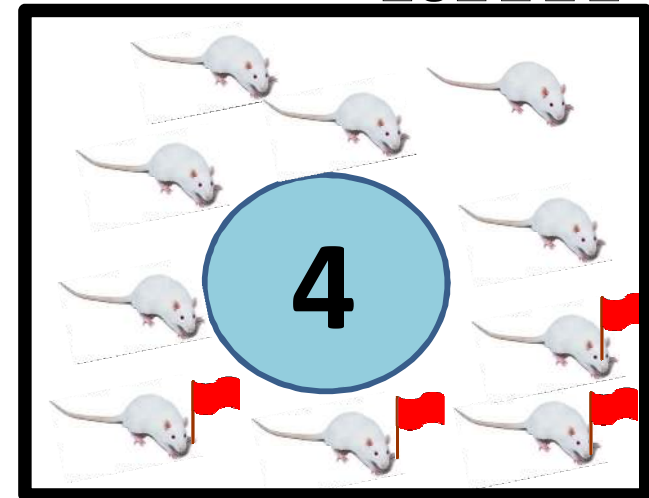


**Carcinogen + MRN-100**

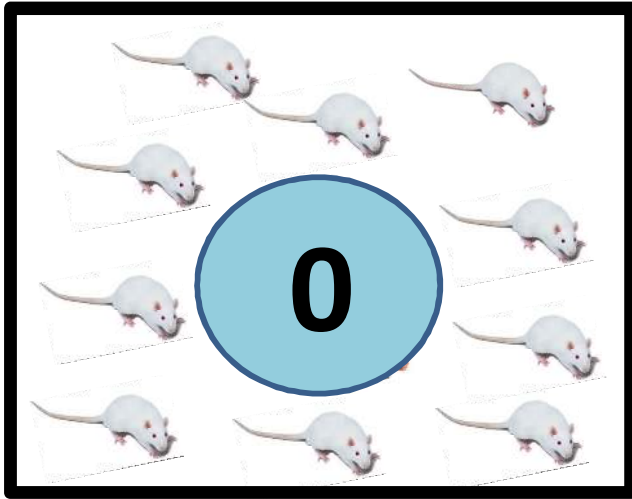


**8 month**

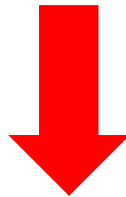
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# Esophogus: Total Number of Foci

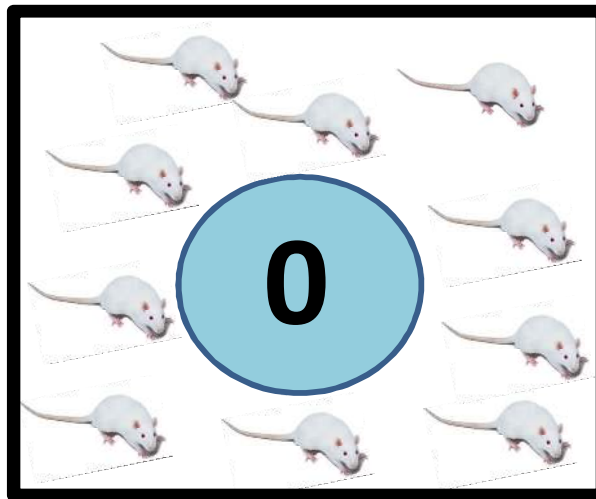


**CONTROL**



**8 month**

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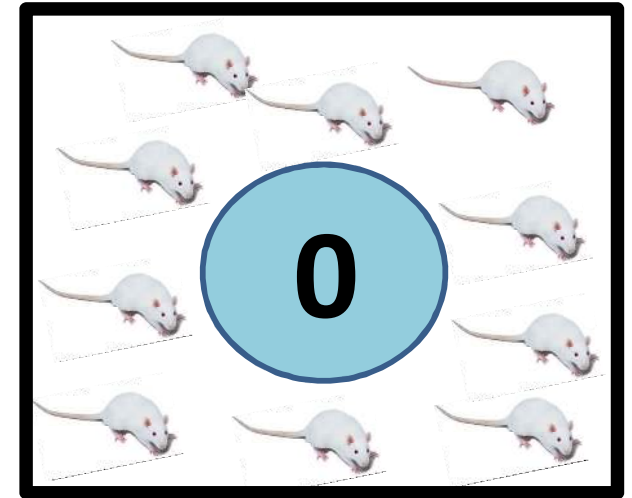


**Carcinogen**



**8 month**

□8□□□□

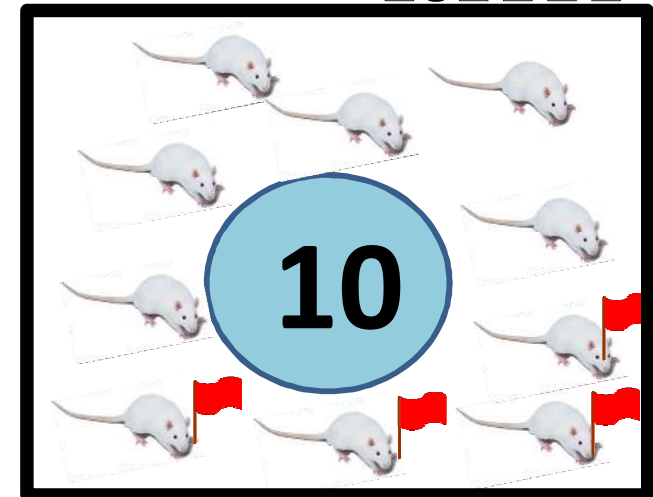
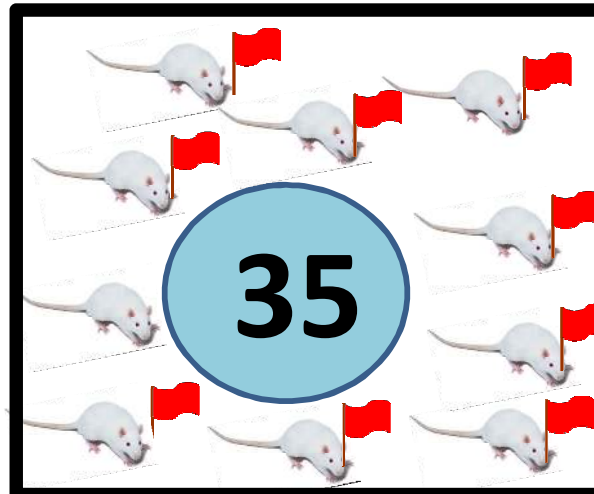
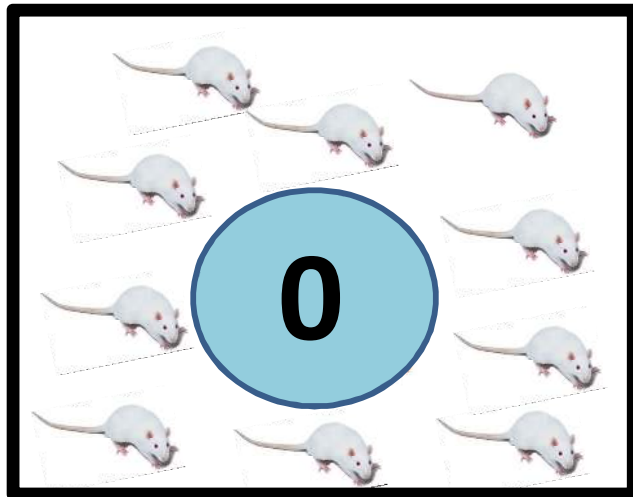


**Carcinogen + MRN-100**

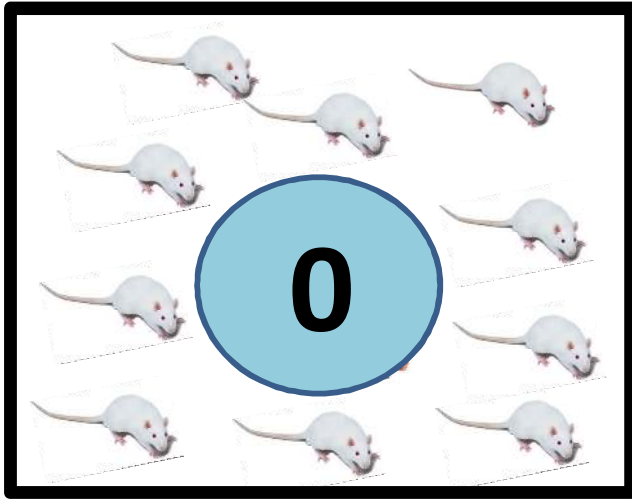


**8 month**

□8□□□□



# Stomach: Total Rats with Foci

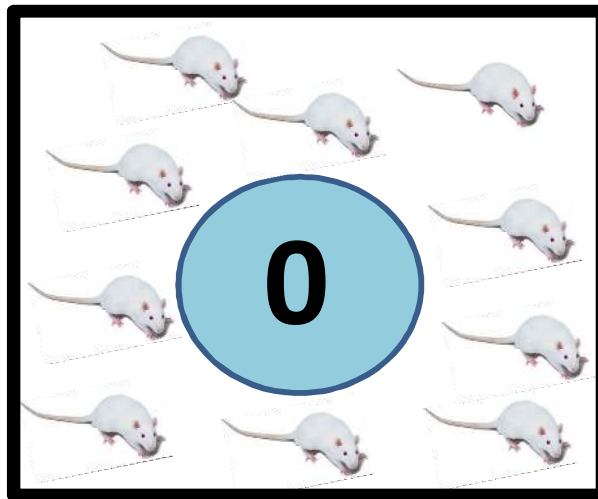
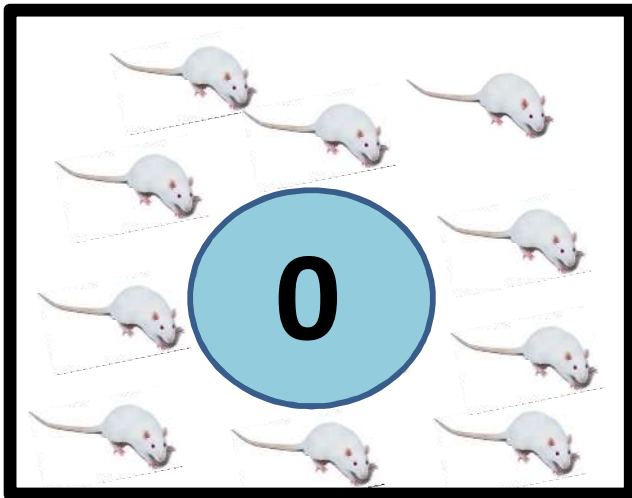


**CONTROL**



**8 month**

□8□□□□

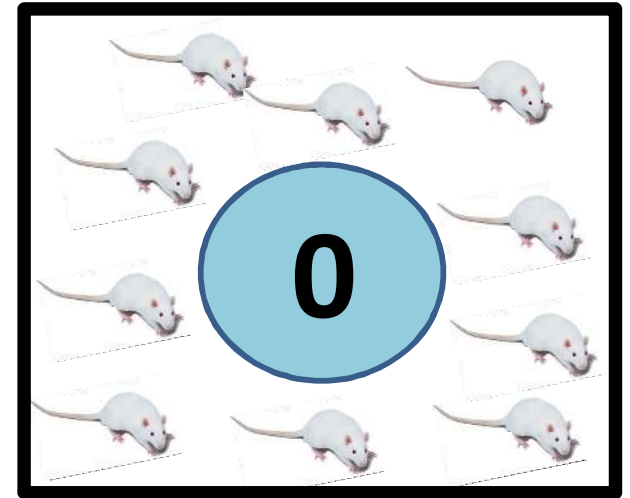
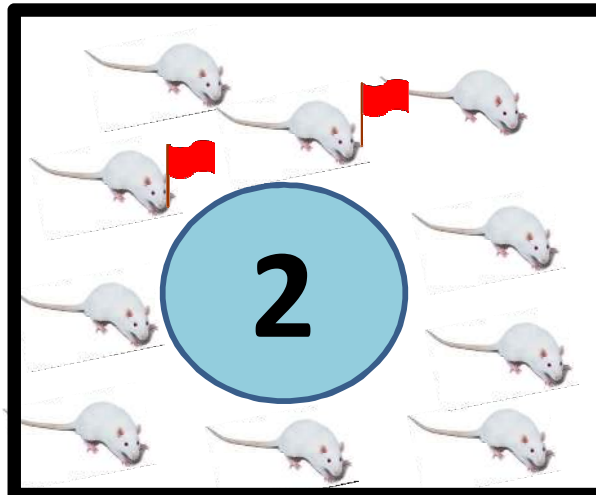


**Carcinogen**



**8 month**

□8□□□□

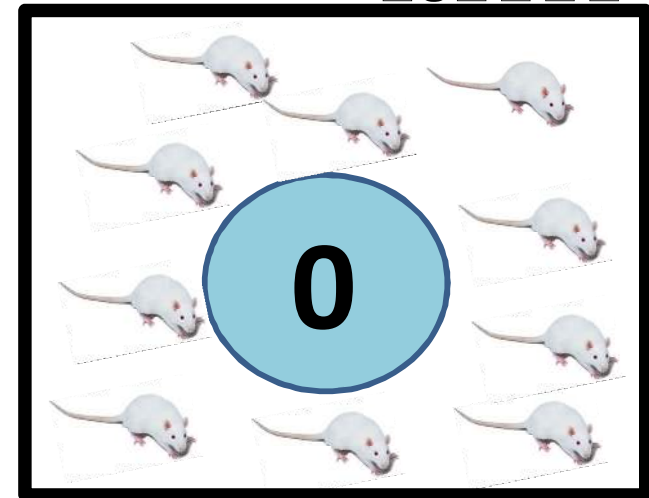


**Carcinogen + MRN-100**

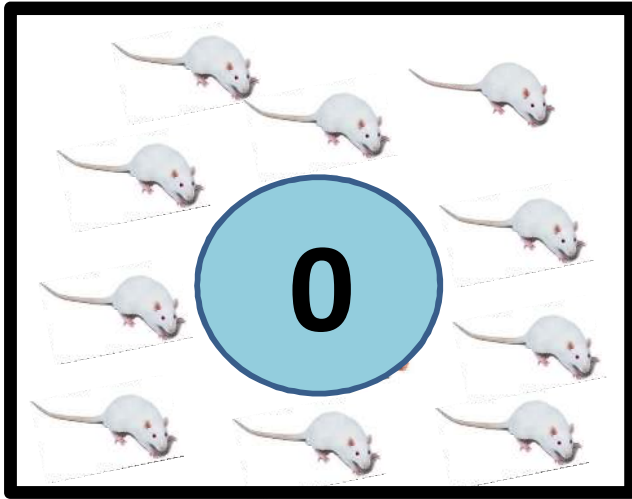


**8 month**

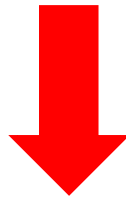
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# Stomach: Total Number of Foci

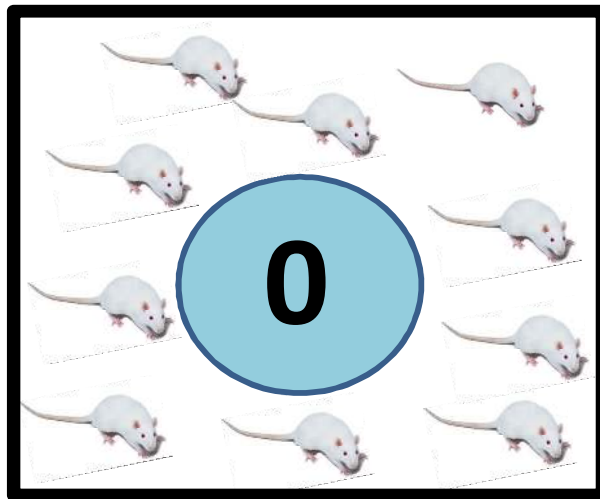
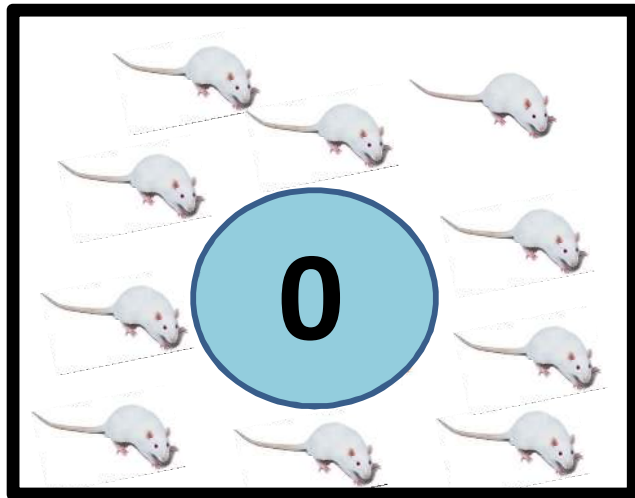


**CONTROL**



**8 month**

□8□□□□

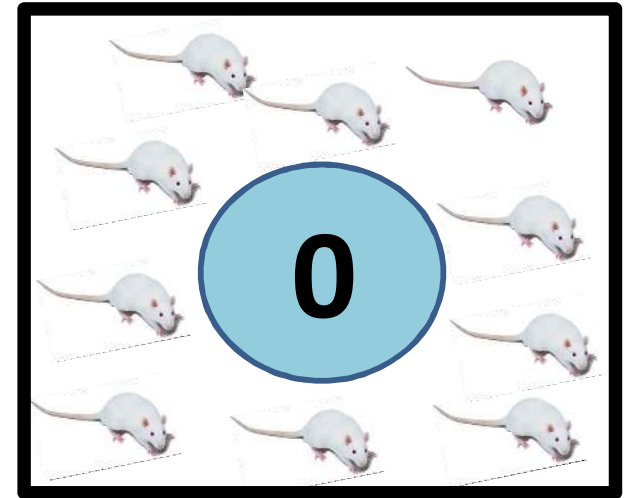
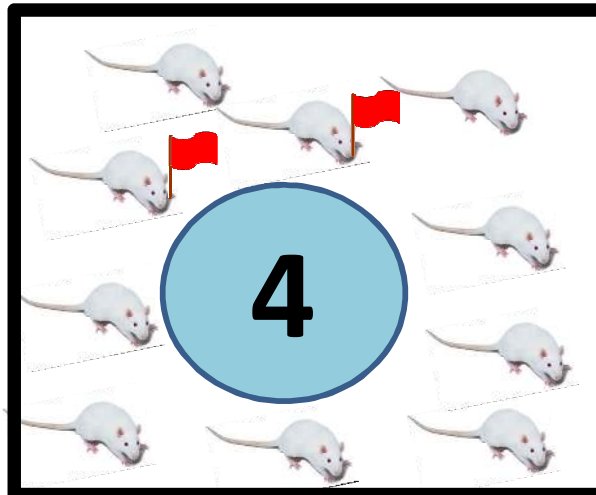


**Carcinogen**



**8 month**

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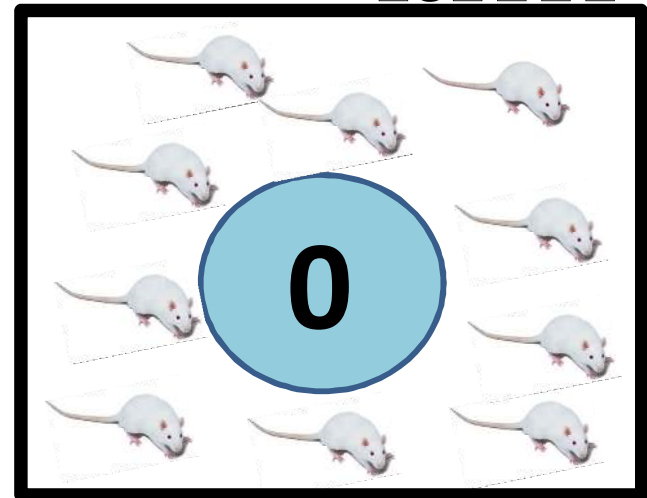


**Carcinogen + MRN-100**



**8 month**

□8□□□□

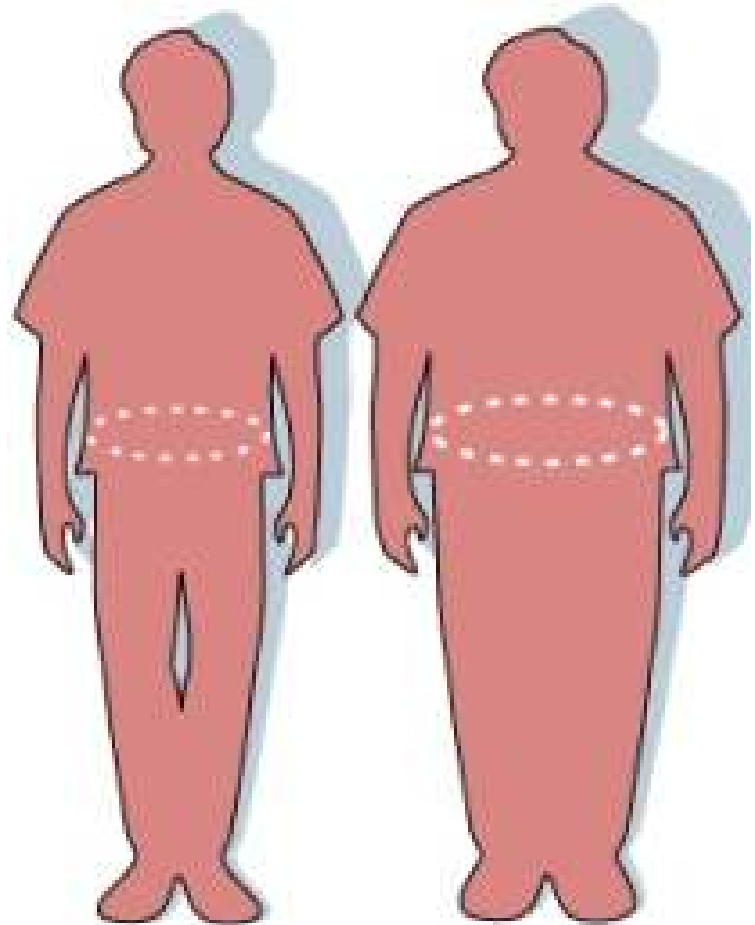


# Characteristic Body Weight Loss in Cancer Patients

Almost one-half of hospitalized adult cancer patients have lost at least 10 percent of their body weight.

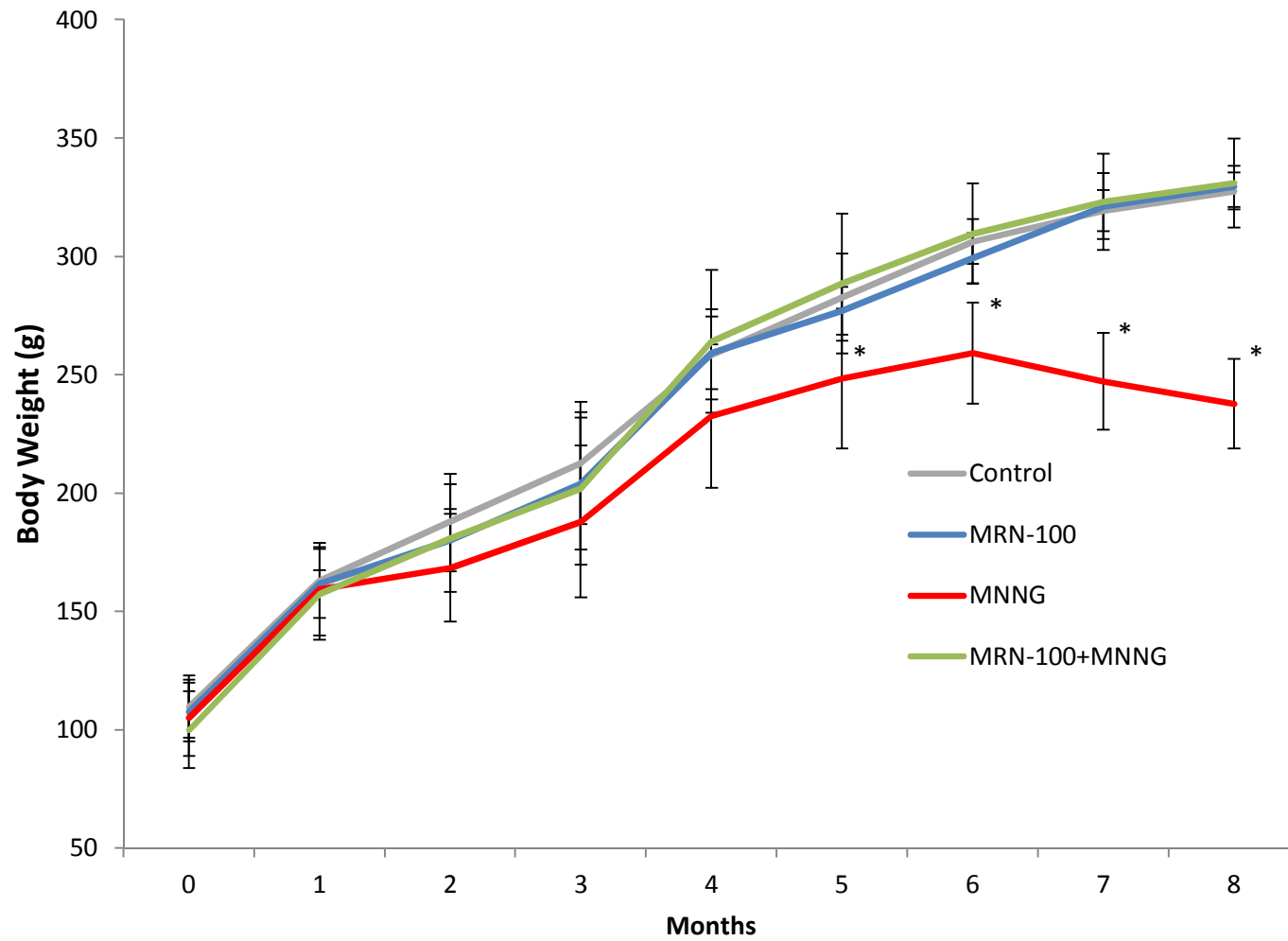
One-quarter of these patients have lost 20 percent or more.

Virtually all patients with disseminated (scattered and abundant) metastasis show evidence of involuntary weight loss.

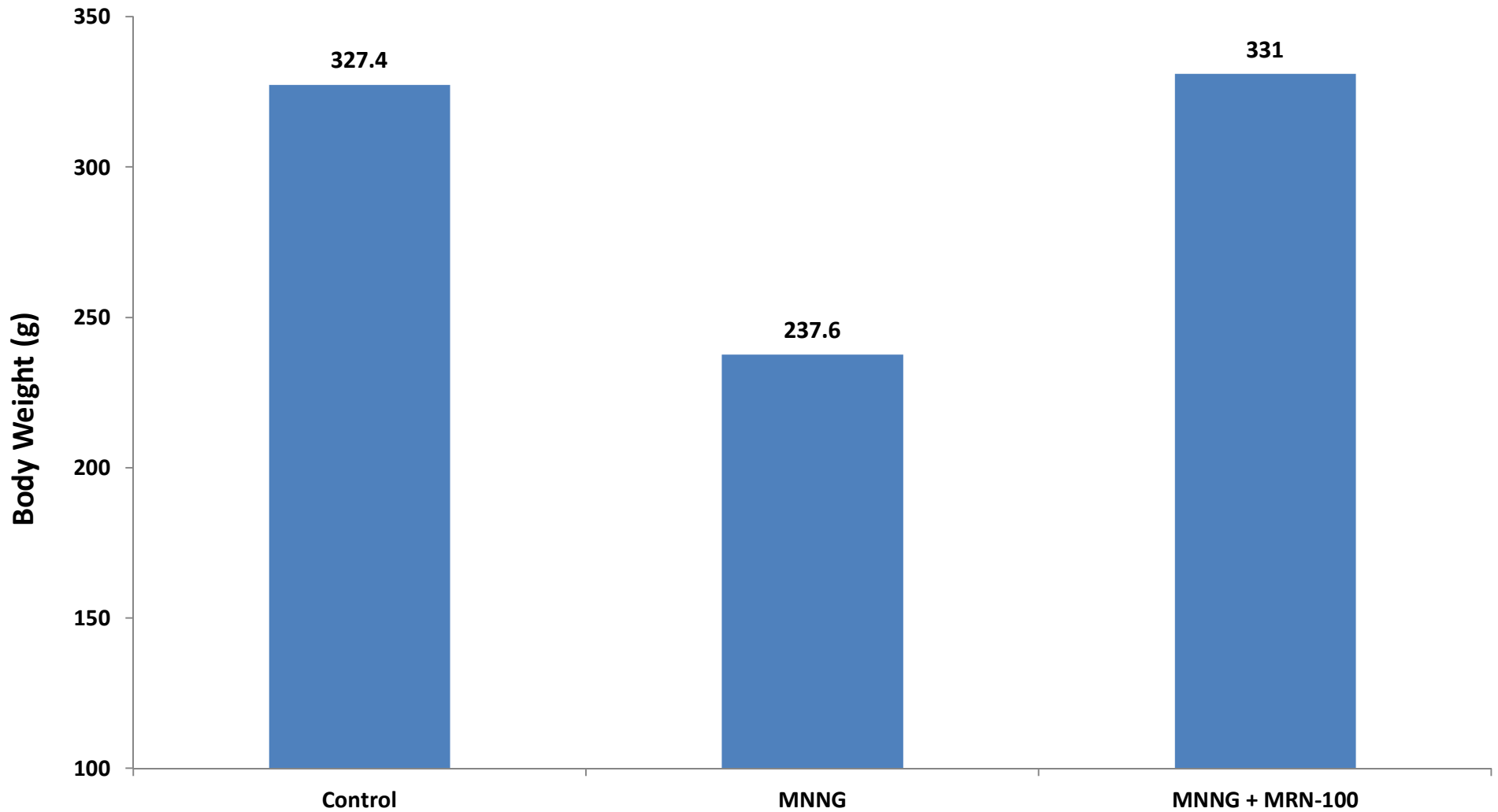




# Body Weight

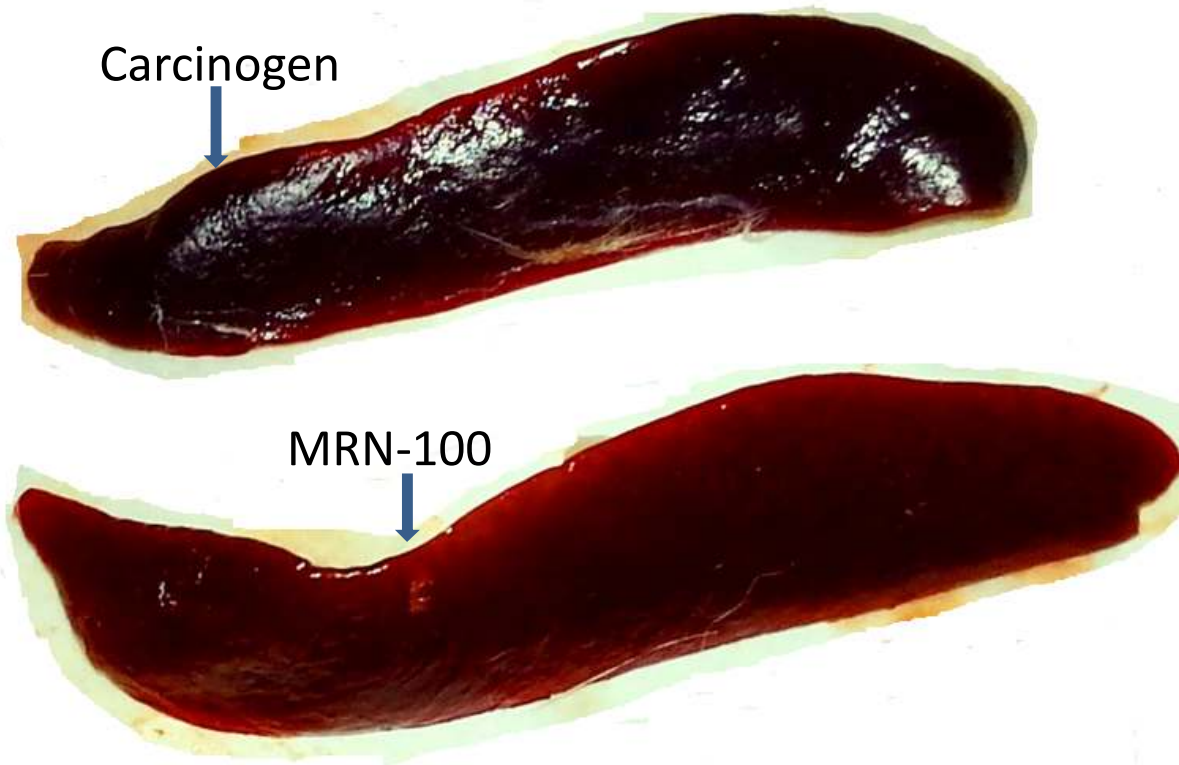


# MRN-100 Prevents Body Weight Loss from Gastric Cancer in Rats After 8 Months

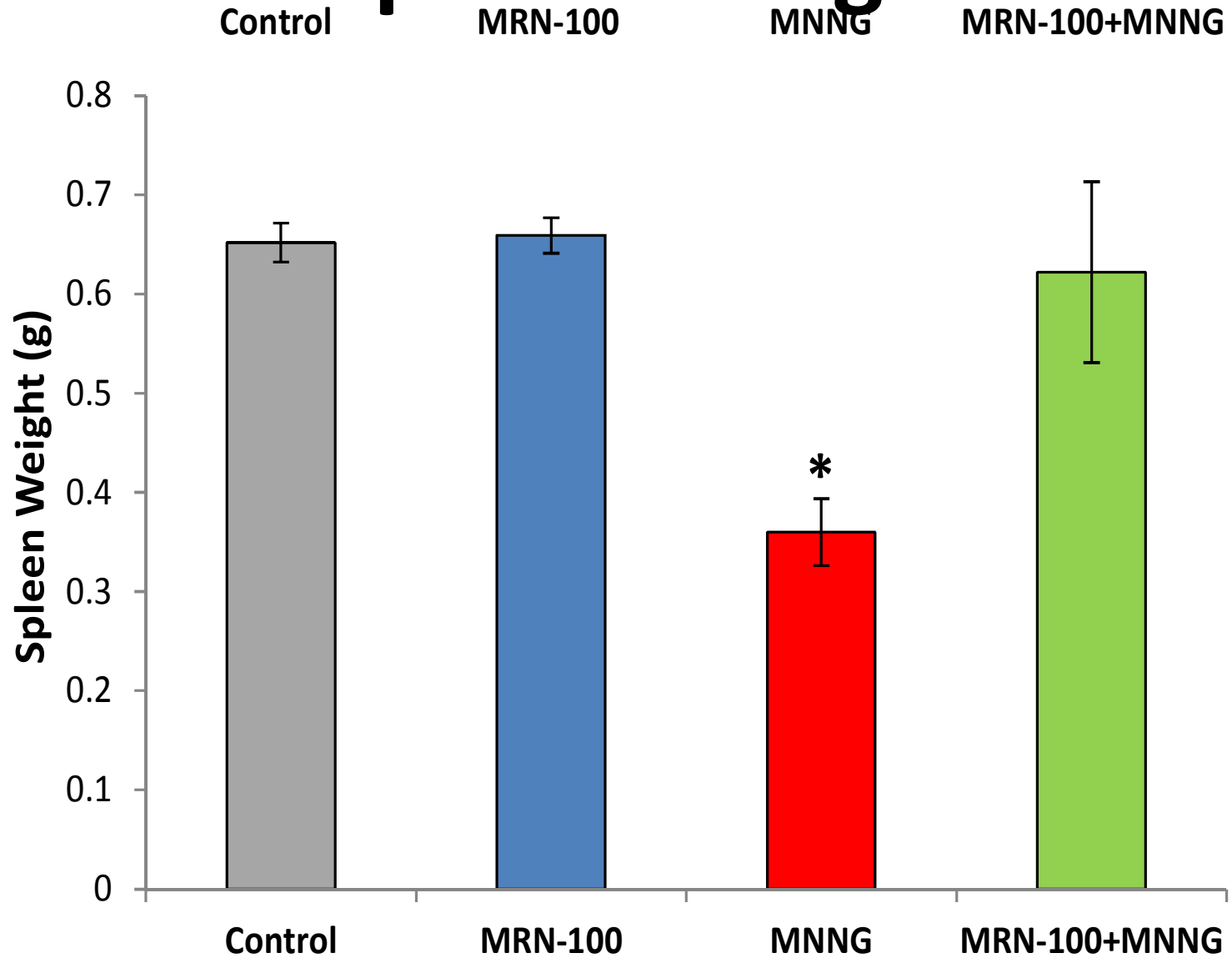




# Spleen weight



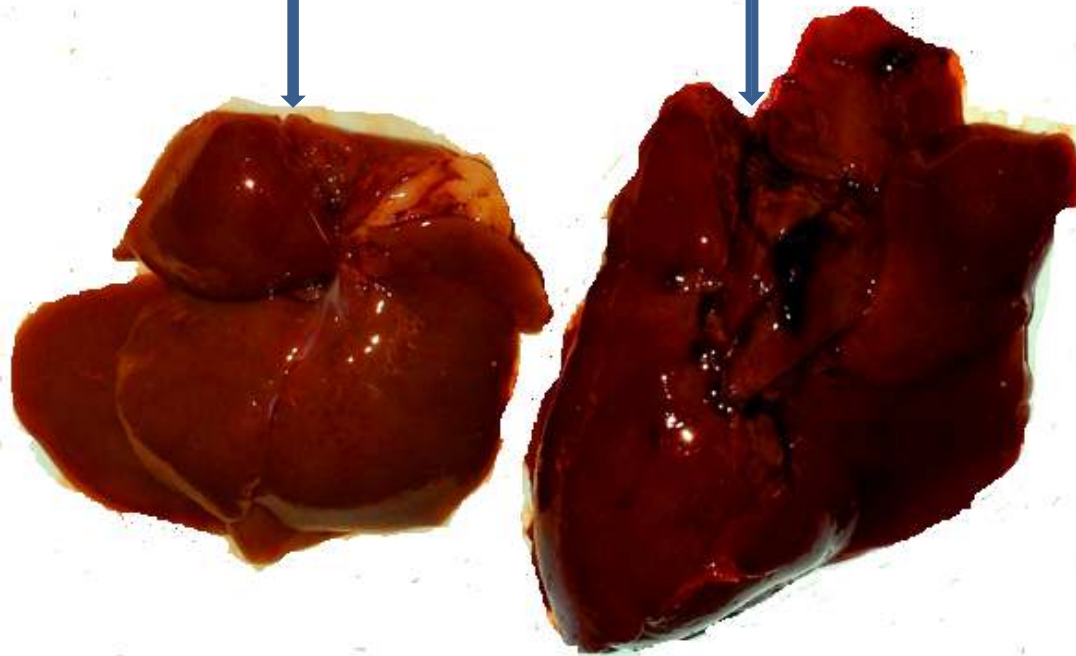
# Spleen weight



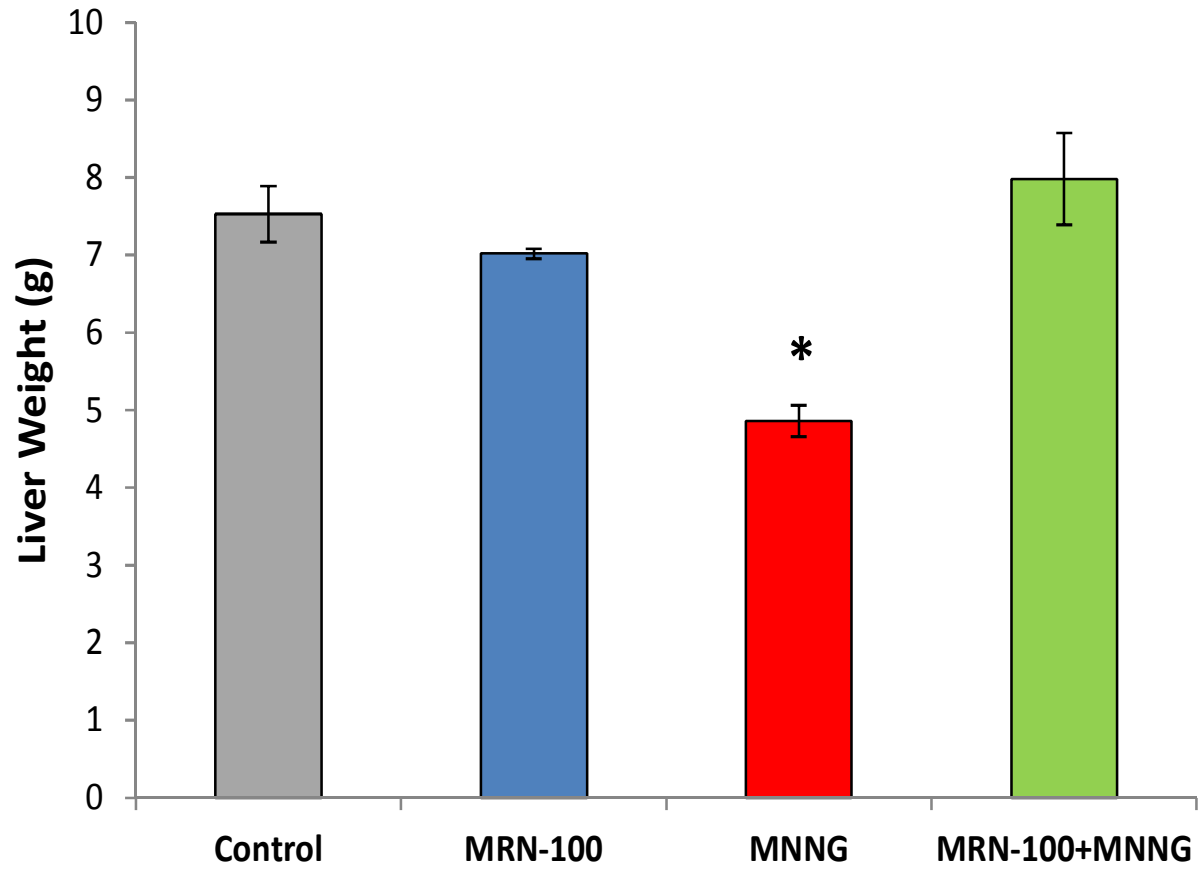
# Liver weight

Carcinogen

MRN-100



# Liver weight



0.8 -  
0.7  
0.6  
0.5  
nt (g)

The major problem concerning the natural antitumor agents is to define their mechanisms of action

**Mechanisms of protection  
against esophageal and  
gastric cancer by MRN-100**

**is via**

# Anticancer by MRN-100

## Mechanisms of action



Antioxidant



Immune modulator

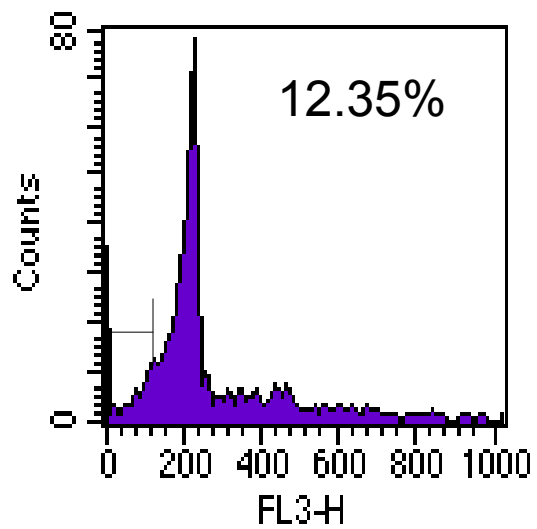
Future  
studies

**1-**

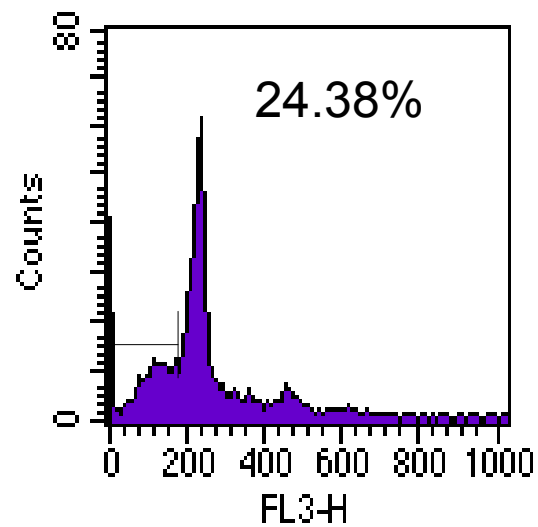
# ***Antioxidant Potential***



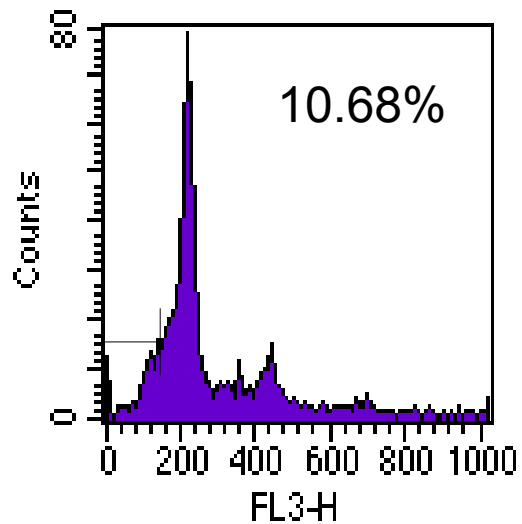
Cells



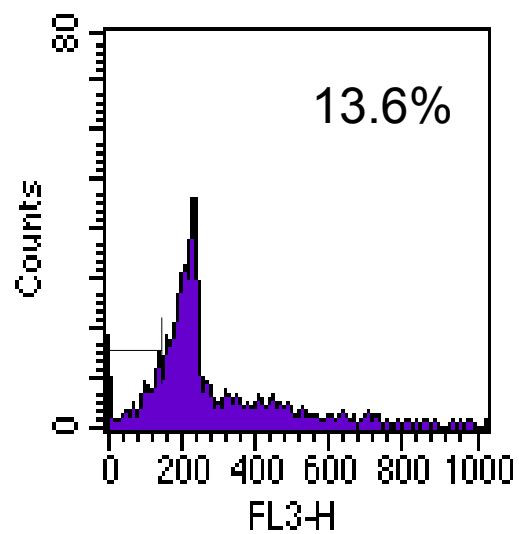
Cells+ H2O2



ACM System  
Water



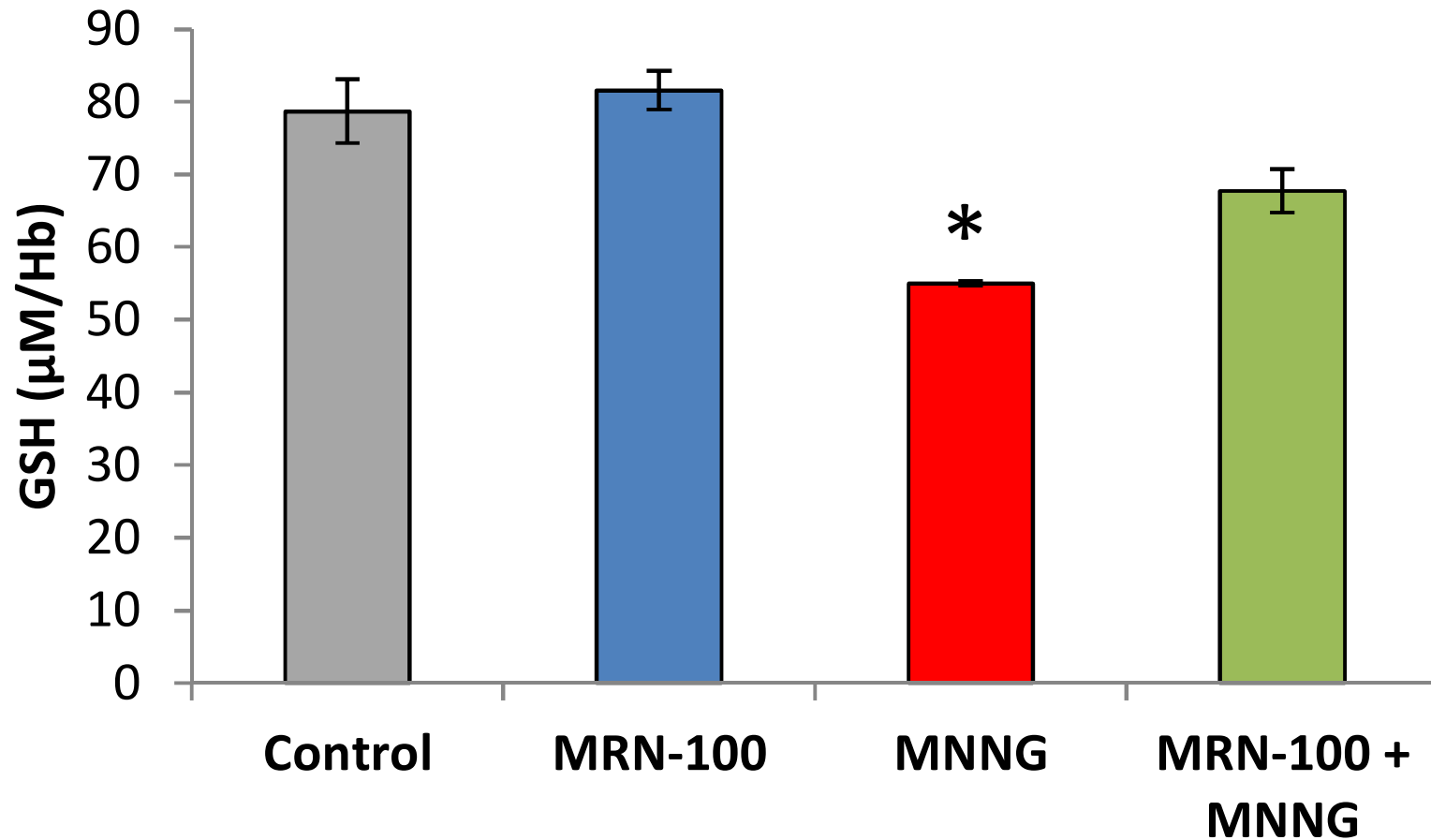
ACM Water +  
H2O2



# MRN-100 augments antioxidant defense system

## 1- Free radical scavenger (GSH)

B

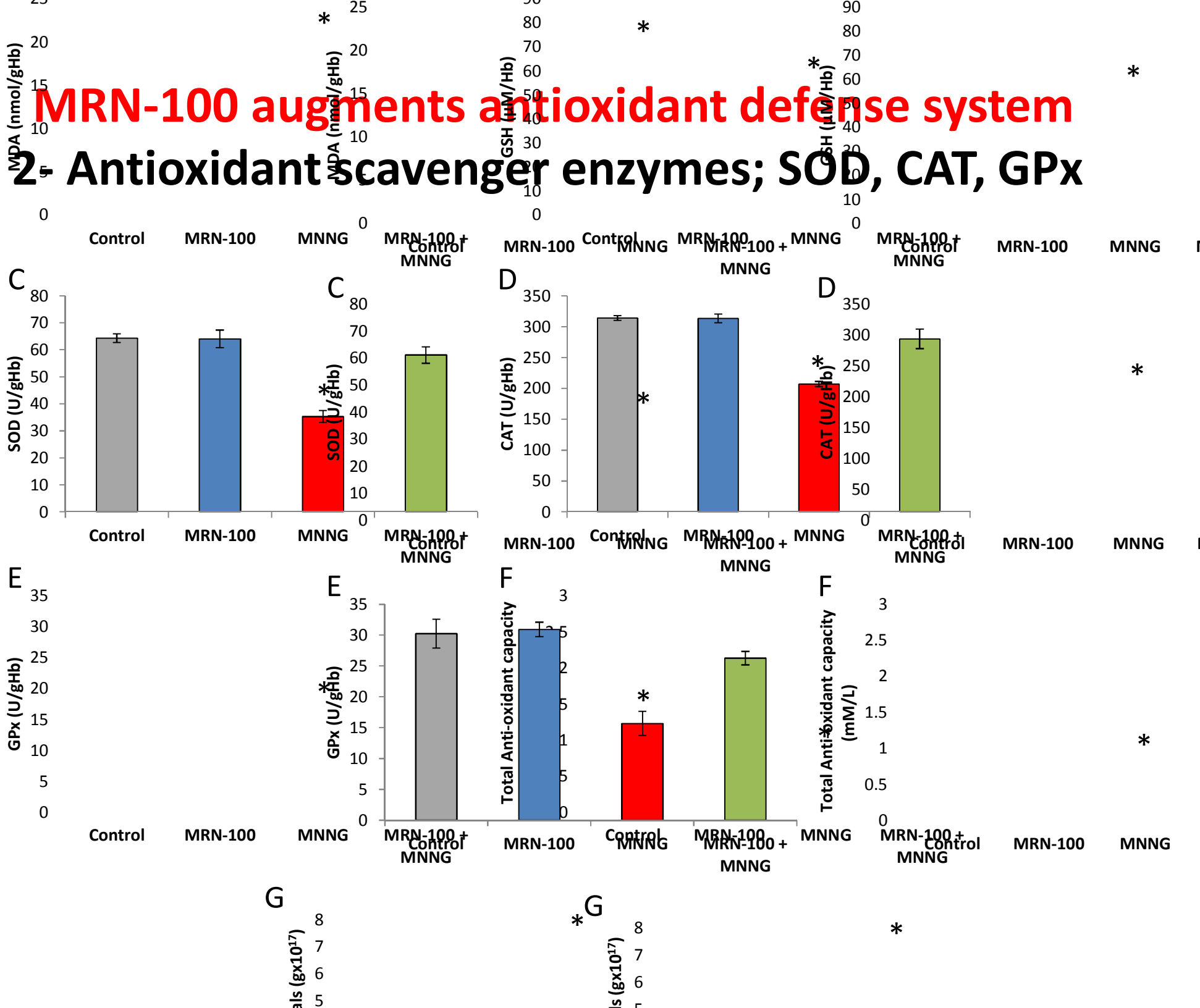


D

350  
300

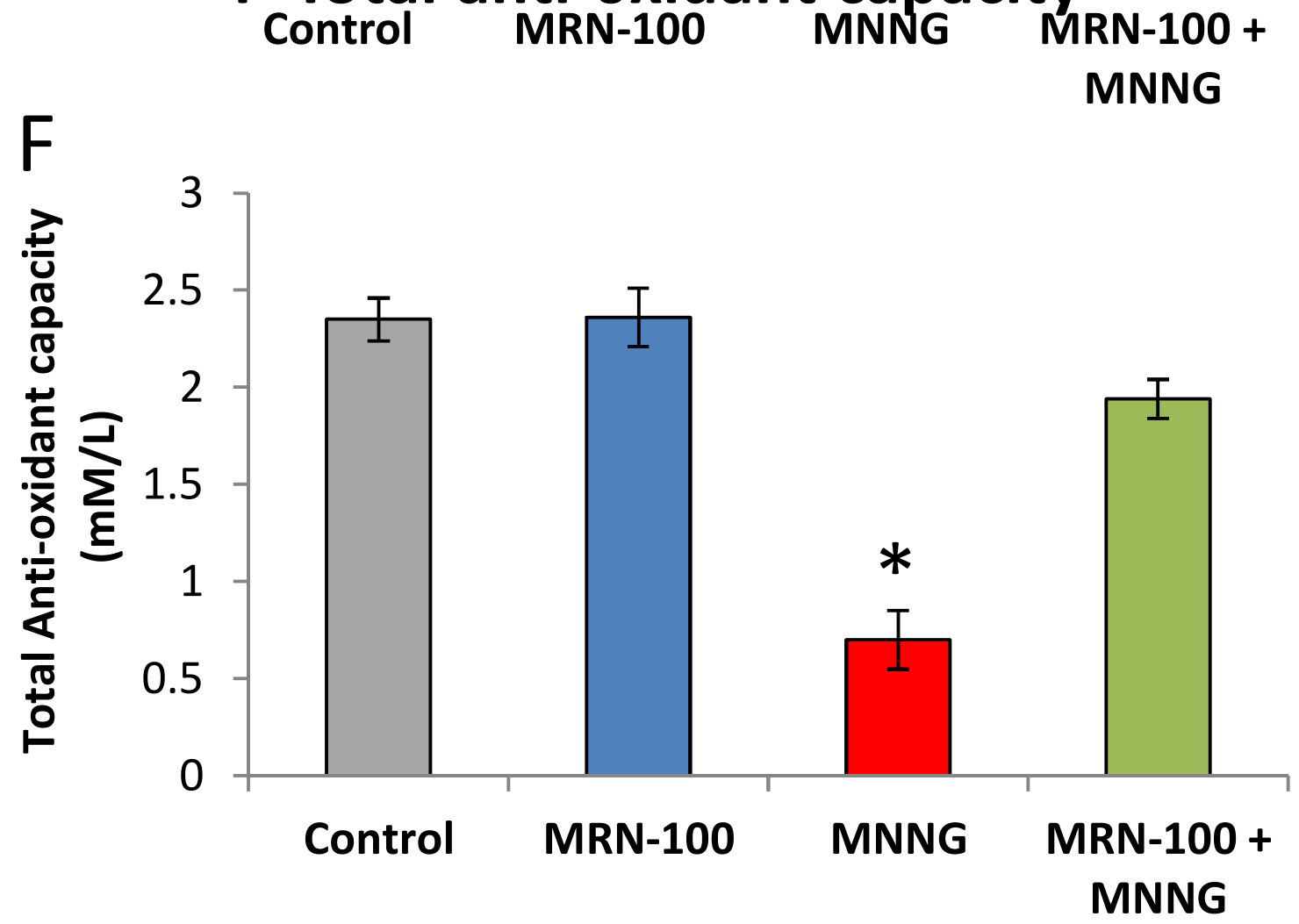
# MRN-100 augments antioxidant defense system

## 2- Antioxidant scavenger enzymes; SOD, CAT, GPx

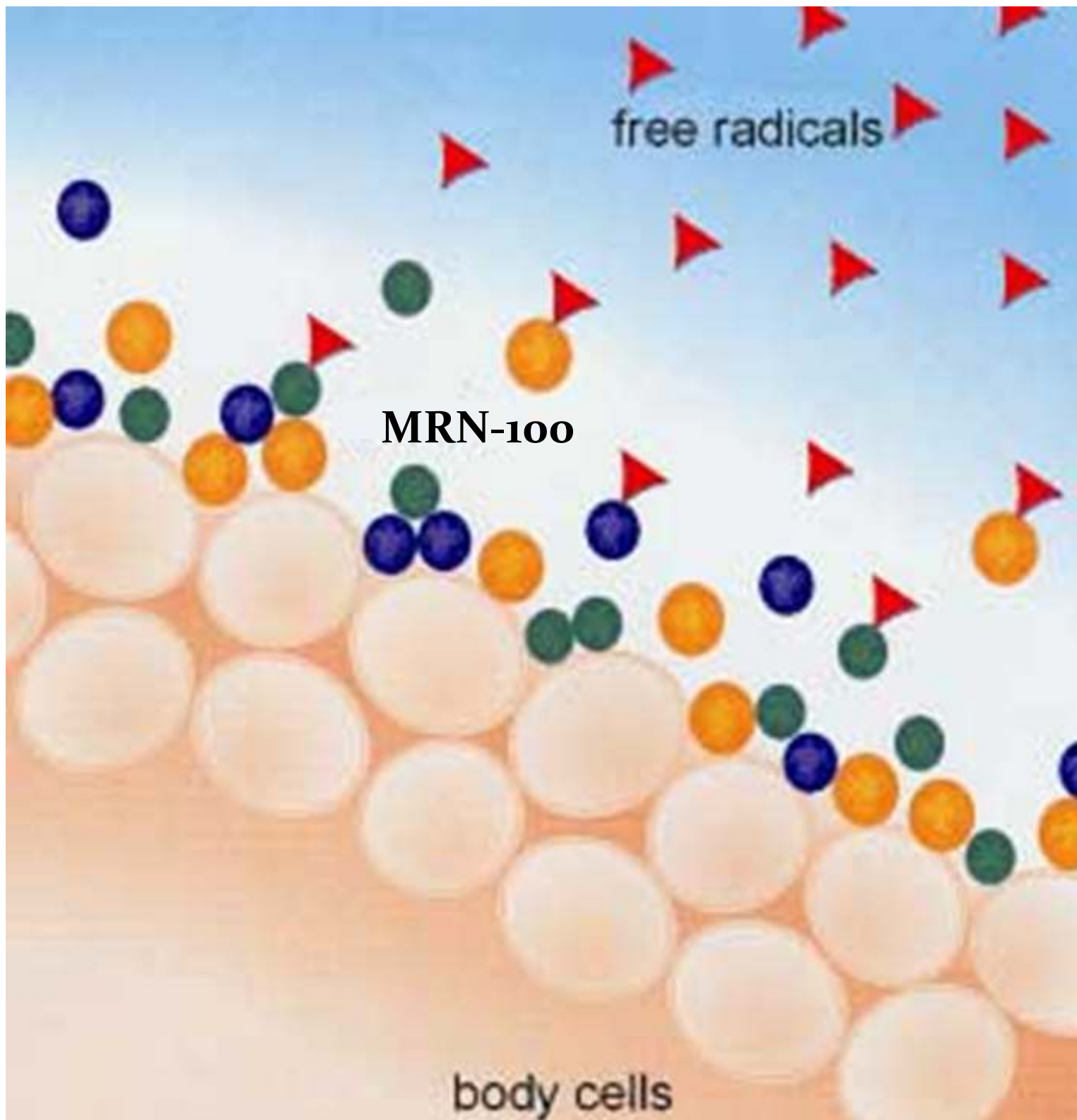


# MRN-100 augments antioxidant defense system

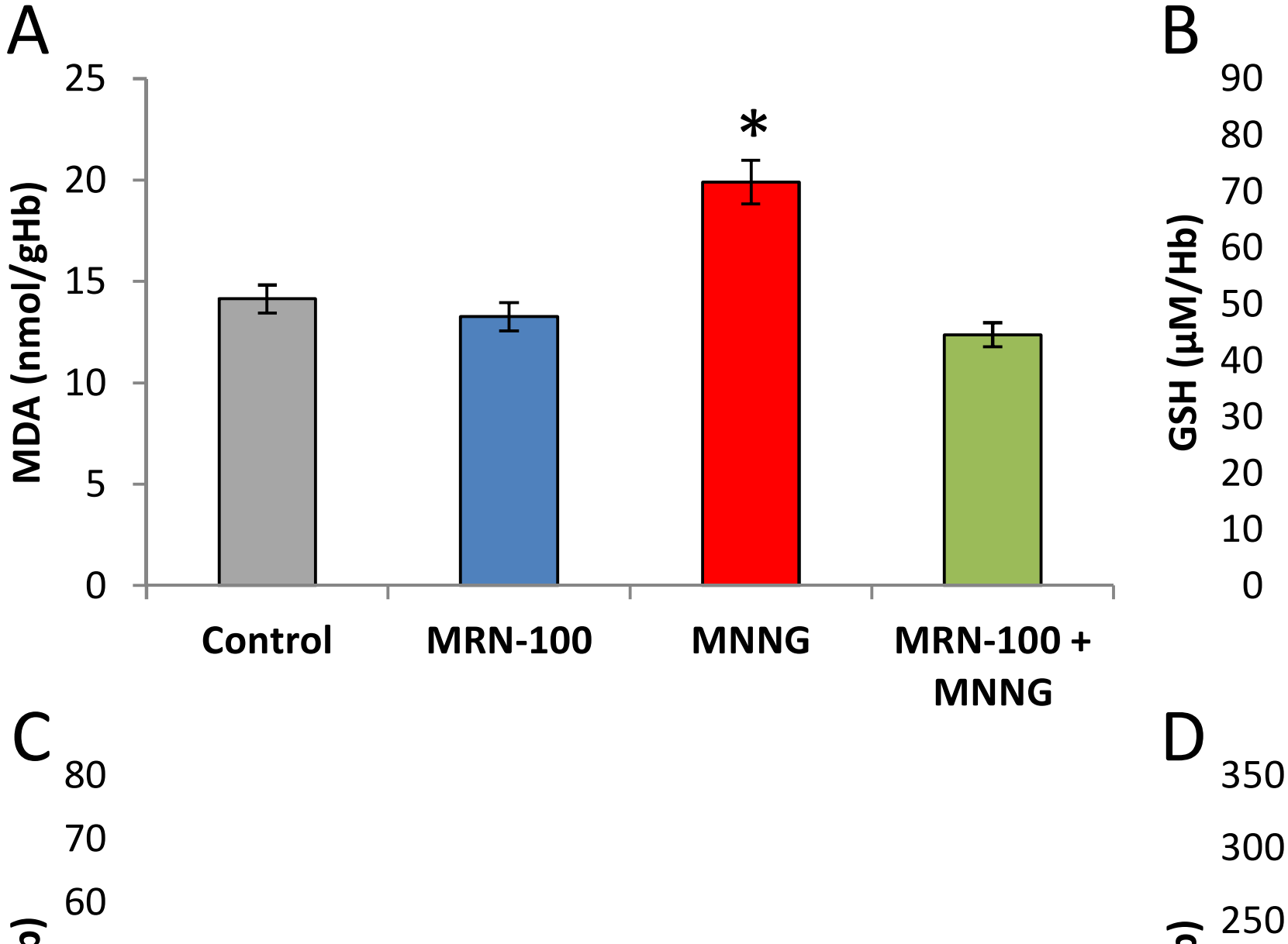
## 4- Total anti-Oxidant capacity



\*



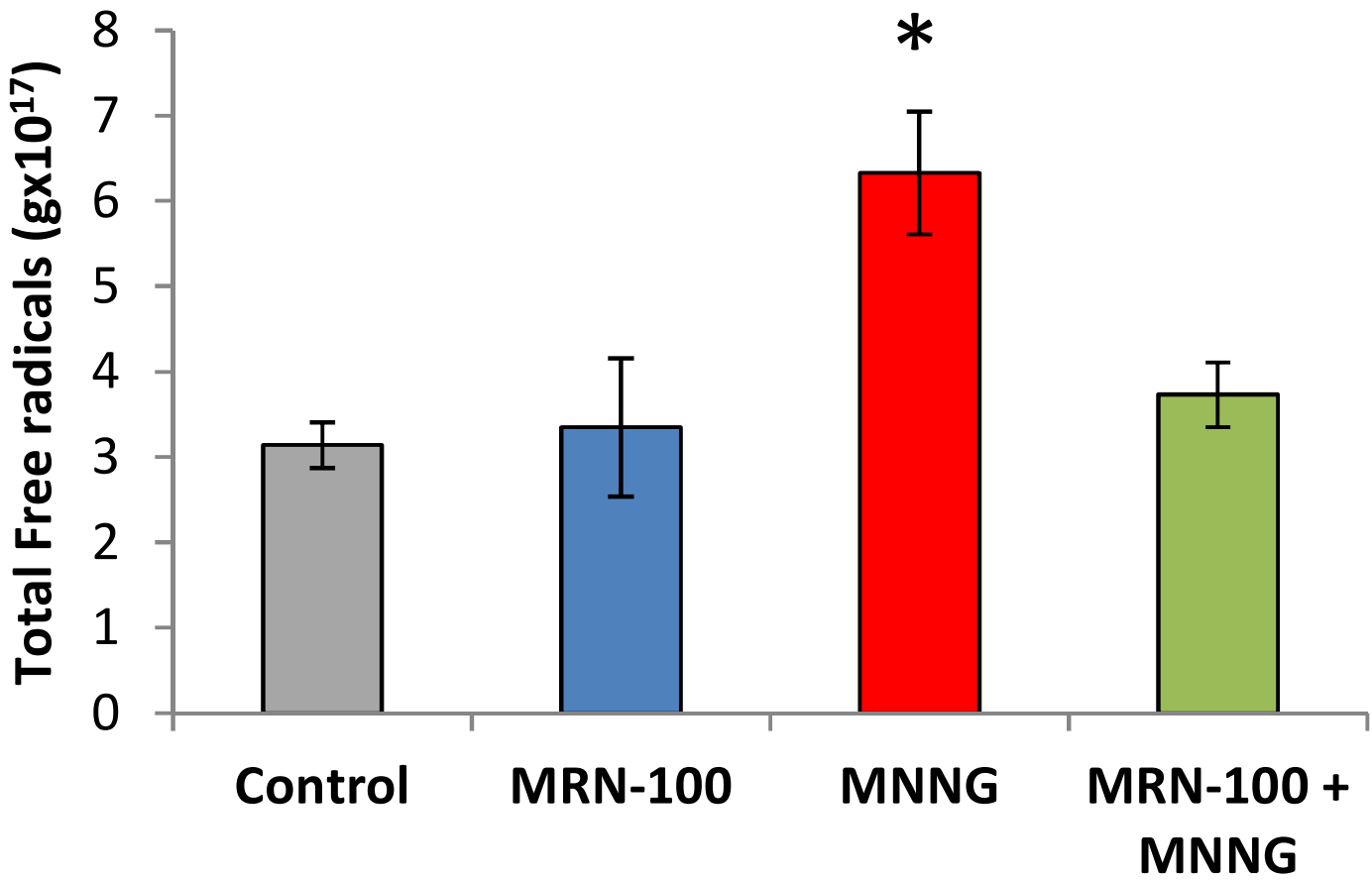
**MRN-100 augments antioxidant defense system.**  
**3- Modulating lipid peroxidation.**(lipid peroxidation biomarker MDA)



# MRN-100 augments antioxidant defense system

MRN-100 MNNG MRN-100 + MNNG Control MRN-100 MNNG

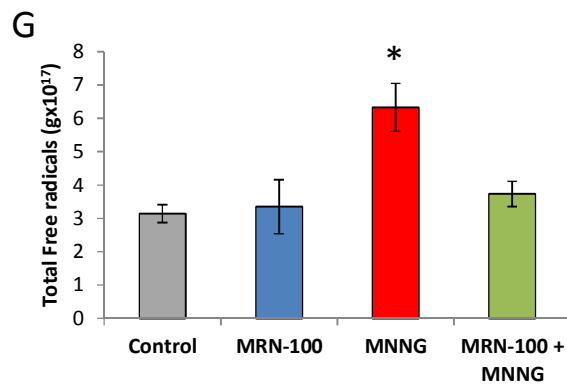
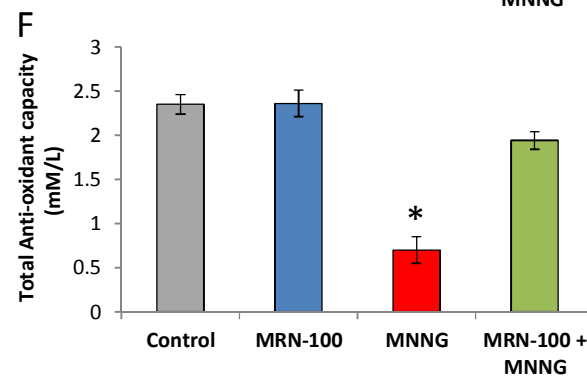
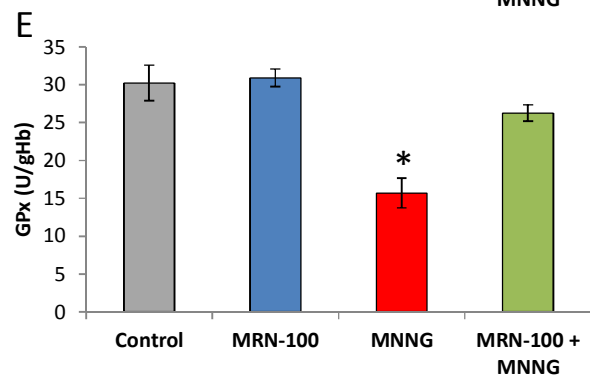
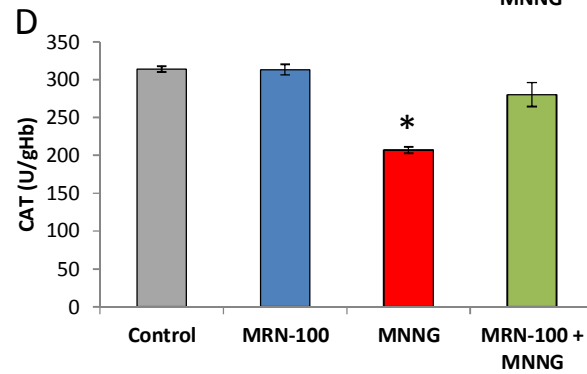
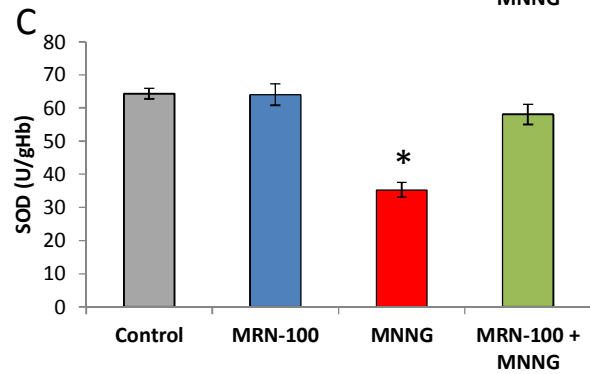
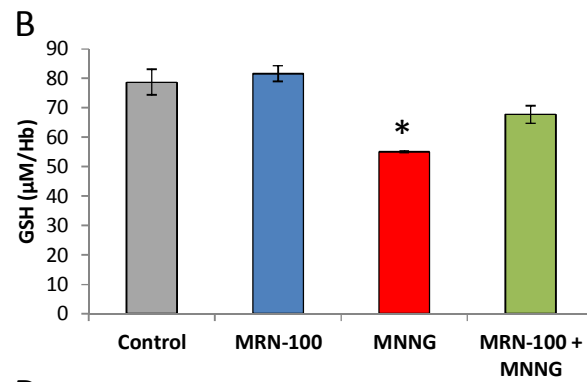
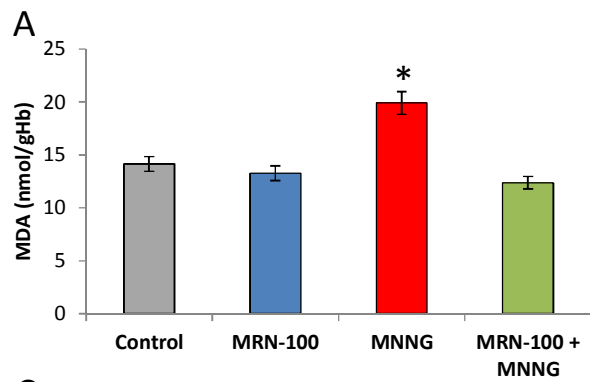
G



# Augmenting antioxidant defense system

- **Free radical scavenger (GSH)**
- **Antioxidant scavenger enzymes; SOD, CAT and GPx**
- **Modulating lipid peroxidation.**  
(lipid peroxidation biomarker MDA, NO)





メディカル・サイエンス・ダイジェスト

## 特集 生活習慣病と ミトコンドリア異常

特集編輯 伊藤 裕  
(慶應義塾大学腎臓内分泌代謝内科)

はじめに  
—メタボリックドミノはミトコンドリアの病—

伊藤 裕  
(慶應義塾大学腎臓内分泌代謝内科)

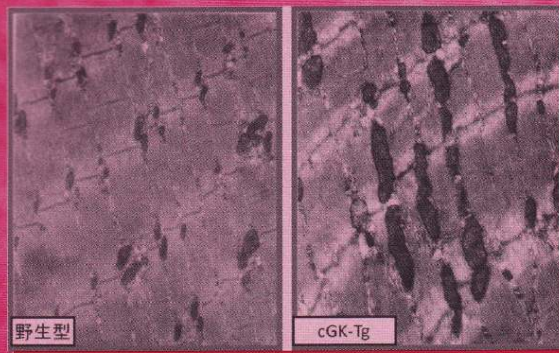
ミトコンドリアゲノムとヒトの寿命  
福 典之・田中 雅嗣  
(東京都健康長寿医療センター研究所)

ホルモンによるミトコンドリア制御  
宮下 和季・伊藤 裕  
(慶應義塾大学腎臓内分泌代謝内科)

ミトコンドリアと代謝異常  
杉本 研・桑木 宏実  
(大阪大学老年・腎臓内科学)

慢性腎臓病 (CKD) 発症と  
ミトコンドリア酸化ストレス  
佐藤 恵美子・伊藤 貞嘉 他  
(東北大学病院腎高血圧内分泌科)

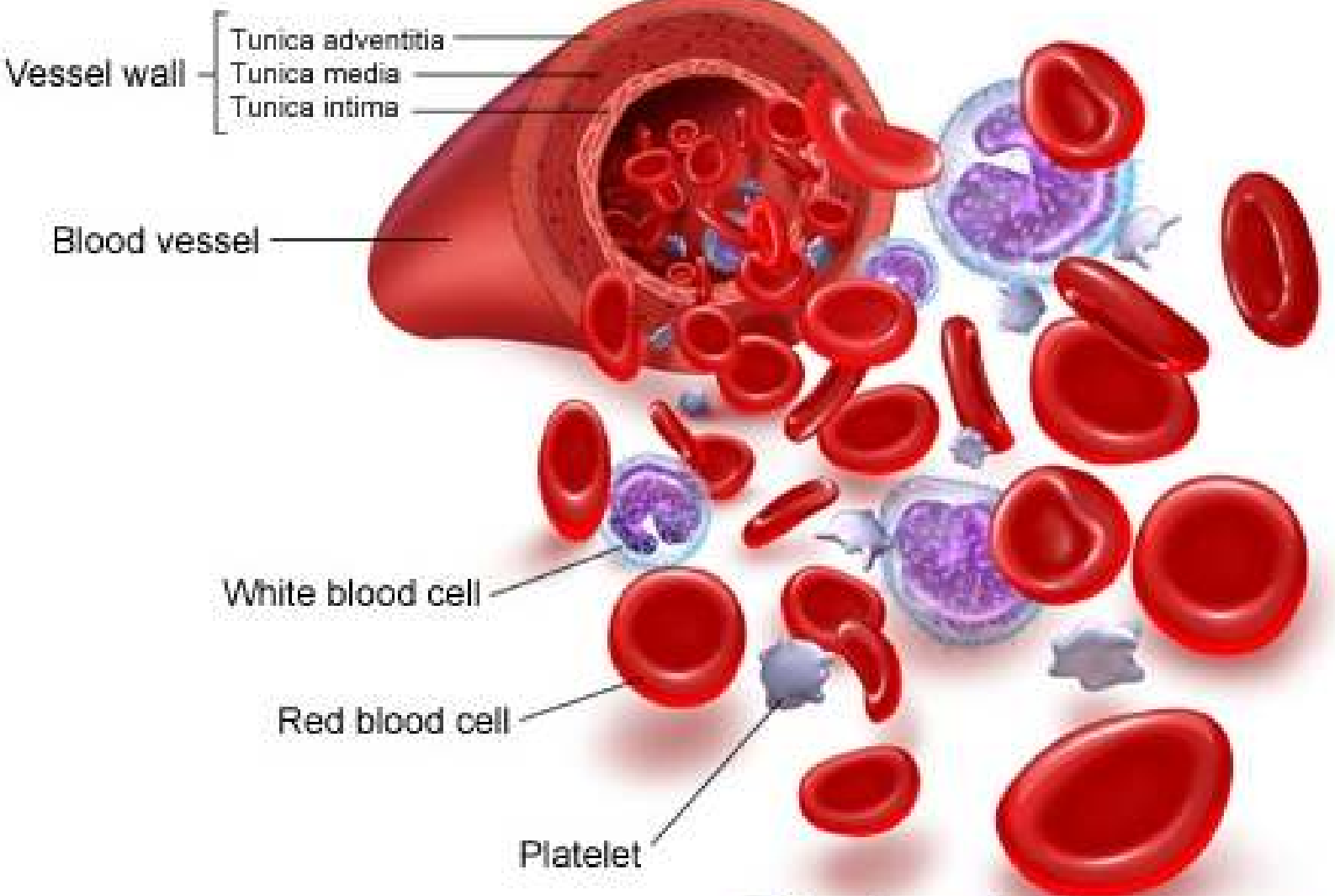
Digestシリーズ  
—Perry症候群— 始まりは一人の患者から  
坪井 義夫  
(福岡大学神経内科学)



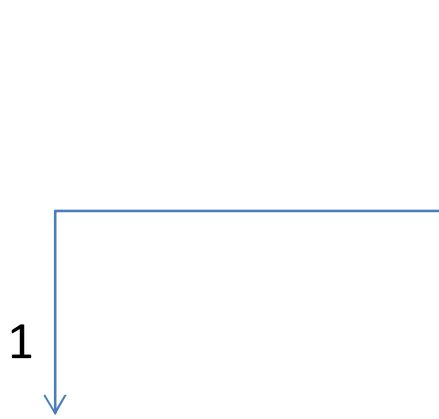
**2-**

***Immune modulation***

# Blood Constituents



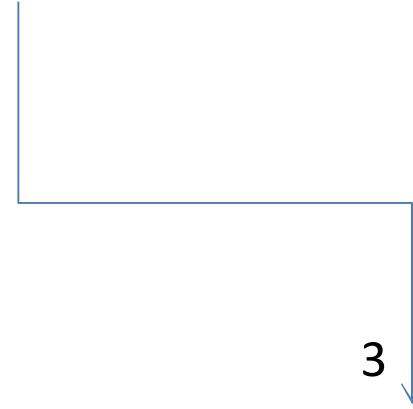
# Hematology Parameters



**Lymphocytes**



**Red Blood Cells (RBCs)  
Hemoglobin Content**



**Platelets**

# Effect of MRN-100 on hematological parameters in gastric cancer

	Group			
	Control	MRN-100	MNNG	MNNG+ MRN-100
<b>RBCs (10<sup>6</sup>/cmm)</b>	8.80±0.21	8.94±0.13 (1.53%)	7.08±0.29 <sup>**</sup> , <sup>††</sup> (-19.58%)	8.32±0.09 <sup>##</sup> , <sup>†</sup> (-5.47%)
<b>Hb(g/dl)</b>	13.82±0.33	13.93±0.24 (0.84%)	11.82±0.48 <sup>**</sup> , <sup>††</sup> (-14.48%)	13.88±0.17 <sup>##</sup> (0.48%)
<b>Hematocrit (%)</b>	43.02±1.17	43.12±0.59 (0.23%)	38.57±0.60 <sup>**</sup> , <sup>††</sup> (-10.34%)	41.38±0.71 <sup>#</sup> (-3.80%)
<b>WBC's (10<sup>3</sup>/cmm)</b>	8.78±0.66	8.61±0.46 (-1.97%)	11.44±0.32 <sup>*</sup> , <sup>†</sup> (30.36%)	8.78±1.12 <sup>#</sup> (0.04%)
<b>Lymphocytes(%)</b>	64.25±2.81	65.62±1.27 (2.13%)	50.93± 4.14 <sup>**</sup> , <sup>††</sup> (-20.73%)	60.7±3.33 <sup>#</sup> (-5.53%)
<b>Neutrophils (%)</b>	26.05±1.95	27.03±0.99 (3.77%)	42.58±5.10 <sup>**</sup> , <sup>††</sup> (63.47%)	29.62±1.77 <sup>##</sup> (13.69%)
<b>Monocytes (%)</b>	4.65±0.43	4.63±0.36 (-0.36%)	4.70±0.21 (1.08%)	4.68±0.78 (0.65%)
<b>Platelets (10<sup>3</sup>/cmm)</b>	803.5±29.67	805.5±24.87 (0.25%)	1011.17±66.87 <sup>**</sup> , <sup>††</sup> (25.85%)	810.17±61.48 <sup>##</sup> (0.83%)

Data represents the mean±SE of 6 mice/group.

\*Significantly different from control group at 0.05 level.

\*\*Significantly different from control at 0.01 level.

†Significantly different from **MRN-100** group at 0.05 level.

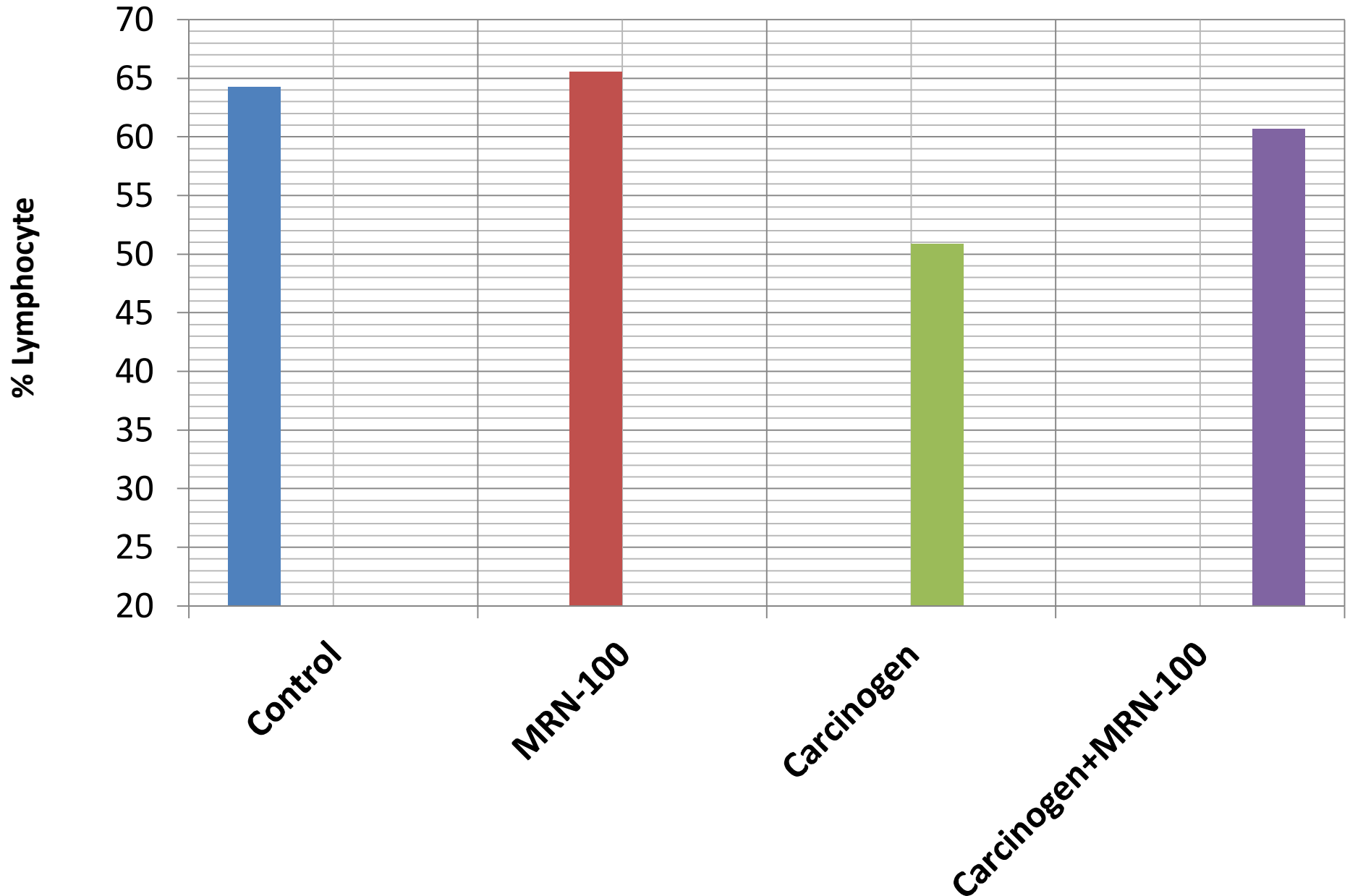
†† Significantly different from **MRN-100** group at 0.01 level.

# Significantly different from MNNG group at 0.05 level.

## Significantly different from MNNG group at 0.01 level.

(% change of control group).

# MRN-100 Protects Against Loss of Lymphocytes

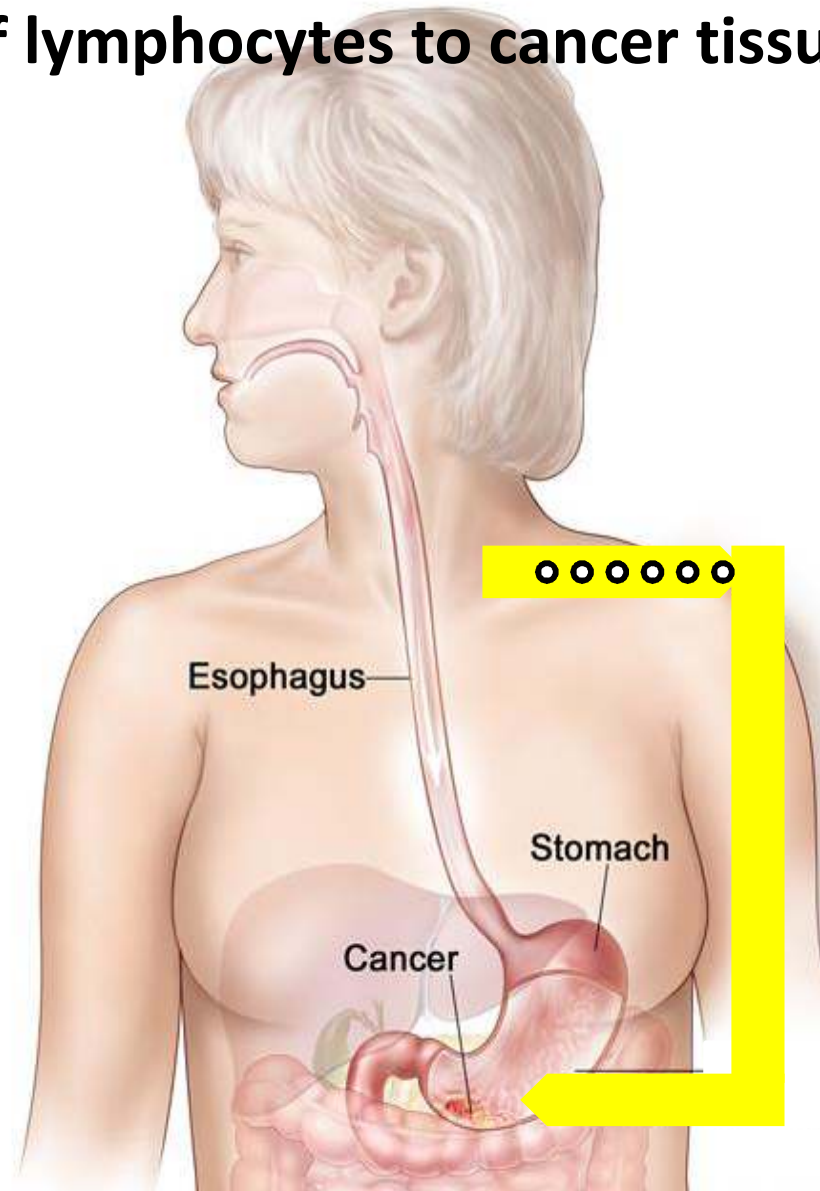


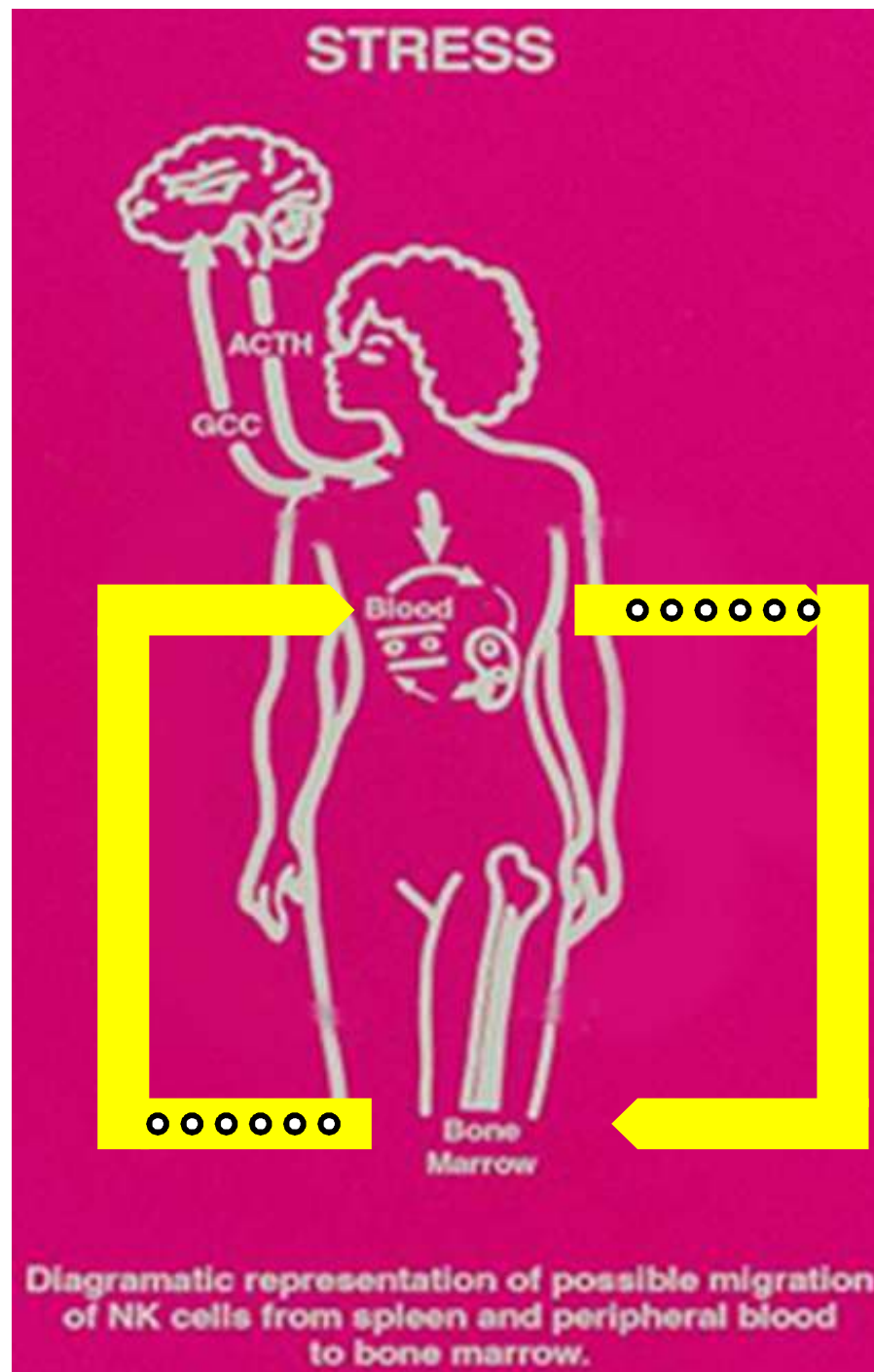
# **Mechanisms underlying the loss of lymphocytes**

- 1. Migration of lymphocytes to cancer tissues**
- 2. Phagocytosis (eat up) of lymphocytes by tumor cells**



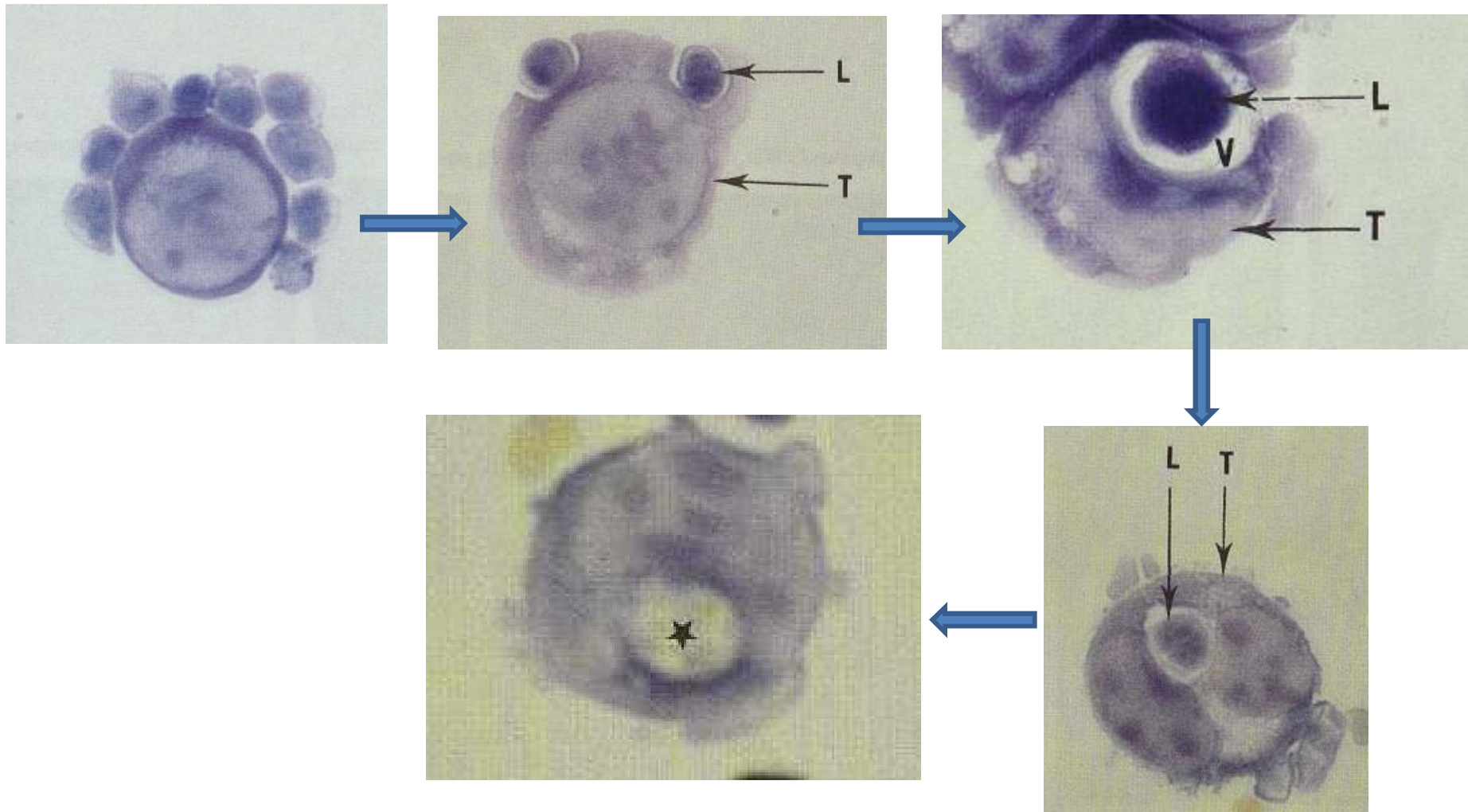
# 1. Migration of lymphocytes to cancer tissues





Ghoneum M. et al. Immunol. 60:461-65. (1987).

## ***2-Phagocytosis (eat up)of lymphocytes by cancer cells*** **(LAZ-559, B cell lymphoma of human origin).**



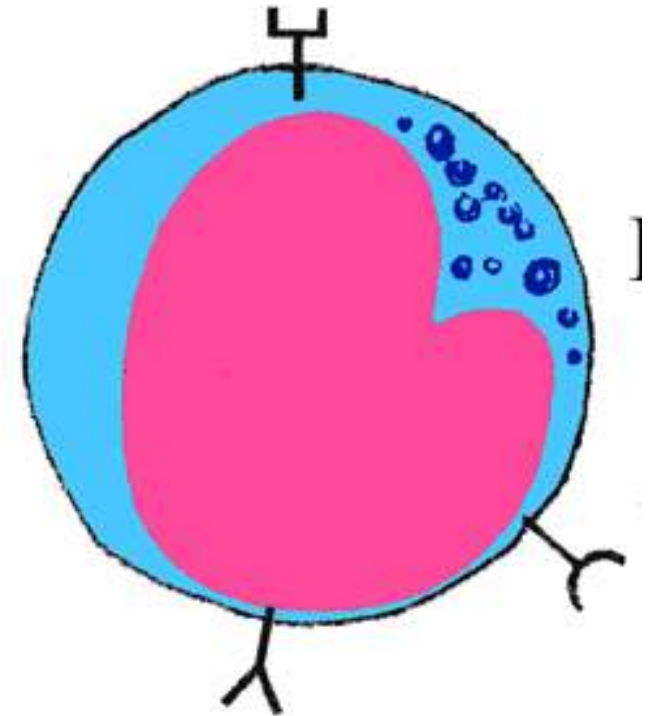
[Ghoneum M, Grewal IS. Hematol Oncol. 1990 ;8\(2\):71-80.](#)

# **MRN-100 Enhances Natural Killer Cell Anti-Cancer Activity**

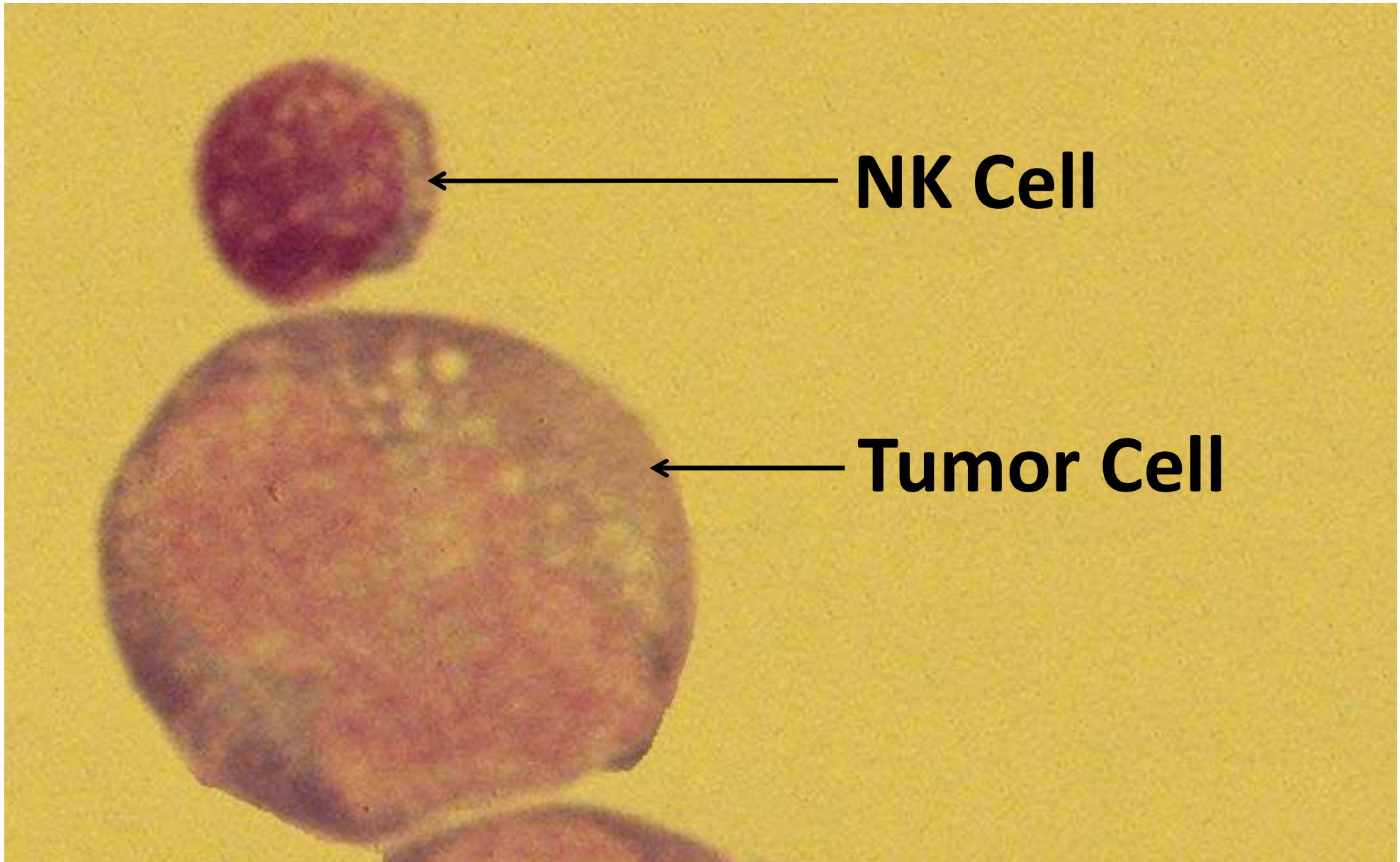
***Natural Killer (NK) Cells: The first line of  
defense against cancer***

# *Dissecting the pathway of NK cell killing the cancer cell*

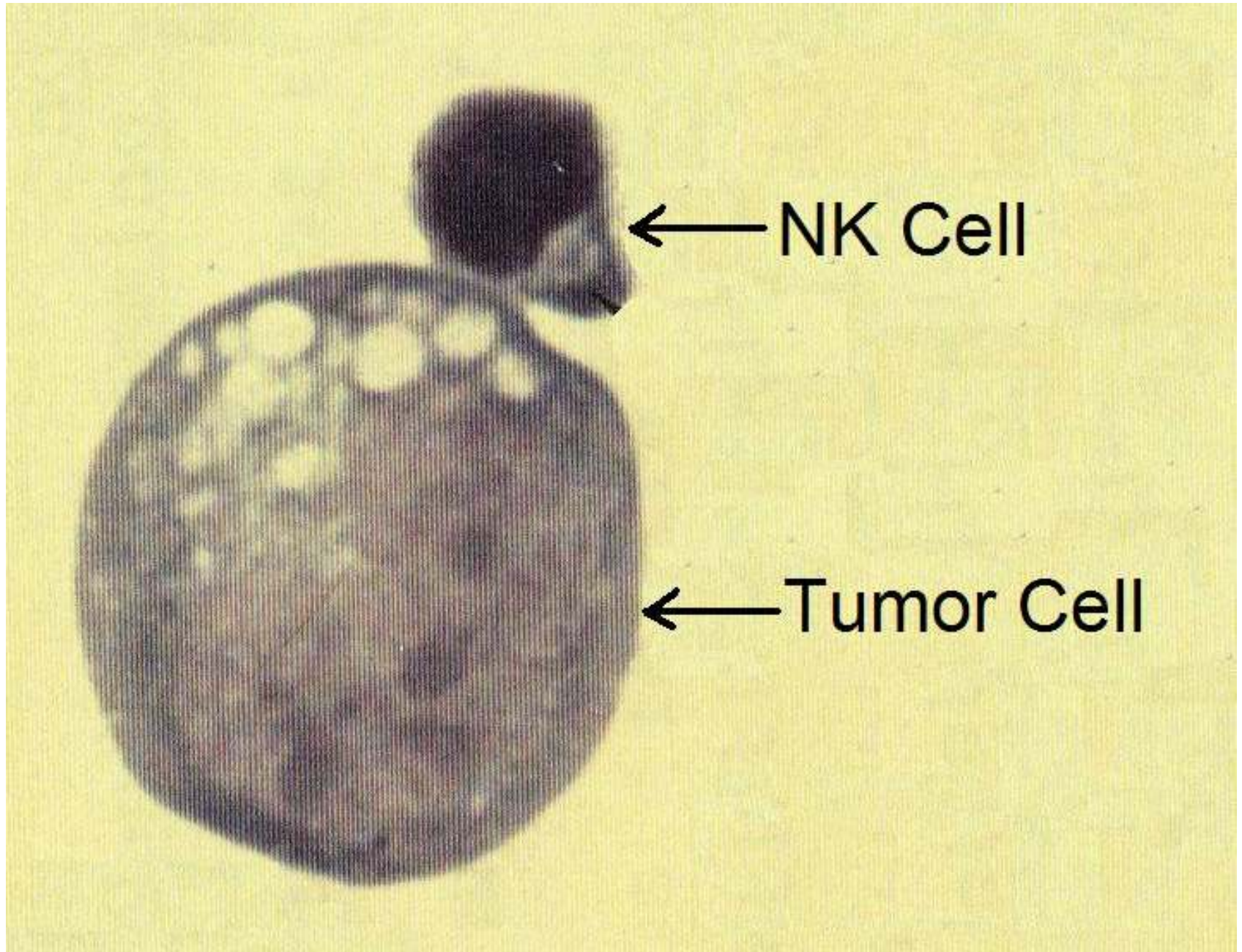
1. NK cell binds to cancer cell
2. NK cell discharges the granules inside the cancer cell, which causes holes in the cancer cell
3. Death of cancer cell
4. NK cell attacks new cancer cell (recycle)



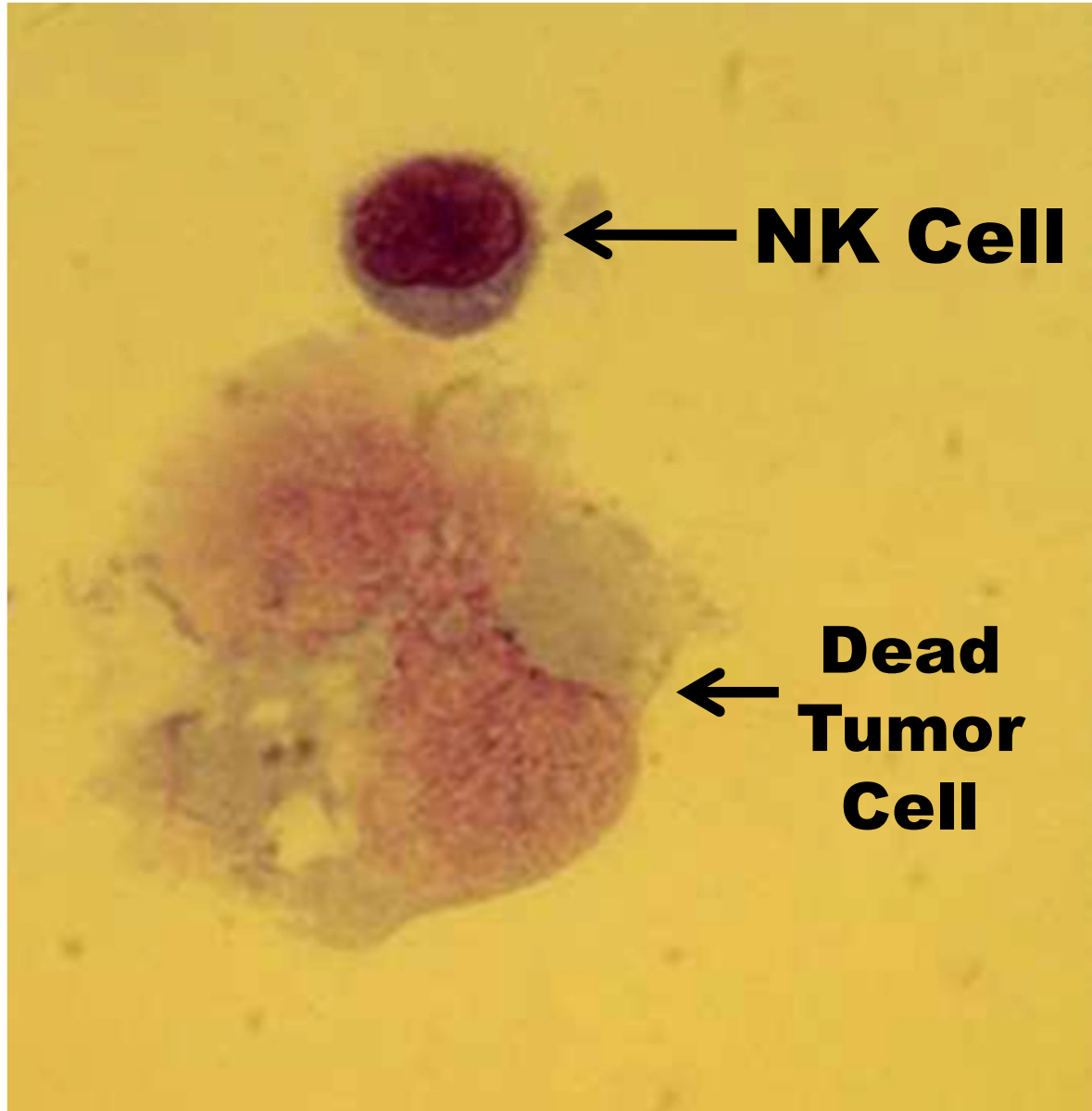
# 1. NK cell binds to cancer cell



## ***2. NK cell induces holes in cancer cell***

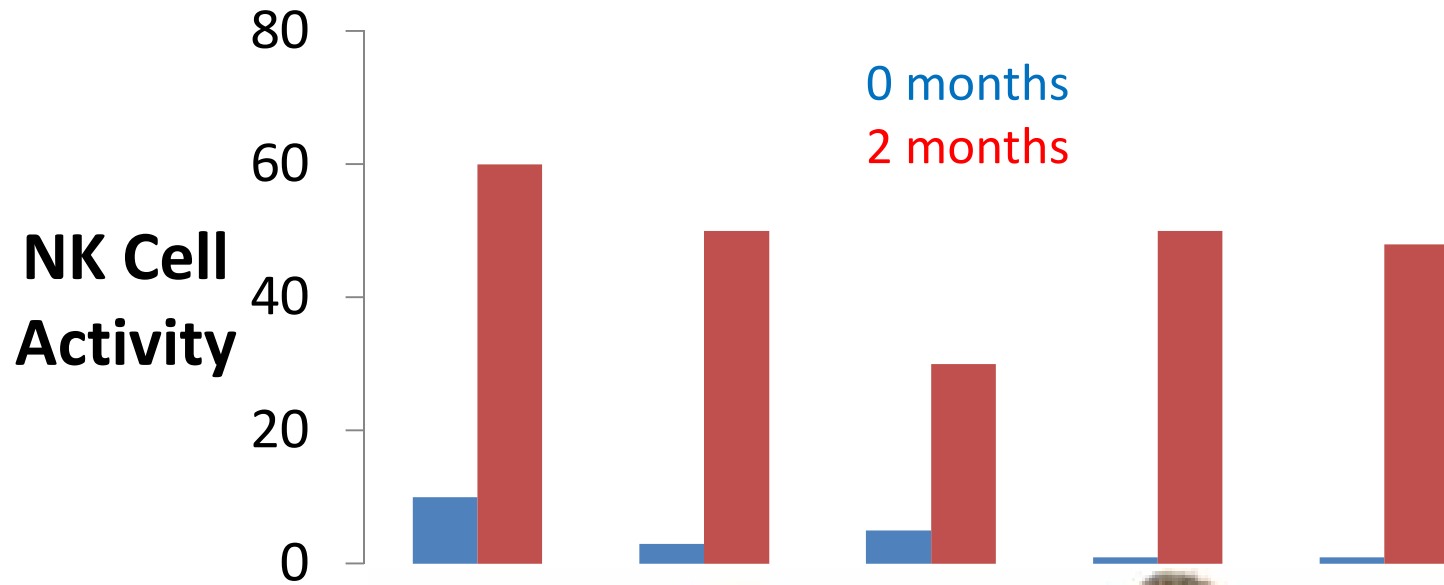


### ***3. Cancer cell is dead***





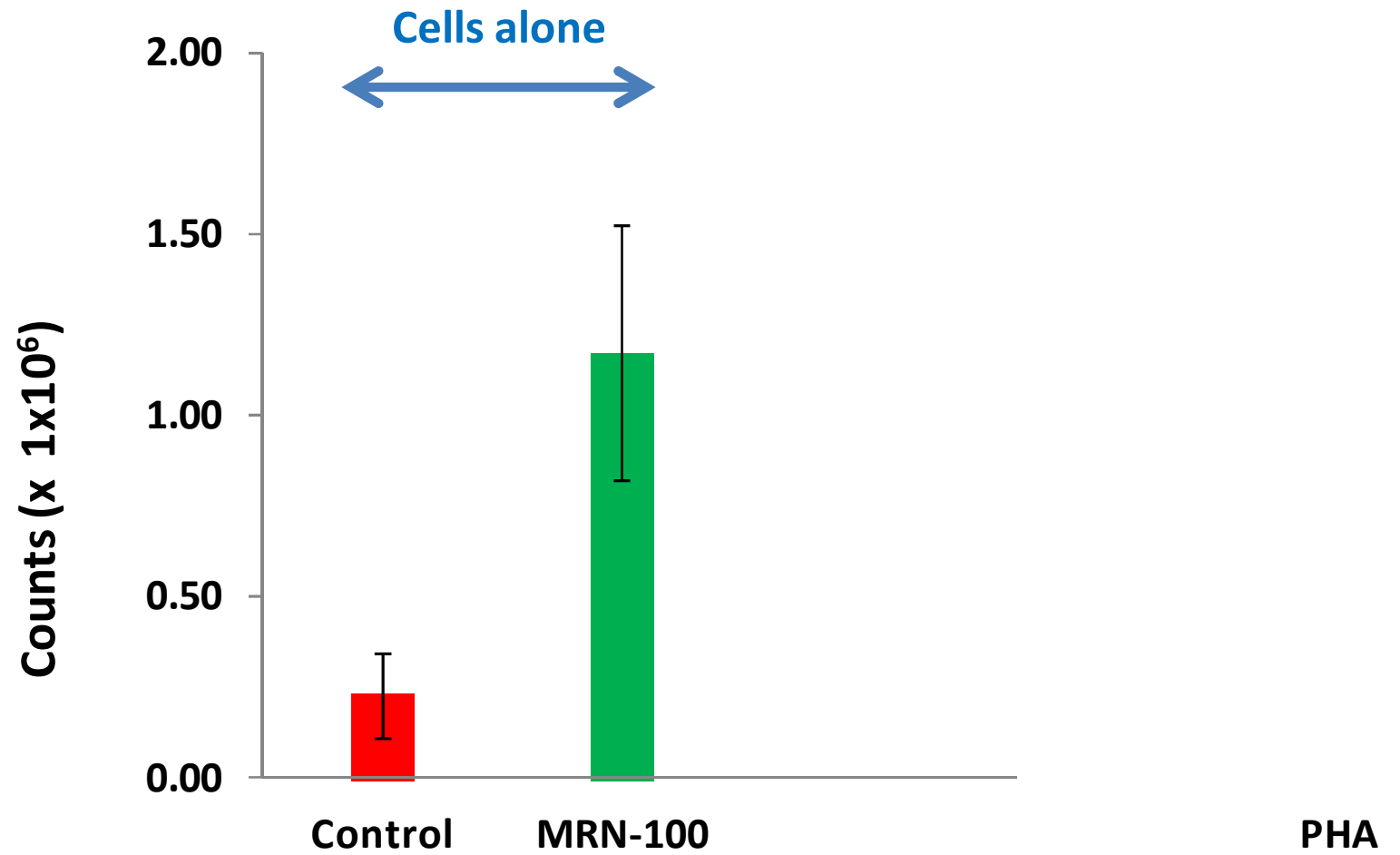
# MRN-100 Enhances Human NK Cell Activity



**Members of the Society of Natural Immunity  
Honolulu, Hawaii, Nov. 10-12 1985**



# MRN-100 Enhances Human T Cell Proliferation



**MARN-100 activates DC**

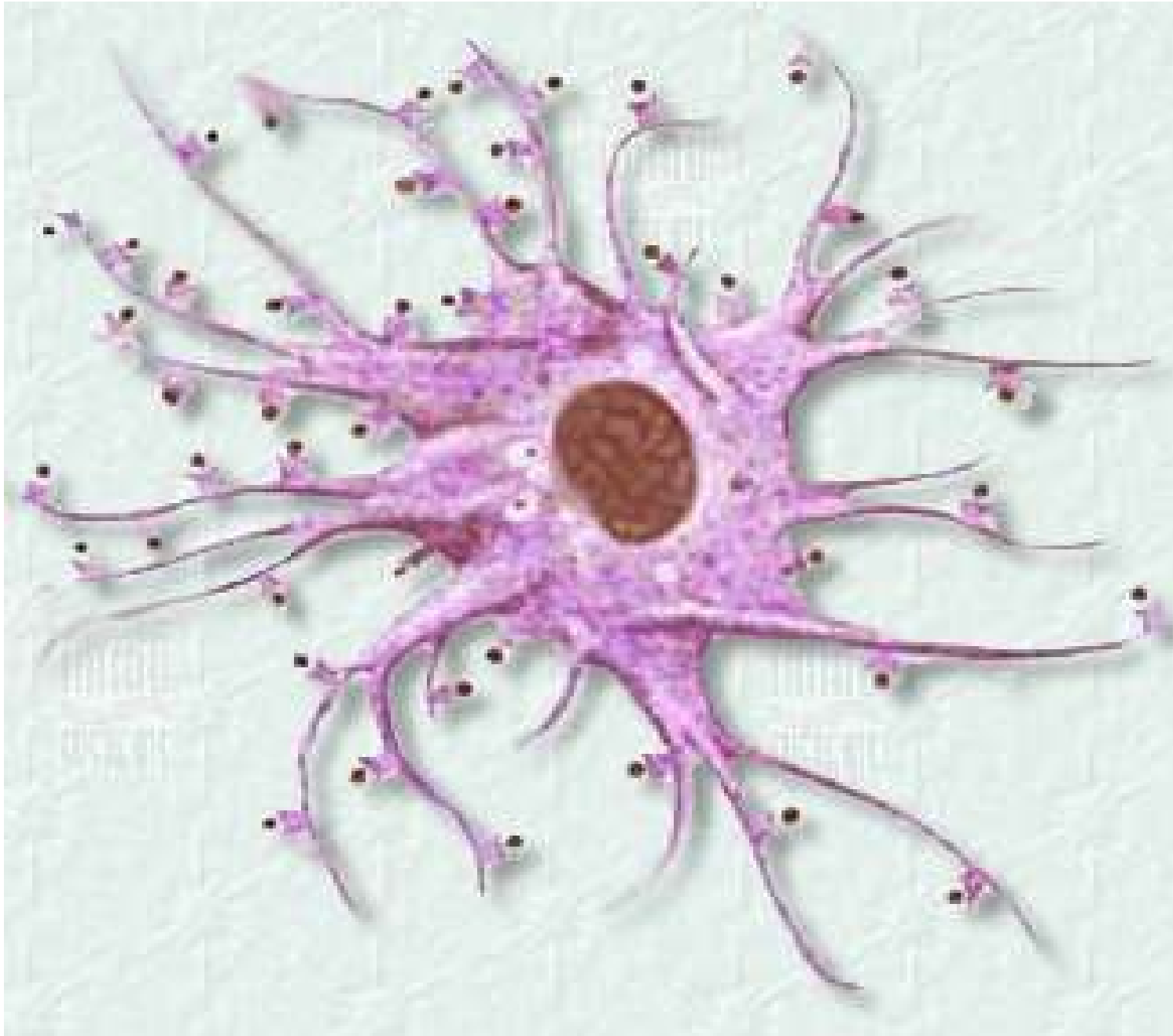


# DC

washington  
**DC**™



# Dendritic cells (DCs)



# **Dendritic Cell**

**(The MOST Efficient Antigen Presenting Cells, APC)**

**Their main function is to process antigen material and present it on the surface to other cells of the immune system, thus functioning as antigen-presenting cells.**

**They act as messengers between the innate and adaptive immunity.**

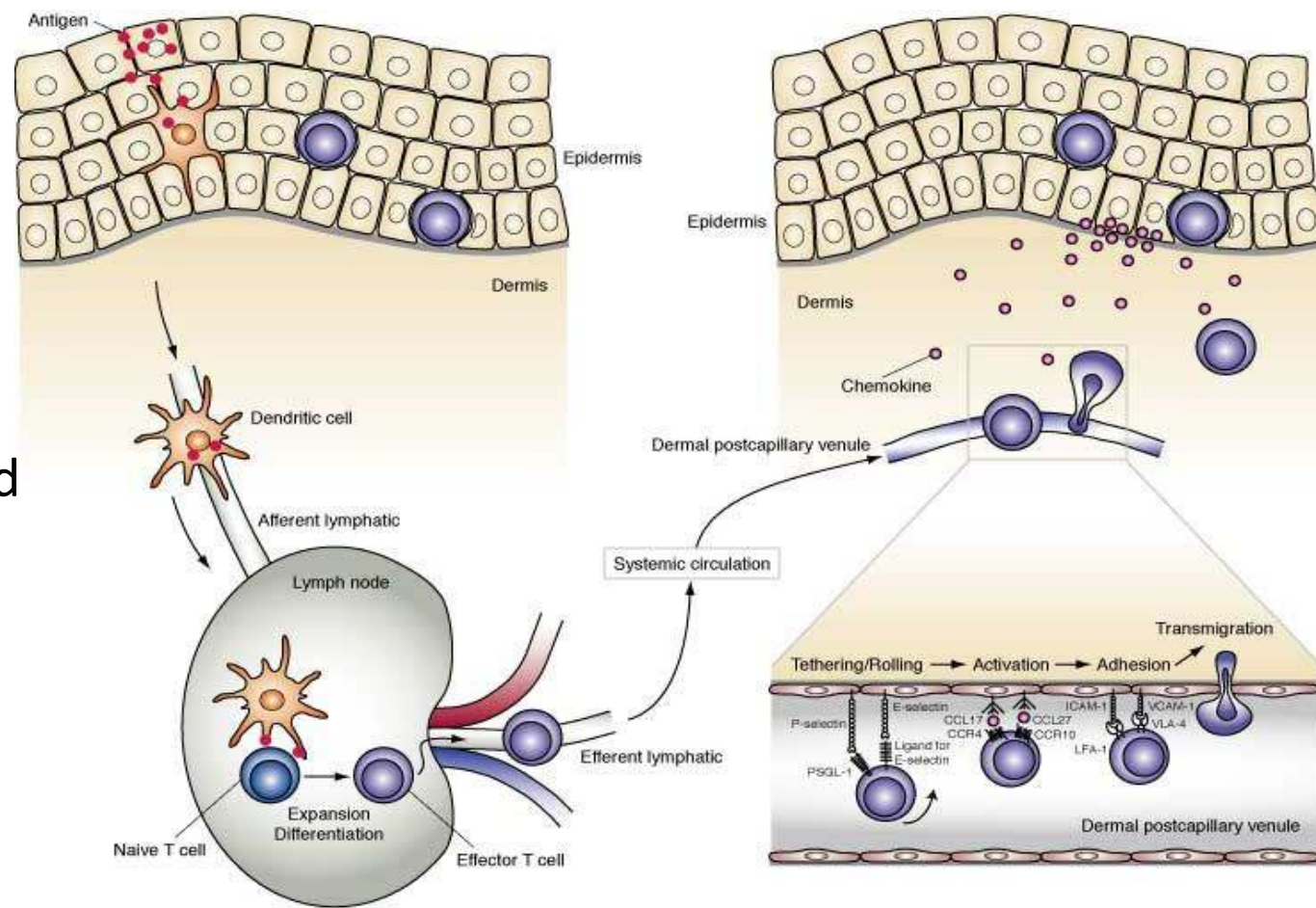


# DC and T cells migration to and from the skin

1-Germs (antigens) that enter the skin are loaded on DCs, which migrate to draining lymph nodes

2- In the lymph nodes, naive T cells are activated by the germ-loaded DCs and start to multiply

3-These germ- responsive T cells migrate into the injured site



[Yamamichi N](#), [Oka M](#), [Inada K](#), [Konno-Shimizu M](#), [Kageyama-Yahara N](#), [Tamai H](#), [Kato J](#), [Fujishiro M](#), [Kodashima S](#), [Niimi K](#), [Ono S](#), [Tsutsumi Y](#), [Ichinose M](#), [Koike K](#). [Biochem Biophys Res Commun](#). 2012 Jul 20;424(1):124-9.

Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Tokyo 113-8655, Japan.

Rebamipide has potential tumor-suppressive effects on gastric tumorigenesis via the recruitment of dendritic cells.

**Rebamipide**, an [amino acid](#) derivative of 2-(1*H*)-quinolinone, is used for mucosal protection, healing of gastroduodenal ulcers.



**MRN-100**

**as a DC Activator  
via**

**1: Increased Expression of Co-  
Stimulatory Molecules**

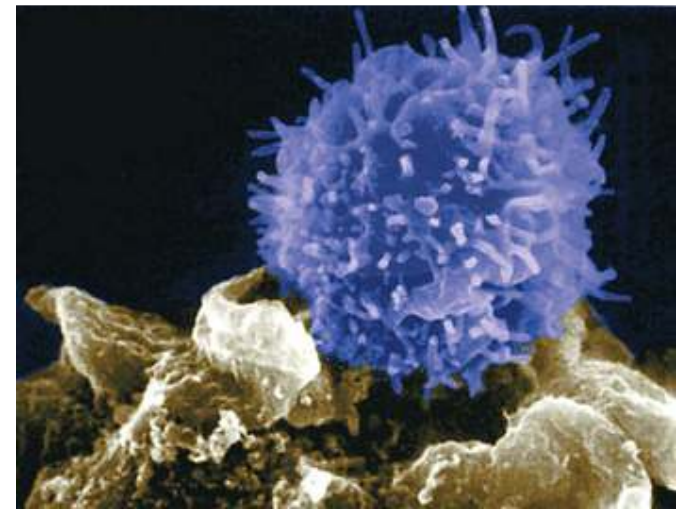
**2: Increased Cytokine Production**

**MRN-100**

**as a DC Activator**

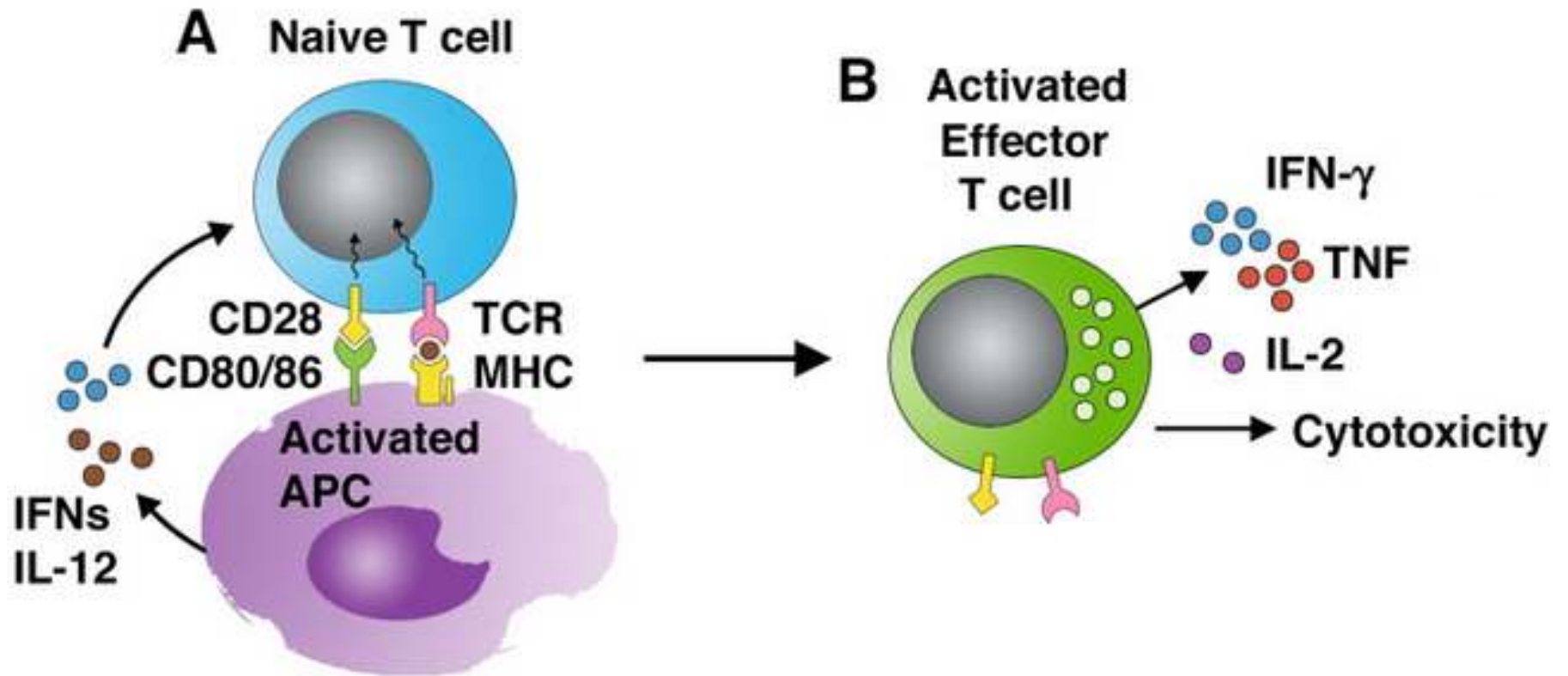
**1: Through Increased  
Expression of Co-  
Stimulatory Molecules**

# T Cells

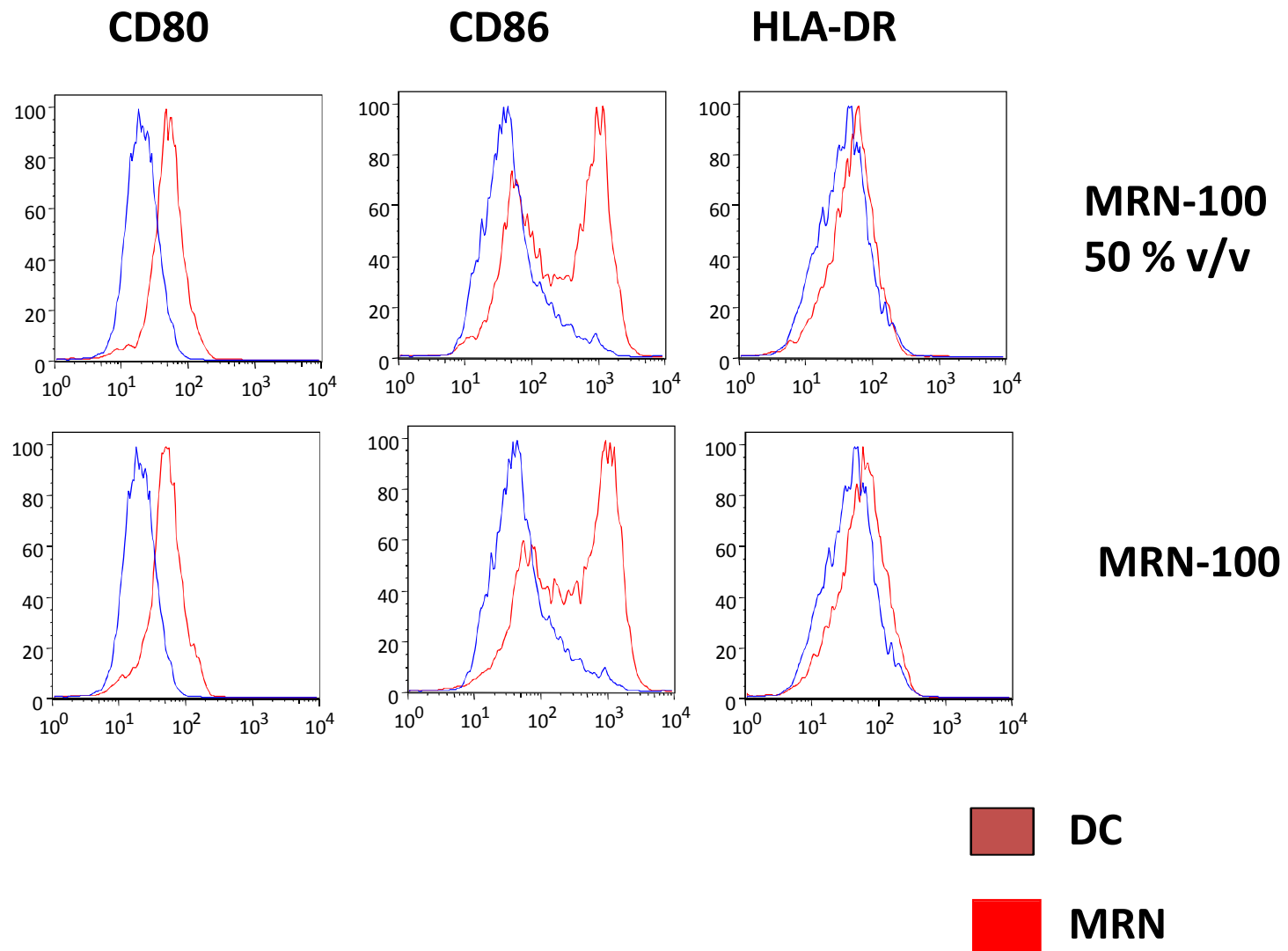


- **T cells are white blood cells**
  - **Involved in cell-mediated immunity**
- **T cells act as soldiers, seeking out and killing invaders**

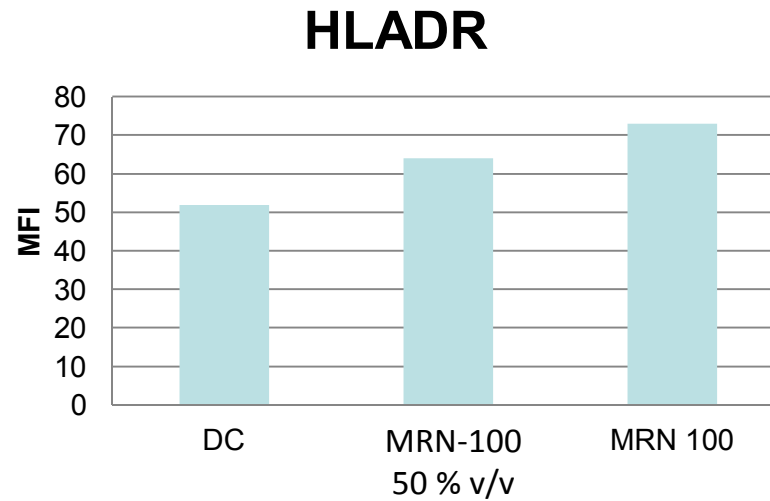
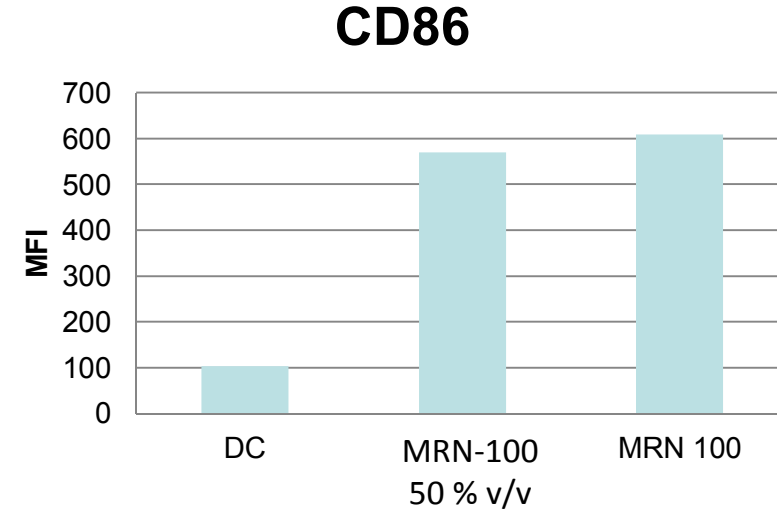
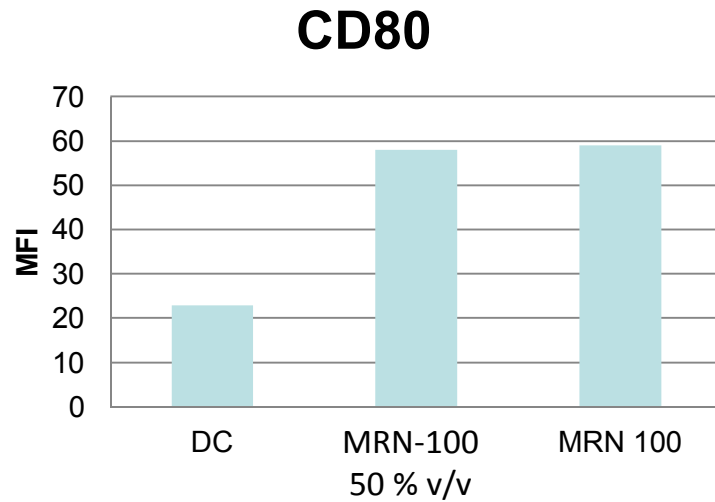
# CD86 Expression



# Different Concentrations of MRN-100 Activate Dendritic Cells



# MRN activated Dendritic cells upregulate Co-stimulatory markers and HLADR





**MRN-100**

**as a DC Activator**

**2: Through Secretion of  
Cytokines**

**Cytokines**: Small proteins

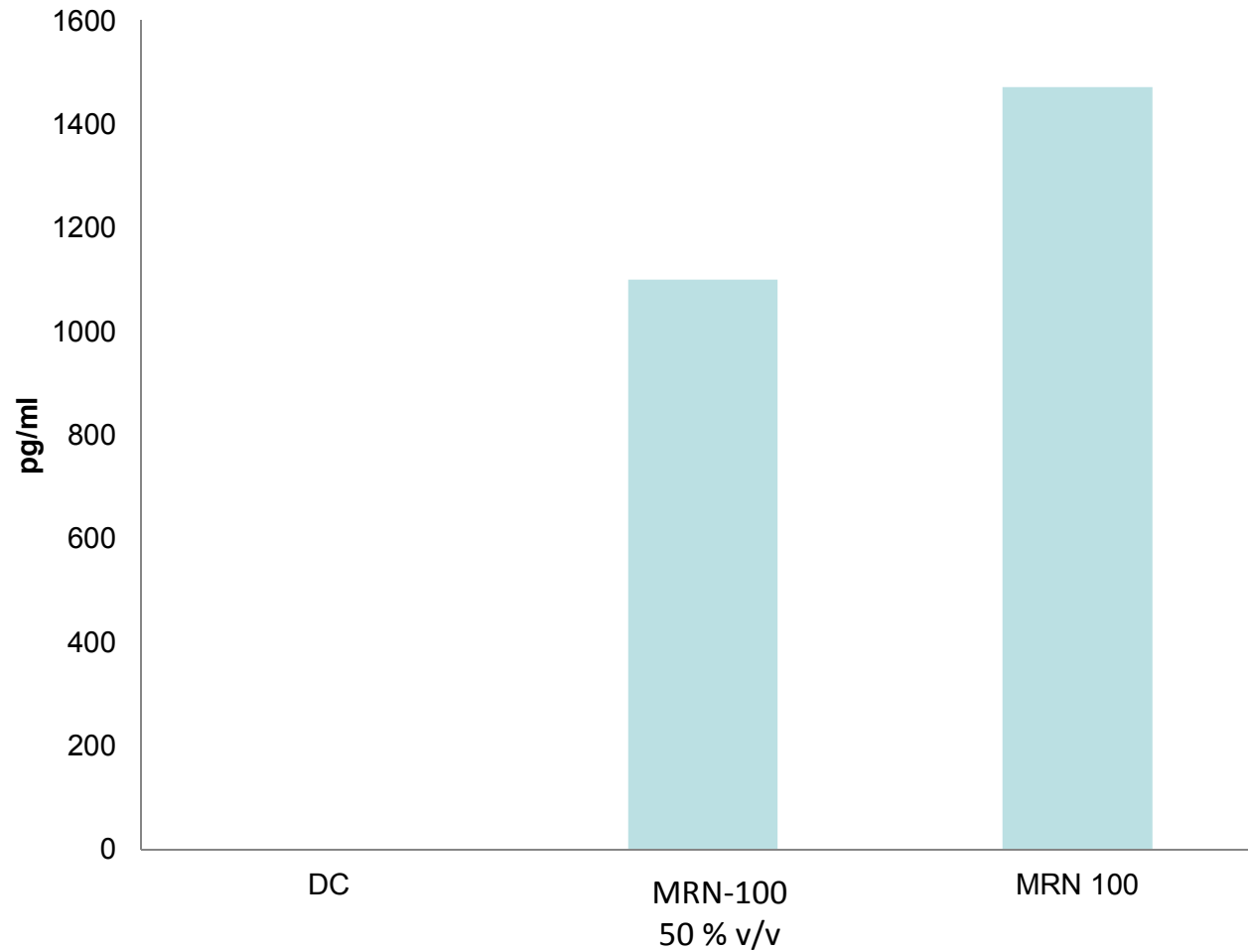
**which:**

**1. Regulate immunity and inflammation**

**2. Are produced in response to an immune stimulus.**

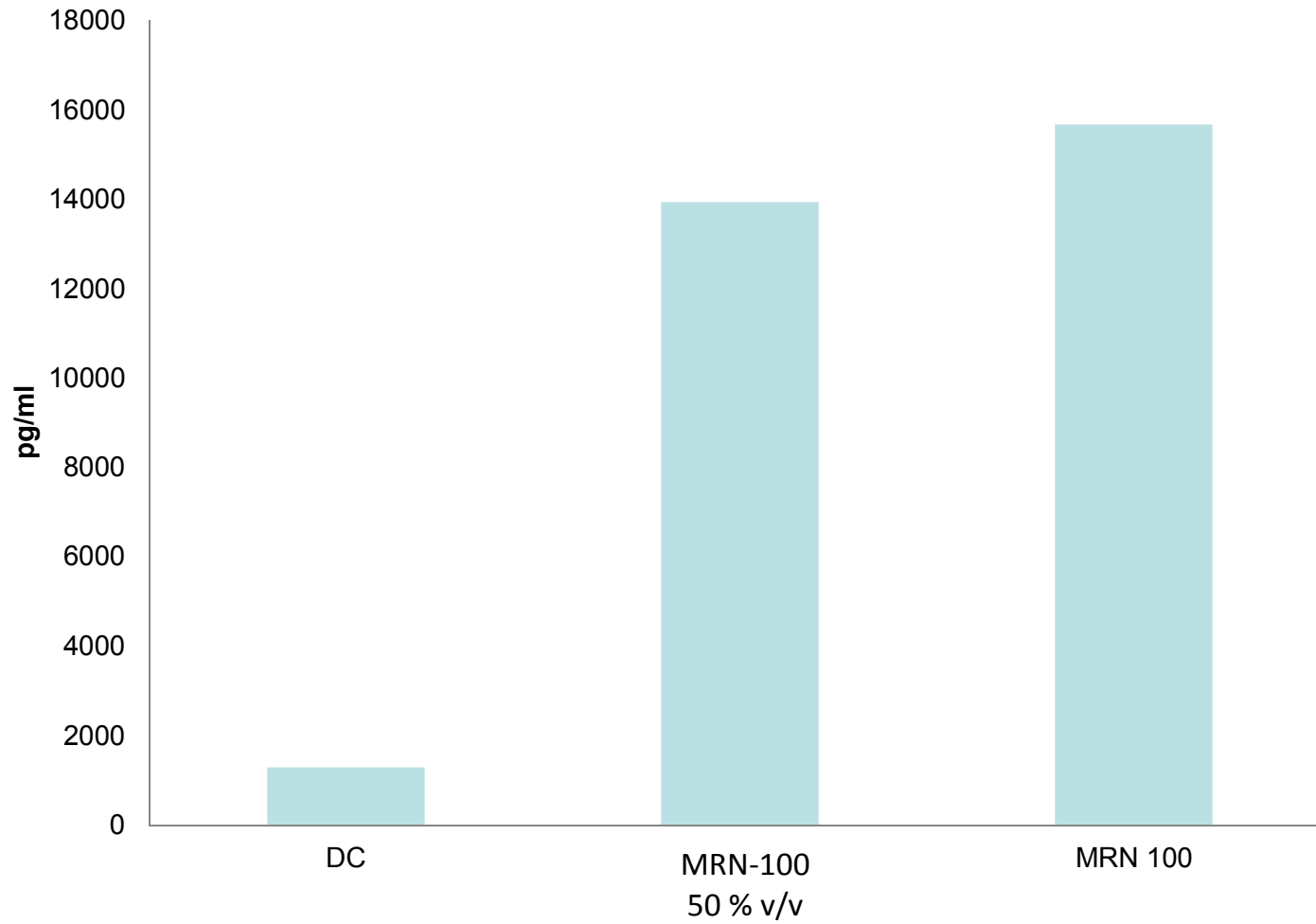
# MRN-100 activates DCs secrete Cytokines

## TNF $\alpha$



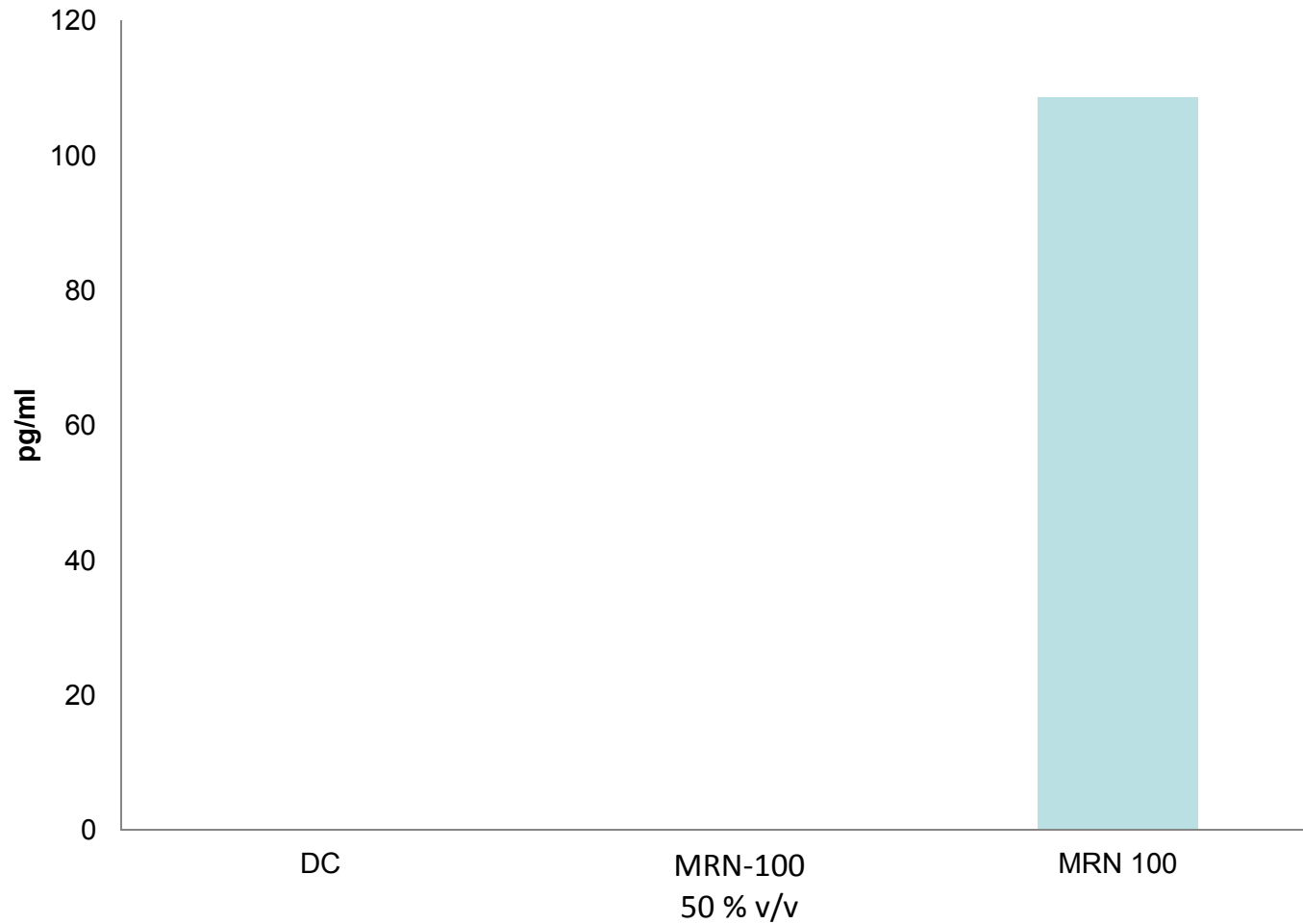
# MRN-100 activates DCs secrete Cytokines

## IL6



**MRN-100** activates DCs secrete Cytokines

**IL1b**



# CYTOKINES



**CELLULAR  
ACTIVATION**

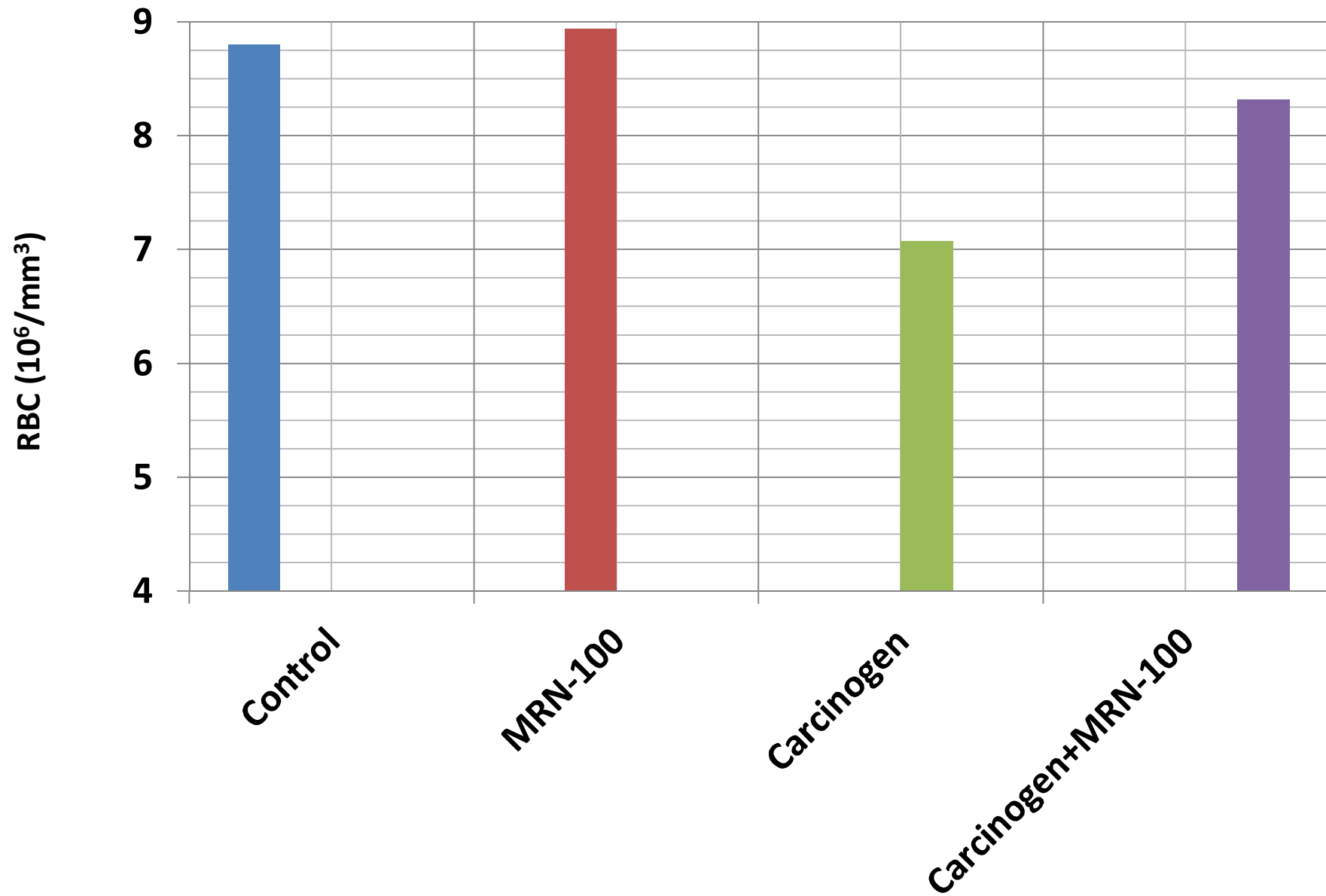


IFN- $\gamma$

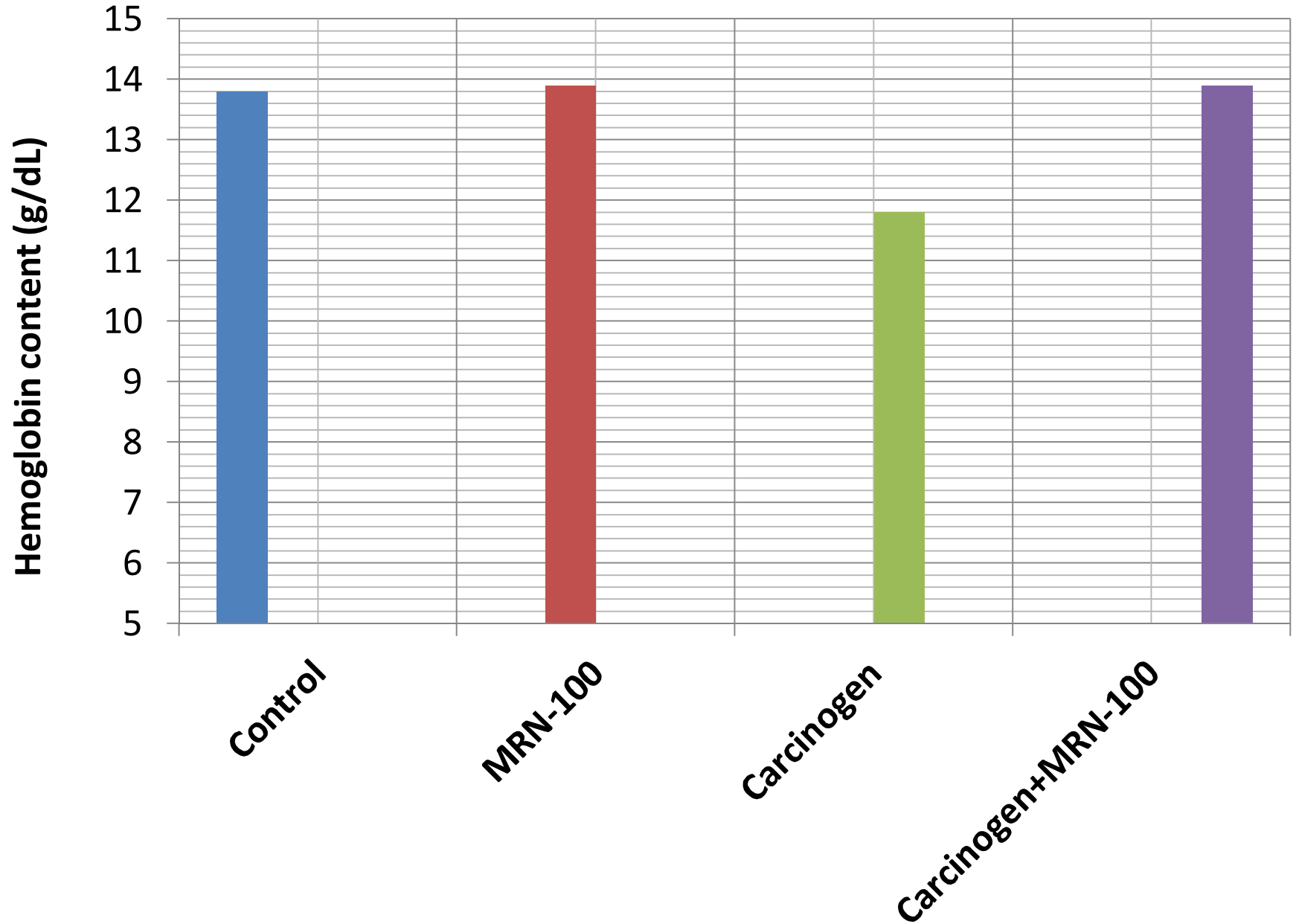
TNF- $\alpha$

IL-10

# MNR-100 Protects Against Loss of Red Blood Cells

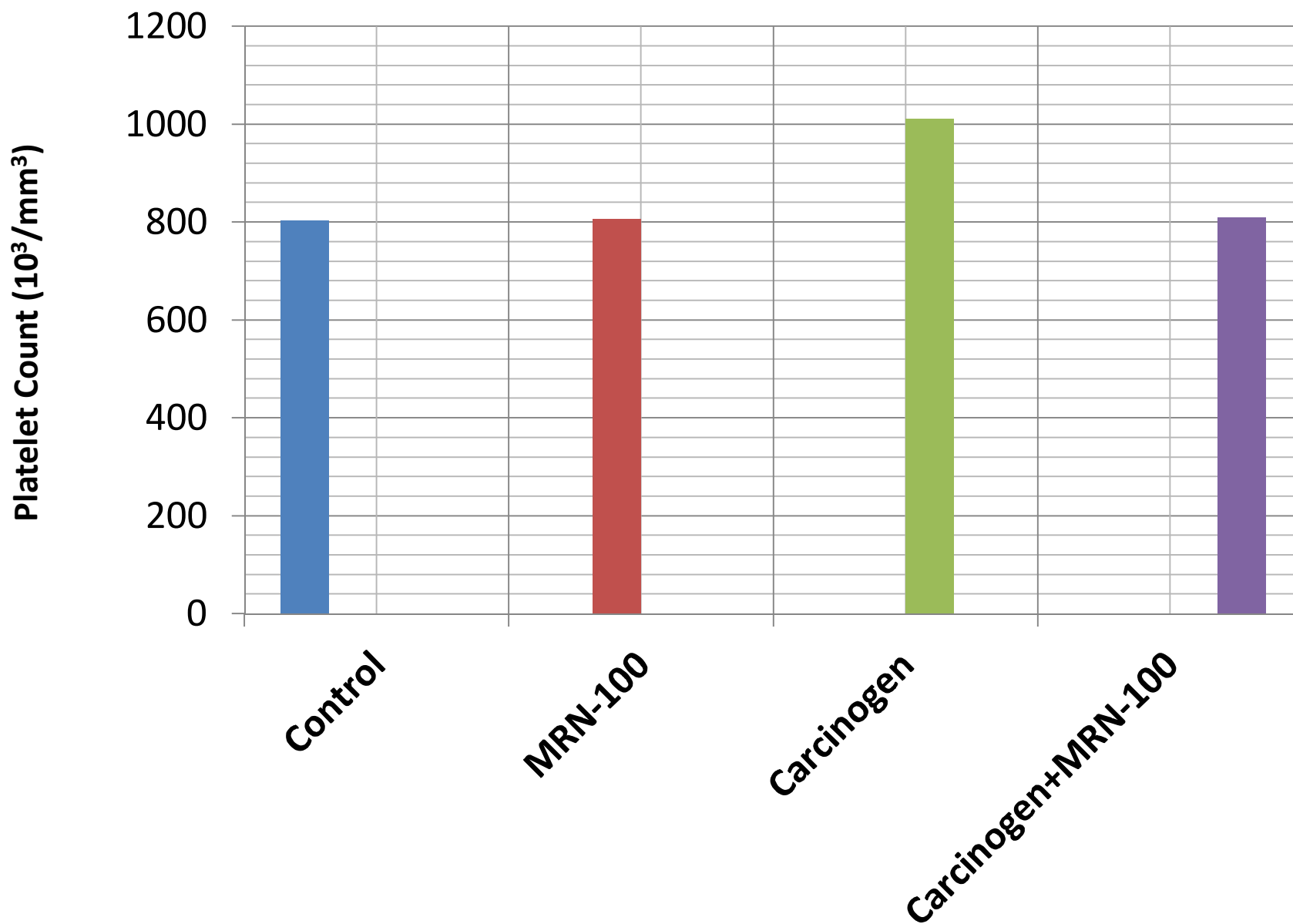


# MNR-100 Protects Against Loss of Hemoglobin Content





# MNR-100 Protects Against Loss of Blood Platelets



# Conclusions

- Our study suggests MRN-100 may be an effective adjuvant for the treatment of gastric and esophageal cancer.
- The mechanism by which MRN-100 exerts its effect may involve its ability to protect against:
  - a. Oxidative stress by carcinogen
  - b. Damage of immune system by carcinogen

# Publications and Presentations related to MRN-100

- Ghoneum M and Kijima Y. Induction of human natural killer (NK) cell activity by p-water (MRN-100). Ann. Conf. on Clinical Immun. New Orleans, LA May 31-June 3 (1996).
- Ghoneum M, Choong K and Namatalla G. p-water (MRN-100) possesses anti-HIV activity in vitro. Palm Springs symposium on HIV/AIDS foundation of HIV therapy. Palm Springs, CA., Mar. 13-16 (1997).
- Ghoneum M, Namatalla G and Kijima Y. Phenotypic analysis of human lymphocyte sub-populations post treatment with p-water (MRN-100). Abstract, proceedings of the 88th Ann. Meeting of American Assoc. for Cancer Res. San Diego, CA., Apr 12-16 (1997).
- Ghoneum M. NK immunorestitution in cancer patients by MRN-100, an iron based compound derived from bivalent and tervalent ferrate. 4<sup>th</sup> Int. Symp. on predictive oncology and therapy. Nice, France. Oct. 24-27, 1998.
- Ghoneum M. MRN-100 depletes glutathione level and increases human head and neck carcinoma Calu-27 sensitivity to natural killer cell cytotoxicity. 4<sup>th</sup> Int. Symp. on predictive oncology and therapy. Nice, France. Oct. 24-27, 1998.
- Tachiki K, Uyemura K, Ghoneum M, Makinodan T. and Yamaguchi, D. Inhibition of tumor cell growth and modulation of cytokine production by the iron based compound MRN-100. American Association for Cancer Research (AACR) Proceedings Cytokines and Cancer: Regulation, Angiogenesis, and Clinical Applications. Vail, Colorado. September 20-24, 2000.
- Badr El-Din NK, Noaman E, Ghoneum M, and Abdel Fattah SM. An Iron-Based Beverage, Hydro-Ferrate Fluid (MRN-100), Protects Against Oxidative Stress in Aging Rats. Abstract In: Annals of Nutrition & Metabolism 55(1)2009. Presented at 19<sup>th</sup> International Congress of Nutrition. Bangkok, Thailand. October 4-9, 2009.
- Ghoneum M. Elbaghdady H, El-Shebly A and Pan D. Protective effect of HydroFerrate Fluid, MRN-100, on survival and hematopoietic cell recovery in  $\gamma$ -radiated Fish, *Tilapia Nilotica*. Health Physics Society (HPS) 57th Annual Meeting (American Conference of Radiological Safety). 22-26 July, 2012 in Sacramento, CA.
- Ghoneum M, Matsuura M and Gollapudi S. An iron-based beverage, hydro ferrate fluid, MRN-100, alleviates oxidative stress in murine lymphocytes *in vitro*. Nutrition J. 8(1); 18 (2009).
- Badr El-Din NK, Noaman E, EL-Banna SM, and Ghoneum M. Reversal of age-associated oxidative stress in rats by MRN-100, a hydro-ferrate fluid. In Vivo. 24:525-34 (2010).
- Ghoneum M and Shaheen M. MRN-100, an iron-based compound possesses anti-HIV activity *in vitro*. Evid Based Complement Alternat Med. 7(4): 427-432 (2010).
- Ghoneum M, Elbaghdady H, El-Shebly A and Pan D. Protective effect of HydroFerrate Fluid, MRN-100, on survival and hematopoietic cell recovery in  $\gamma$ -radiated Fish, *Tilapia Nilotica*. J Rad Res.(submitted, 2012).
- Ghoneum M and Badr El-Din N, Mitochondria and Modulating Oxidative Stress: A Role for HydroFerrate Fluid (MRN-100) in Reversing Age-associated Oxidative Stress and Apoptosis. (Review article in Japanese) Medical Science Digest (MSD) Vol. 38, 2 (2012).

# MRN-100

- Ghoneum M and Kijima Y. Induction of human natural killer (NK) cell activity by p-water (MRN-100). Ann. Conf. on Clinical Immun. New Orleans, LA May 31-June 3 (1996).
- Ghoneum M, Choong K and Namatalla G. p-water (MRN-100) possesses anti-HIV activity in vitro. Palm Springs symposium on HIV/AIDS foundation of HIV therapy. Palm Springs, CA., Mar. 13-16 (1997).
- Ghoneum M, Namatalla G and Kijima Y. Phenotypic analysis of human lymphocyte sub-populations post treatment with p-water (MRN-100). Abstract, proceedings of the 88th Ann. Meeting of American Assoc. for Cancer Res. San Diego, CA., Apr 12-16 (1997).
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# Acknowledgements

- Sastry Gollapudi, Ph.D. UCI, USA
- Nariman Bader El-Din, Ph.D. El Mansoura University, Egypt
- Lucilene Tolentino, MD. CDU, USA
- Lina Wang, MD. USC, USA
- Motohiro Matsuura, Ph.D. Jichi Medical University, Japan





**Linus Pauling, 2 time Nobel Prize Winner,  
Vitamin C advocate**





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**SUBCOMMITTEES**  
DOMESTIC RELATIONS  
PUBLIC TRANSPORTATION AND HIGHWAYS

April 22, 2004

Dr. Mamdooh Ghoneum Ph.D  
3240 Kelton Ave,  
Los Angeles, CA 90034

Dear Dr. Ghoneum:

On behalf of the State of Tennessee, we would like to extend our appreciation for your participation in the Alternative Medicine Seminar.

The information you provided was very beneficial to many Tennesseans with these diseases affecting the immune system.

The research you are conducting in the area of cancer research and immune system disease is valuable to so many people, and we thank you.

The State of Tennessee owes you our gratitude in assisting our citizens with alternative therapies in dealing with the treatment of many severe diseases.

Again, we thank you and look forward to having you back in our state again.

Respectfully yours,

Nathan Vaughn  
2<sup>nd</sup> District State Representative



Japanese Society of Complimentary and Alternative Medicine.

Japanese Immunology Society



# 感謝状

Manulook Ghoneum, Ph. D. 殿

あなたに私共 東洋医学免疫研究会  
の研究に際し 始終 一直 誠意を以つ  
て事にあたし多大な成果をおげ貴会  
の業種に冥加して下さりました。  
本日 ここに貴会を代表し 深く感謝  
の意を表します。

平成七年十一月二十六日



東洋医学免疫研究会

会長 佐藤 正

原宿免疫センター

理事 瀬戸 良



  
THE FILIPINO-CHINESE MEDICAL SOCIETY, INC.  
3<sup>RD</sup> SCIENTIFIC MEETING AND  
2<sup>ND</sup> ONCOLOGY SYMPOSIUM  
"ROLE OF IMMUNOTHERAPY IN CANCER"  
SPONSORED BY:  
 TAN YAN KEE FOUNDATION  
JULY 18, 2005





The  
FILIPINO-CHINESE MEDICAL SOCIETY, INC.

presents this

## PLAQUE OF APPRECIATION

to

**MAMDOOH GHONEUM, Ph. D.**

In grateful recognition of his invaluable contribution  
as GUEST SPEAKER of the  
3<sup>RD</sup> Scientific Meeting and 2<sup>ND</sup> Oncology Symposium of the  
Filipino-Chinese Medical Society, Inc., discussing the topic  
"ROLE OF IMMUNOTHERAPHY IN CANCER".

Given at Century Park Hotel this 18th day of July,  
year two thousand and five.

A handwritten signature in black ink, appearing to read "Carmencita Lo".

CARMENCITA LO, M.D.  
President

A handwritten signature in black ink, appearing to read "Nelson Lim".

NELSON LIM, M.D.  
Secretary

A handwritten signature in black ink, appearing to read "Susan Lee".

SUSAN LEE, M.D.  
Chairman  
Scientific Committee

A handwritten signature in black ink, appearing to read "Teresita Dy Uy".

TERESITA DY UY, M.D.  
Chairman  
Committee on Honors & Awards





The Embassy of the  
Arab Republic of Egypt

The Egyptian Cultural  
& Educational Bureau

*Honor the Cancer Research of*

**DR. MAMDOOH GHONEUM**

Charles Drew University of  
Medicine and Science  
University of California, Los Angeles

Washington, DC  
March 25, 2010



Wadi Halfa

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International Boundary  
National Capital  
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Road





