### The Role of MRN-100 in Fighting Cancer and Alzheimer's Disease

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# 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: ~10% uninsured (~33 Million)

### **Preventive Care**

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

# Outline

- 1. Bedil Ai Study: 2016 and 2017 new data
- 2. MRN-100 Exerts Anti-Cancer Activity
  - a) Immune modulation
- 3. Anti-Alzheimer's
  - a) Introduction and Findings
  - b) Antioxidant potential
- 4. Safety: is MRN-100 safe?
- 5. Conclusion
- 6. Acknowledgements



## Bedil Ai.

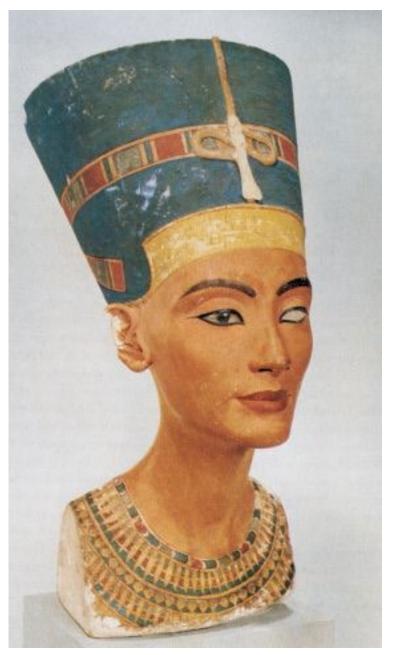
# Bedil Ai may be useful agent for improving eye vision.

# **MRN-100**

### **Compound Synthesis:**

MRN-100 is obtained from phytosin, a plant extract that contains iron and neutral lipid compounds, and can be found in rice, wheat, or radish seeds. When phytosin is dispersed in distilled water, ferric chloride is added, the lipid compounds are removed, and the iron compound obtained is subjected to fractional determination with respect to bivalent ferrate and trivalent ferrate in order to generate MRN-100.

### **Queen Nefertiti**



Nefertiti: Egyptian Queen known for her beautiful eyes

#### **Two Different Color Eyes**



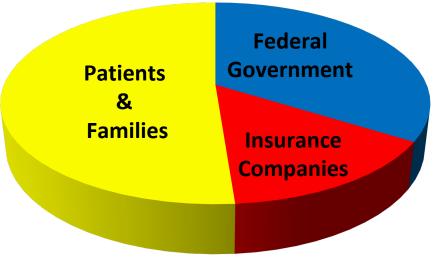
#### **Spiders** can have eight eyes



Why animals have so many eyes is still a mystery in many cases.

### Paying to correct eye vision problems

- The nation's annual cost of eye and vision disorders is about \$140 billion
  - According to National Opinion Research Center specialists at the University of Chicago
- Covering the bills:



• \$238 per person per year

https://www.mesvision.com/includes/pdf\_Broker/MESVision%20Facts%20and%20Statistics.pdf http://glassescrafter.com/information/percentage-population-wears-glasses.html http://www.usatoday.com/story/news/nation/2013/06/30/vision-related-diseases-cost/2453119

### **Experimental Design**



Autorefractor





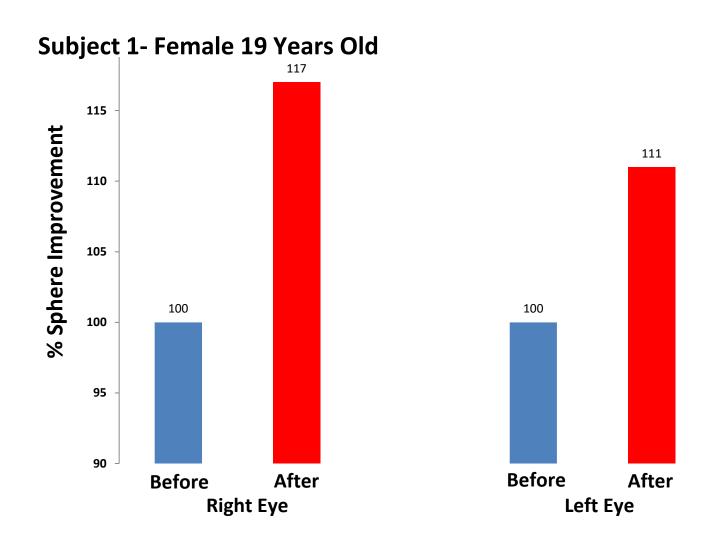
Manual refraction test with a instrument called **phoropter** 

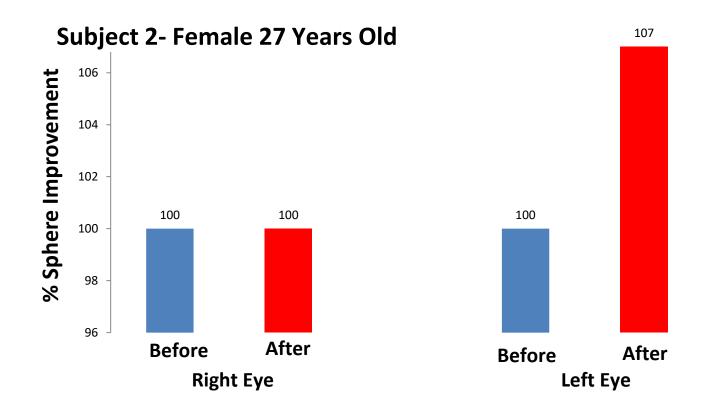
Bedil Ai for 1 month

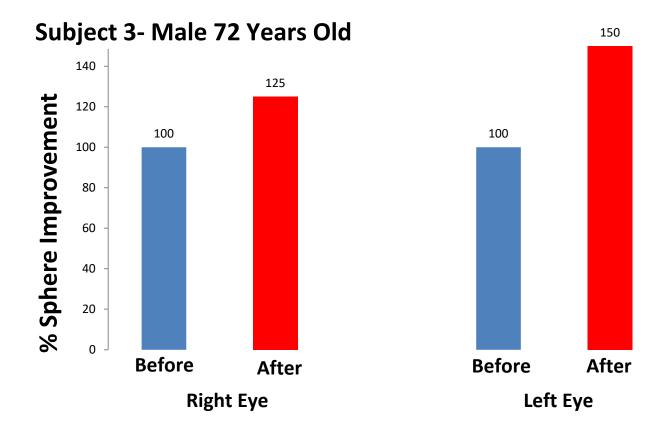
2<sup>nd</sup> Eye Exam

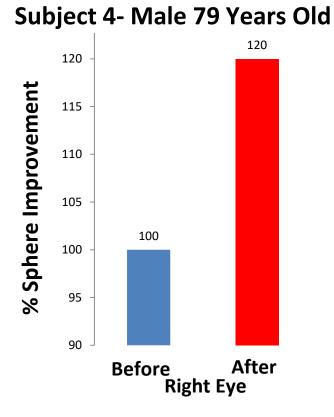
Refraction: The test that your eye doctor uses to determine your exact eyeglass prescription.

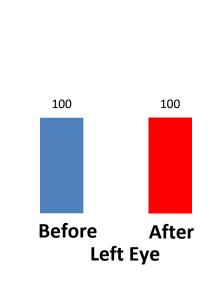


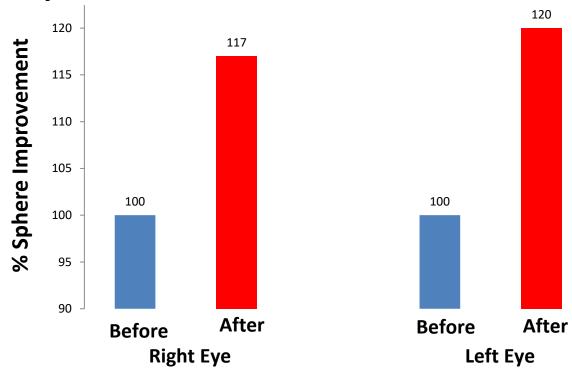




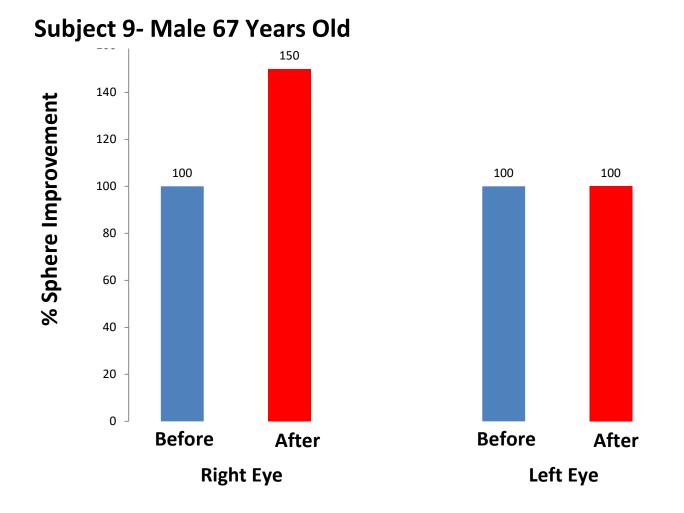


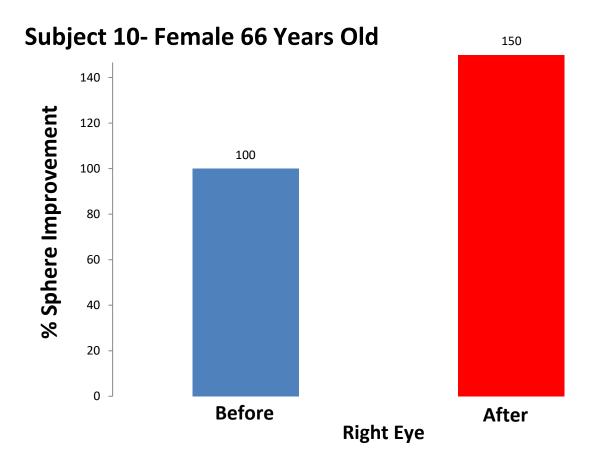


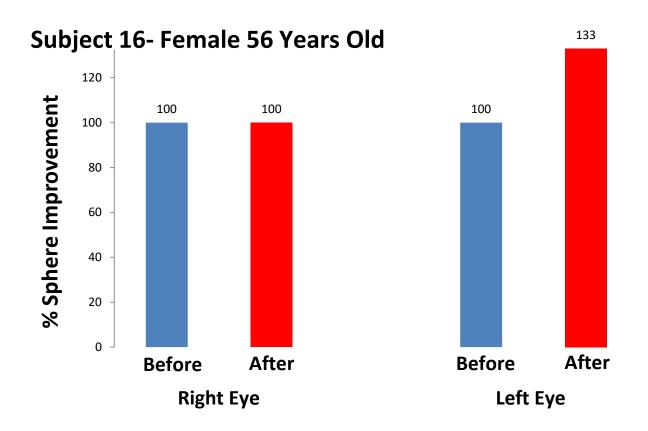


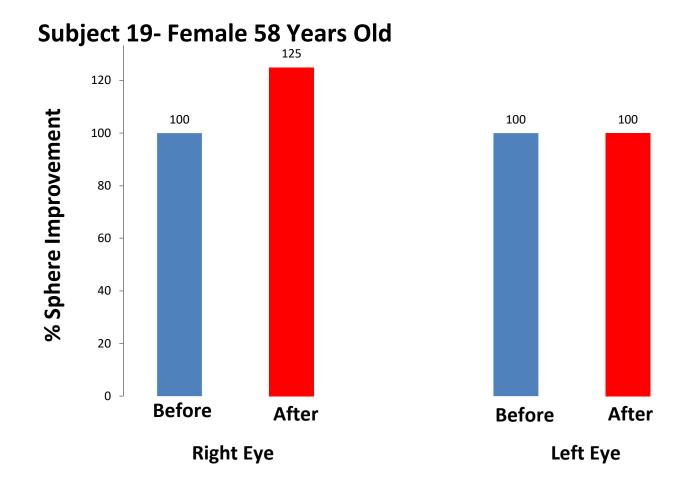


Subject 8- Female 70 Years Old

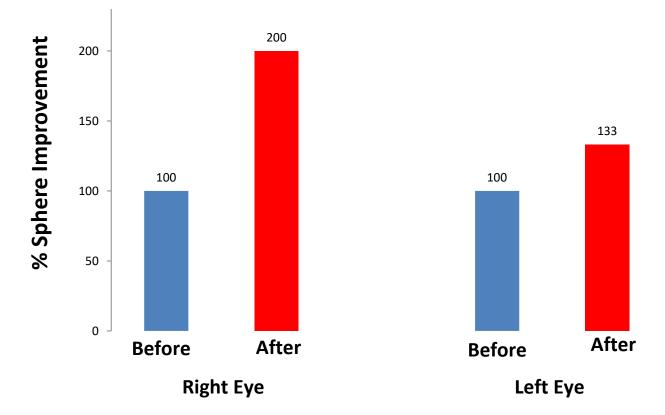




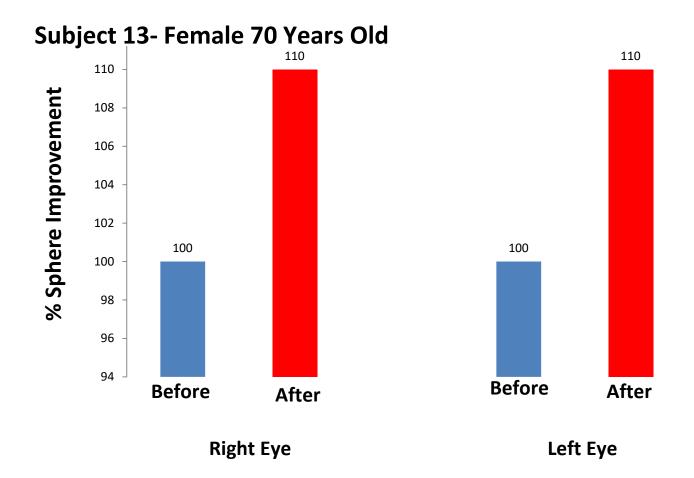


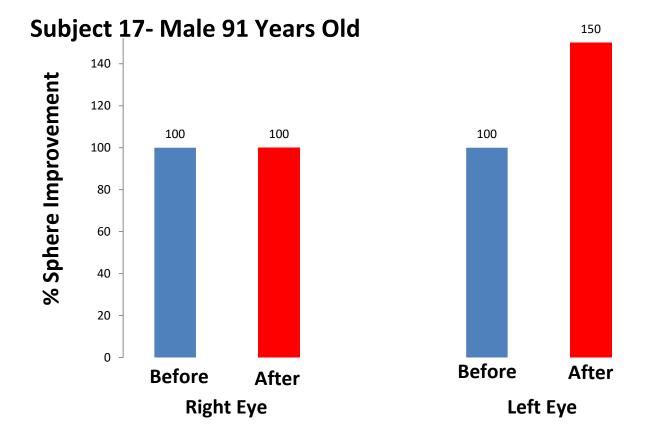


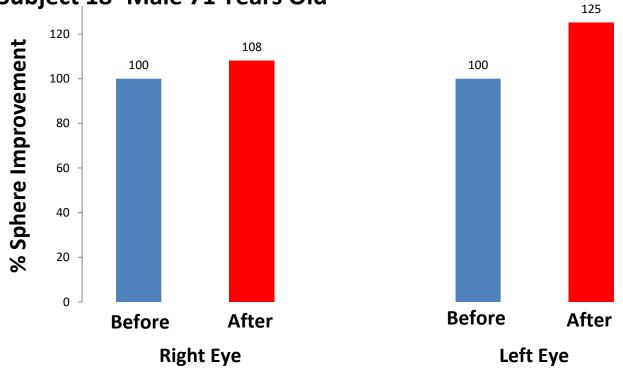
# New Data 2017



#### Subject 12- Female 69 Years Old







#### Subject 18- Male 71 Years Old

**Patient 10 Personal Comments:** 

After one month of using spray, could read tiny text on personal check (underneath check number in upper right-hand corner). Example: 497 11-35/1210 CA 90792.



### **Patient 17 Personal Comments:**



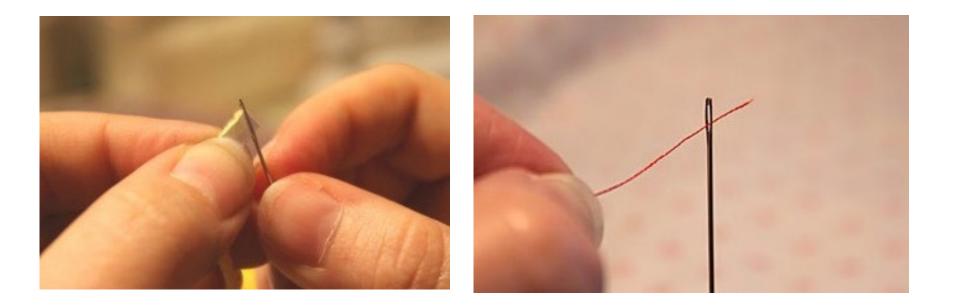
After using spray, tears stopped running and was able to see golf ball more clearly.

#### **Patient 18 Personal Comments:**



Dr. said glasses were too strong after 1 month and needed to be changed.

### **Patient 19 Personal Comments:**



Says that after using spray for one month, can now thread a needle (before she could not).

#### **Additional Comments By Subjects in 2017:**

Subject 13's doctor noted no eye pressure (glaucoma) after 1 month treatment

Subjects 15 and 16 said they noticed the eye pressure improved

# Conclusion

## New data support earlier results that Bedil Ai may be a useful agent for improving eye vision

# Break

Part II

### An iron-based compound, MRN-100, Exerts Anticancer Effect

### Dr. Mamdooh Ghoneum

Department of Surgery, Drew University of Medicine and Science, Los Angeles, CA, U.S.A.

# **Outline**

- I. Does MRN-100 Exert Anti-Cancer Activity?
  - A. Esophogeal and gastric cancer
  - B. Head and neck cancer
  - C. Leukemia
  - D. Skin cancer
- II. Mechanism that involves immune modulation



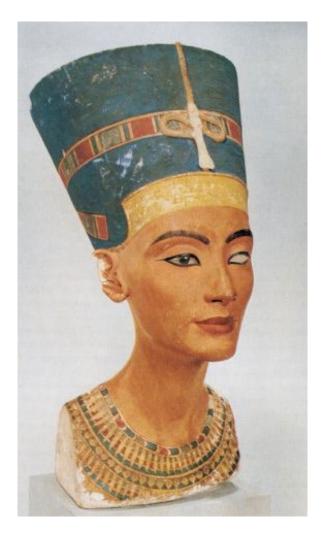
# PART I: The War on Cancer





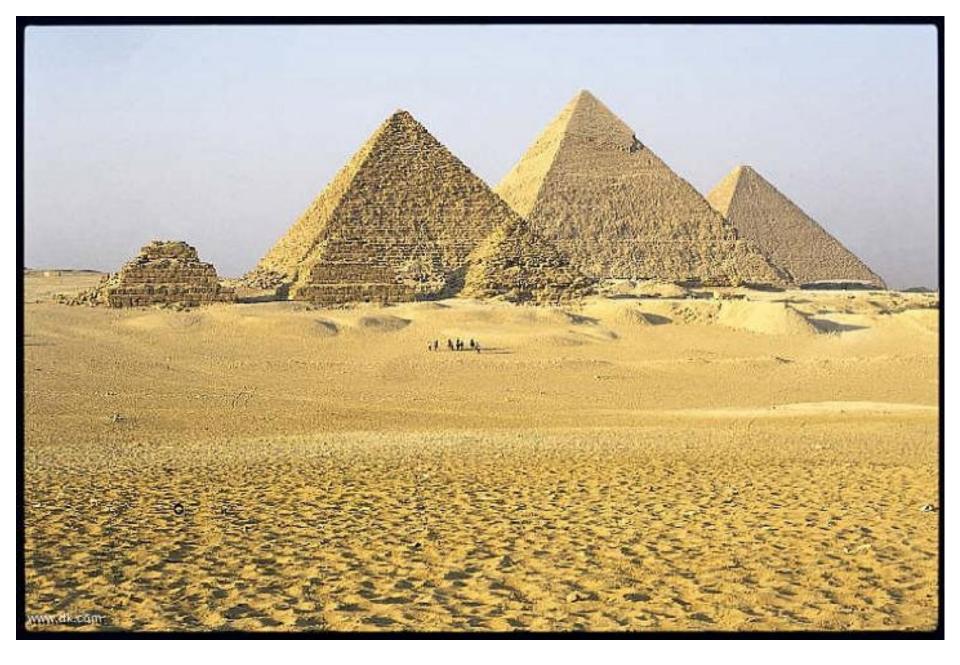






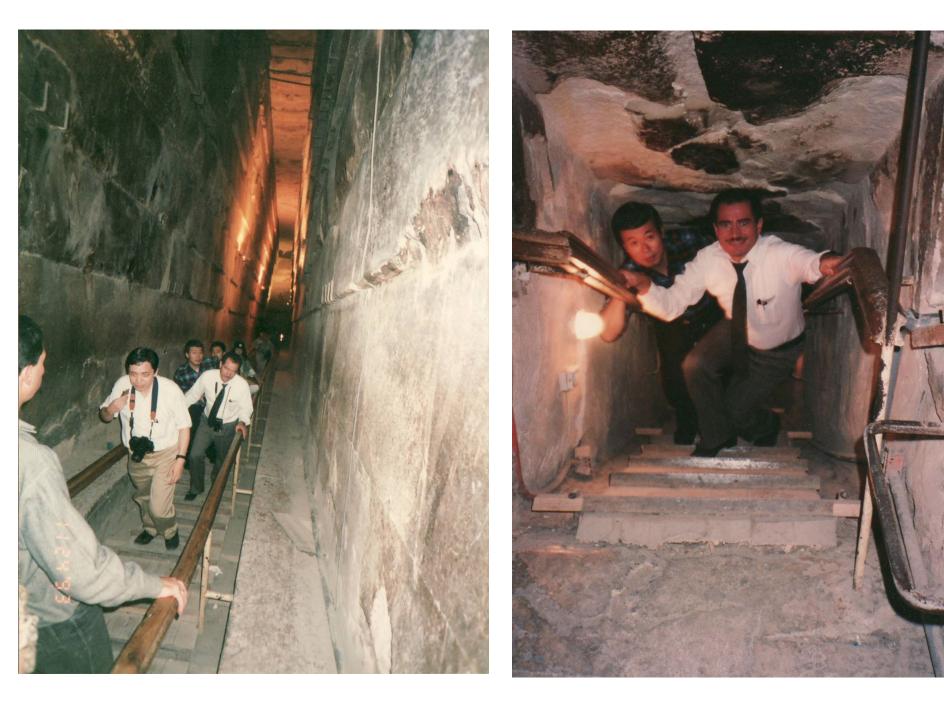
Pharaoh Tutankhamun

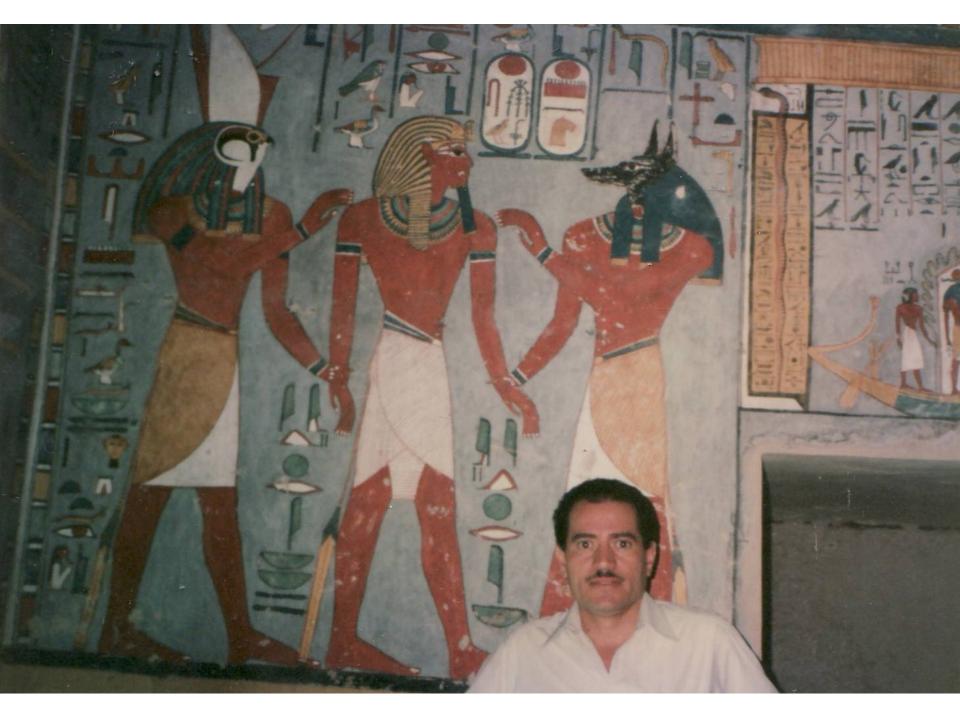
Nefertiti's Bust













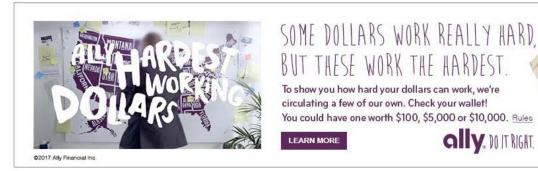
Ancient affliction. A high-resolution CT scan of the lumbar spine region of a 2150-year-old Egyptian mummy has just revealed small, round lesions—the oldest case of metastatic prostate cancer in ancient Egyptians.

(mummy)MNA / DDF - Instituto dos Museus e da Conservação, I.P., Lisbon; (CT, inset) LMP / IMI -Imagens Médicas Integradas, Lisbon

#### Mummy Has Oldest Case of Prostate Cancer in Ancient Egypt By Heather Pringle | Oct. 26, 2011, 5:54 PM

#### HUFFPOST





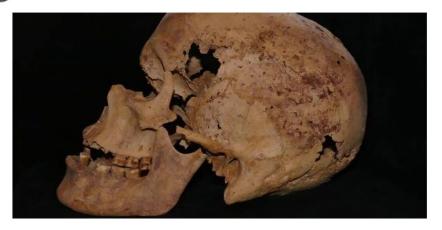
**ally.** Do IT RIGHT.

SCIENCE 03/25/2015 12:53 pm ET



#### Oldest Evidence Of Breast Cancer Seen In Ancient Egyptian Skeleton

By Macrina Cooper-White



The bones date back 4,200 years and bear signs of "the typical destructive damages provoked by the extension of a breast cancer as a metastasis in the bones," according to a written statement issued by Egypt's Ministry of Antiquities.

## "War on Cancer" 1971



\$89 BILLION ANNUALLY =\$89,000,000,000

J. Natl. Cancer Inst. 2008

#### Estimated New Cancer Cases\* in the US in 2017

		Males 836,150	Fema 852,6
Prostate	19%		
Lung & bronchus	14%		
Colon & rectum	9%		T
Urinary bladder	7%		
Melanoma of skin	6%		
Kidney & renal pelvis	5%		
Non-Hodgkin lymphoma	5%		
Leukemia	4%		
Oral cavity & pharynx	4%		
Liver & intrahepatic bile duct	3%		
All other sites	23%		

30%	Breast
12%	Lung & bronchus
8%	Colon & rectum
7%	Uterine corpus
5%	Thyroid
4%	Melanoma of skin
4%	Non-Hodgkin lymphoma
3%	Leukemia
3%	Pancreas
3%	Kidney & renal pelvis
22%	All other sites

\*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

# Total U.S. cancer deaths (1970 -2017)

- 1970: ~330,000 - 2017: ~600,000

# **Chemotherapy and Radiation Therapy**

- 1. Toxic
- 2. Immune-suppressive
- 3. Mutagenic
- 4. Carcinogenic



5. Exhibit an indiscriminative killing that involves cancer cells and many normal cells

We are in great need for new, effective, non-toxic agents for the treatment of cancer



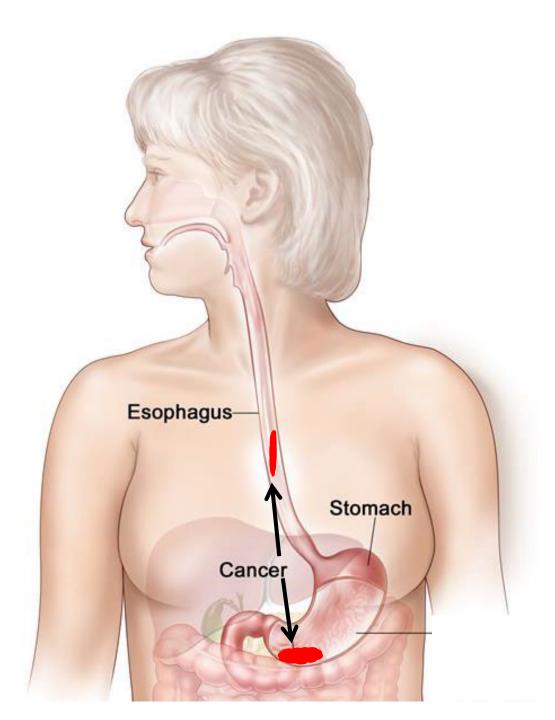
# An iron-based compound (MRN-100)

MRN-100 was provided by ACM Co., Ltd., Japan

# **Does MRN-100 Exert Anti-Cancer Activity?**



MRN-100 protects against chemical-induced esophageal and gastric cancer in Wistar rats.



# **Did You Know ?**

- 1. Gastric and esophageal cancers are two leading causes of cancer-related deaths throughout the world
- 2. <u>In Japan in 2013</u>,

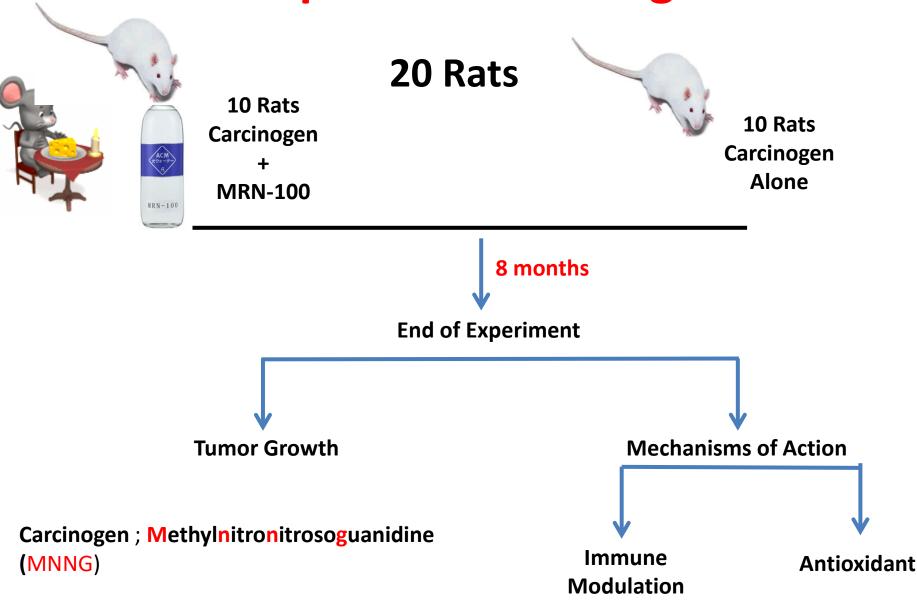
approximately 60,000 total people had gastric cancer and 17,500 new cases of esophogeal cancer were diagnosed.

3. In the United States in 2013,

approximately 40,000 people were diagnosed with esophagus or stomach cancer.



### **Experimental Design**



#### Ghoneum et al. (2014) Nutrition and Cancer.



# RESULTS

#### Glandular dysplasia and adenocarcinoma in gastric tissue



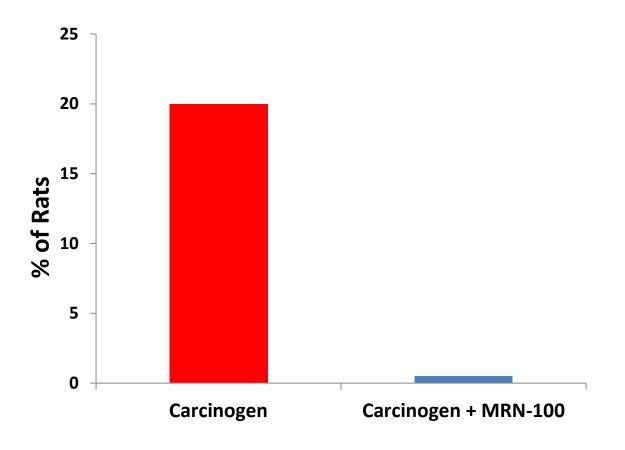






Sodium Chloride 1mL/rat every 3 days

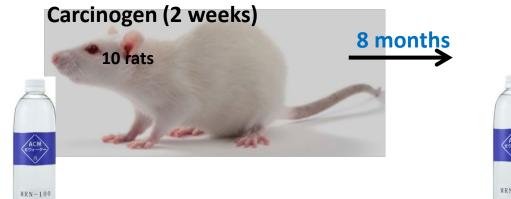
#### % of rats with glandular dysplasia and adenocarcinoma in gastric tissue



# Squamous dysplasia or squamous cell carcinoma in esophageal tissue



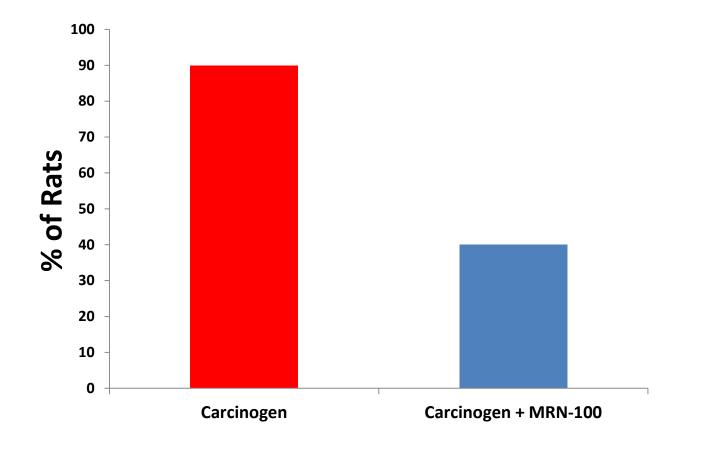




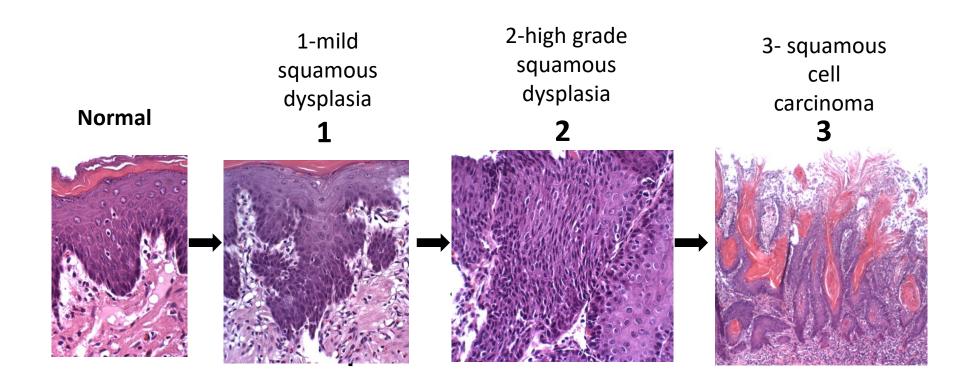


Sodium Chloride 1mL/rat every 3 days

#### % of rats with squamous dysplasia or squamous cell carcinoma in esophageal tissue

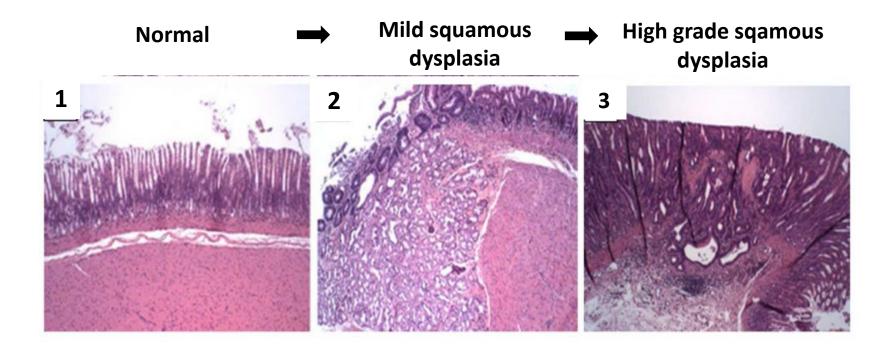


### **Sequence of esophageal cancer development**



Sodium Chloride 1mL/rat every 3 days

### **Experimental Design for gastric cancer**





International Journal of Biological Sciences 2015; 11(3): 295-303. doi: 10.7150/ijbs.10586

Research Paper

#### Hydroferrate Fluid, MRN-100, Provides Protection against Chemical-Induced Gastric and Esophageal Cancer in Wistar Rats

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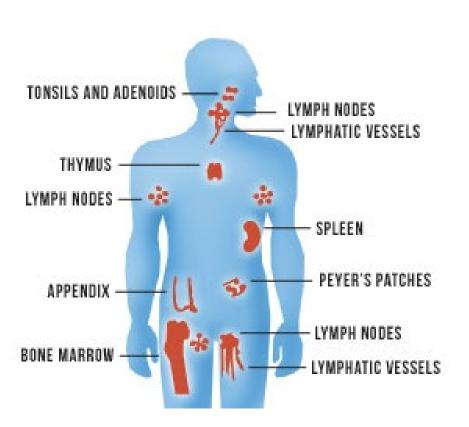
Received: 2014.09.19; Accepted: 2014.12.09; Published: 2015.01.28

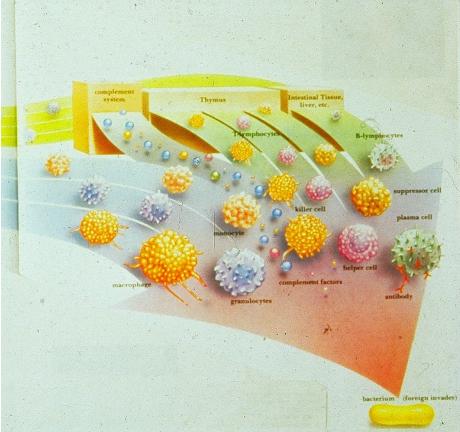
The major problem concerning natural anti-tumor agents is to define their mechanisms of action.

# Immune Modulation

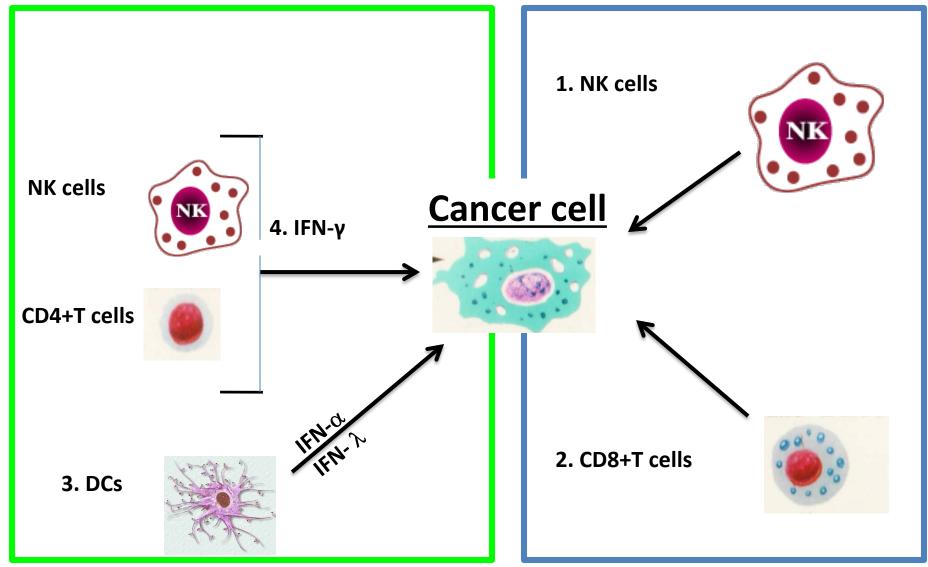
#### **1. Immune tissues**

#### 2. Immune cells

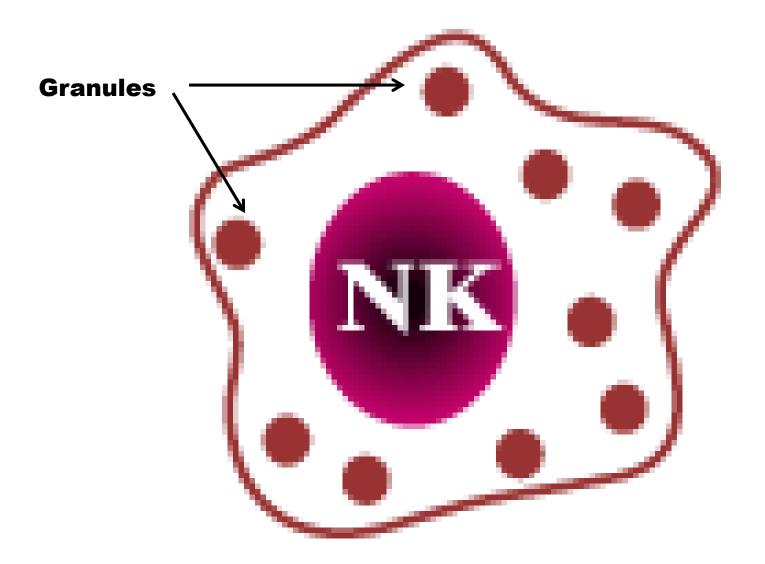




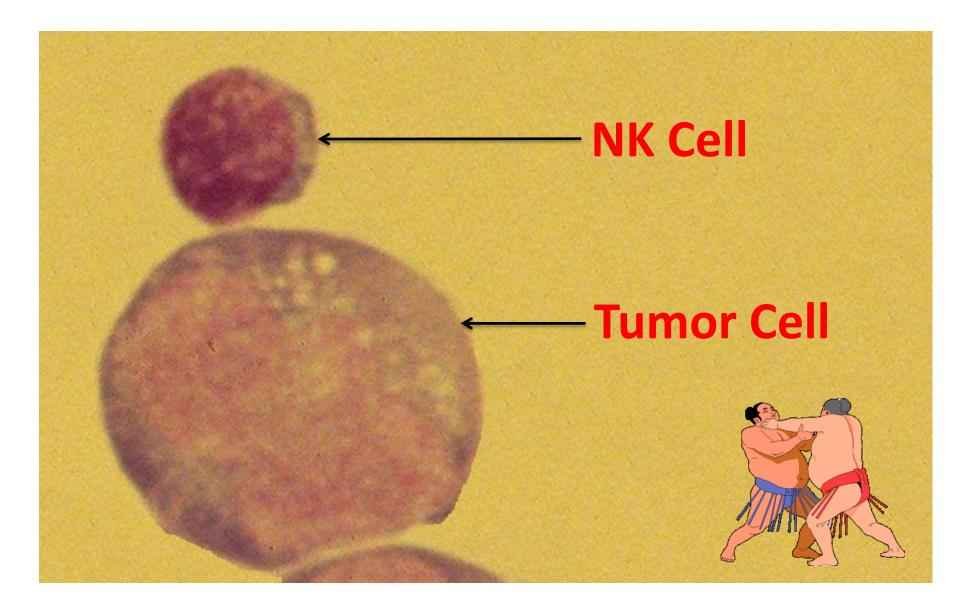
# MRN-100 induces various immune cells to attack target cells



# **Natural Killer (NK) Cells**



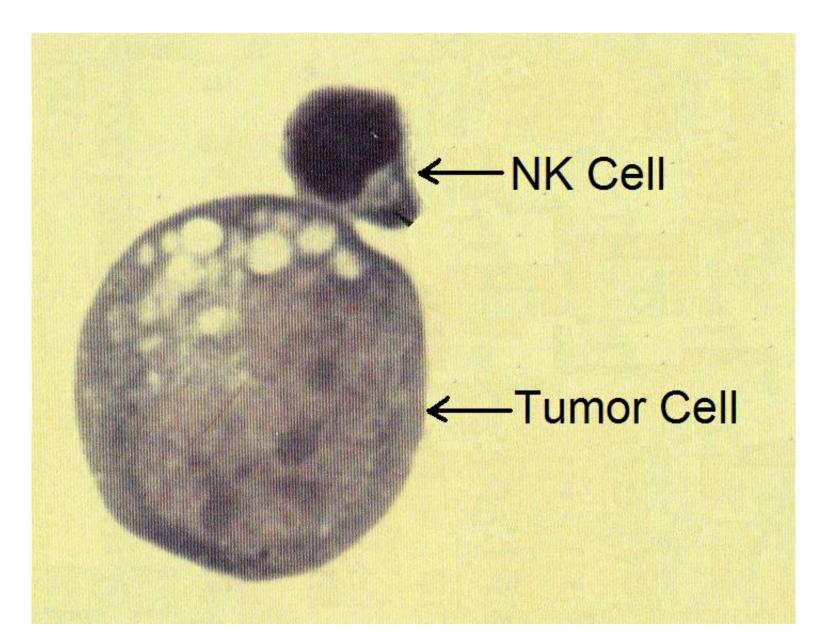
### **1-NK cell binds to cancer cell**

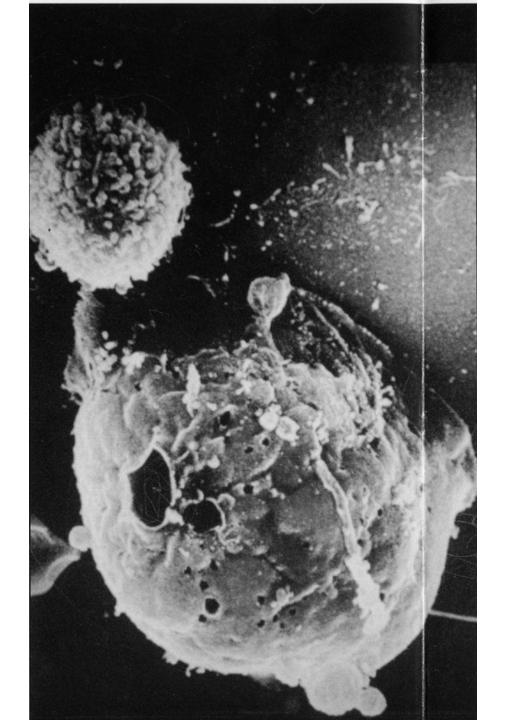


#### 2-NK cell discharges the granules inside the cancer cell

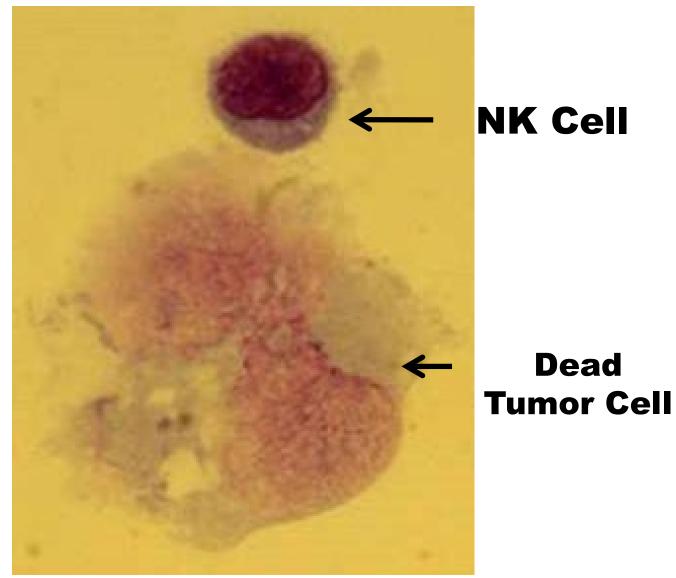


### 3- Granules induces holes in cancer cell

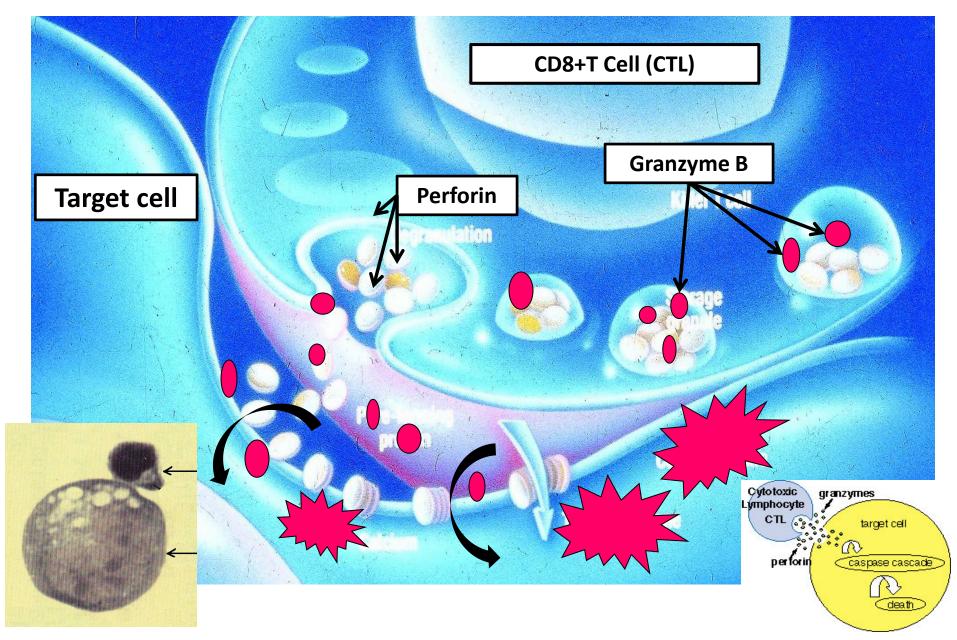




## 4- Cancer cell is dead



### NK/CD8+T cell activity against <u>target</u> cells



### MRN-100 Enhances Natural Killer (NK) Cell Anti-Cancer Activity

NK Cells represent the first line of defense against cancer.

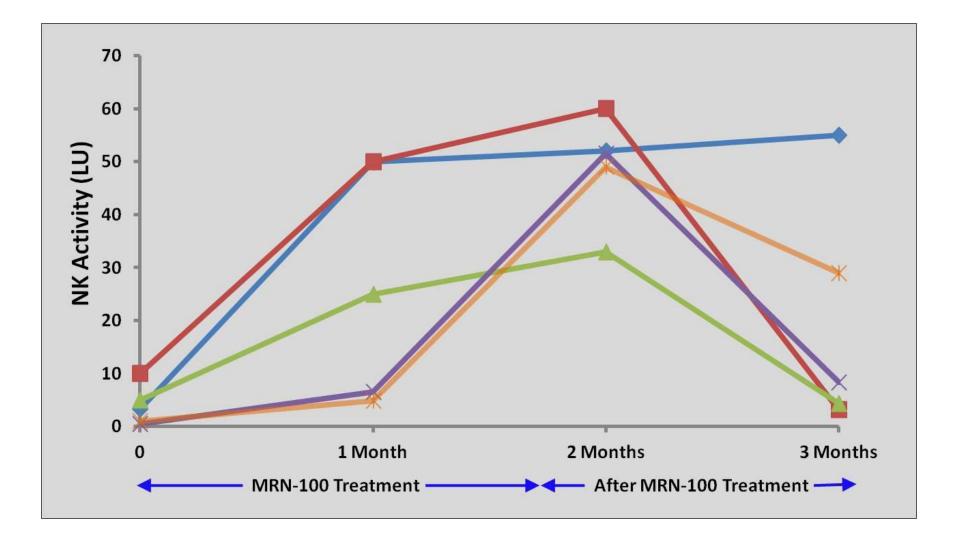
#### **MRN-100 Enhances NK Cell Activity in** 15 Healthy Subjects Before NK Activity (LUs) After 11.1 6.3 5.3 **4.3** 3.8 3.3 2.9 3.3 2.9 0.5 **2** 2.2 1.1 **Healthy Subjects**

MNC from 15 healthy subjects

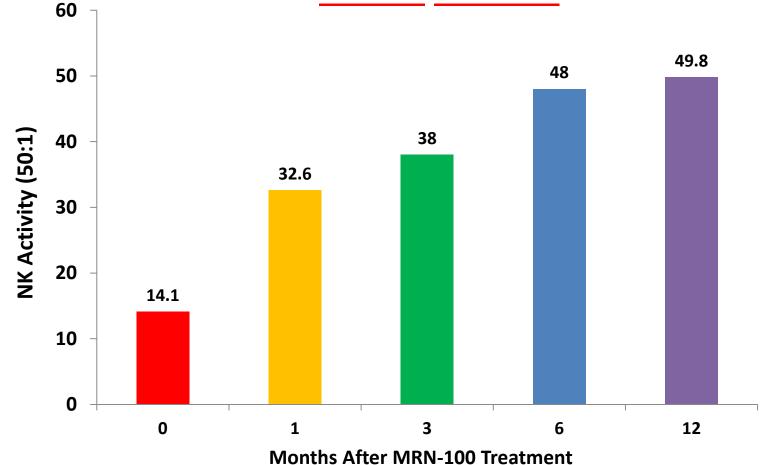
• NK cytotoxicity was measured by <sup>51</sup>Cr-release assay

• Annual Conference of Clinical Immunology, New Orleans, LA, May 31-June 3, 1996

#### **MRN-100 Enhances NK Cell Activity 5 Human** <u>healthy</u> subjects



### MRN-100 Enhances NK Cell Activity of 10 Cancer Patients



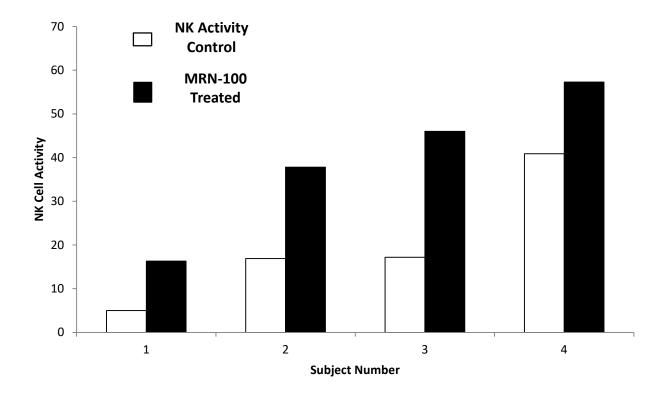
• MNC from 10 subjects with different malignancies

• NK cytotoxicity was measured by <sup>51</sup>Cr-release assay

•4<sup>th</sup> International Symposium on Predictive Oncology and Therapy, Nice, France Oct 24-27, 1998.

With respect to different types of human malignancies

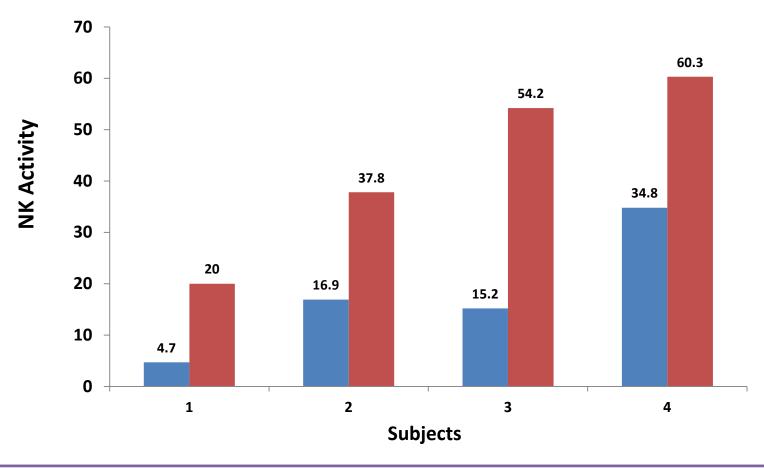
#### MRN-100 increases human <u>head & neck carcinoma</u> Calu-27 sensitivity to human NK cell cytotoxicity in vitro\*



- MNC from 4 healthy subjects
- NK cytotoxicity was measured by <sup>51</sup>Cr-release assay at E:T ratio 100:1
- 4<sup>th</sup> International Symposium on Predictive Oncology and Therapy, Nice,

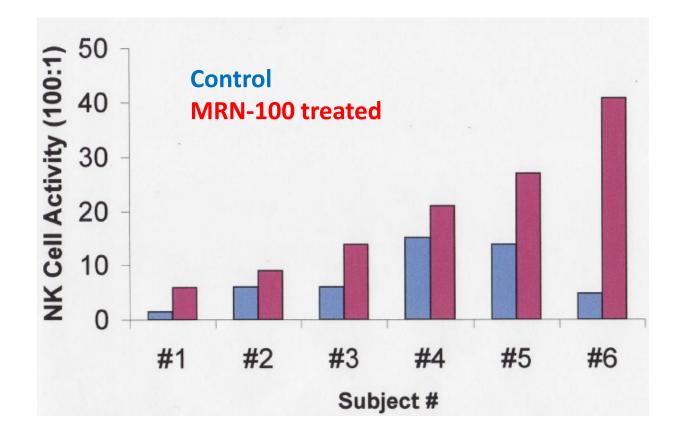
France Oct 24-27, 1998. Cancer Detection and Prevention. Vol 22 Supp 1 1998

# MRN-100 increases human <u>erythroleukemic cell</u> line, K562, sensitivity to human NK cell cytotoxicity in vitro



- MNC from 4 subjects with different types of malignancies
- NK cytotoxicity was measured by <sup>51</sup>Cr-release assay at E:T ratio 100:1
- 4<sup>th</sup> International Symposium on Predictive Oncology and Therapy, Nice, France Oct 24-27, 1998.

#### MRN-100 increases Squamous Cell <u>Carcinoma of the</u> <u>Skin</u> (SCC) sensitivity to human NK cell cytotoxicity



MNC from 6 Healthy subjects/patients with different types of malignancies NK cytotoxicity was measured by <sup>51</sup>Cr-release assay at E:T ratio 100:1 \*Data presented at the 4<sup>th</sup> International Symposium on Predictive Oncology and Therapy. Nice, France, October 24-27, 1998.

# Conclusions

- Our study suggests MRN-100 may be an effective adjuvant for the treatment of gastric and esophageal cancer, and in other types of human malignancies.
- 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

# Break

# Part III MRN-100 and Alzheimer's disease

## Alzheimer's Disease

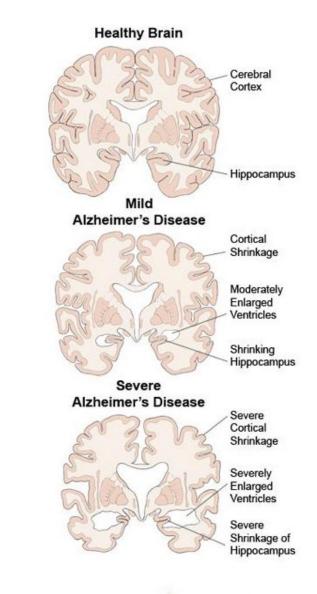


## **Alzheimer's disease**

 Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a progressive decline of memory and cognition

# Definition

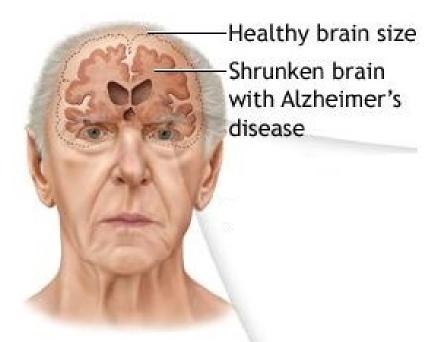
- Alzheimer's disease is a degenerative brain disease and the most common cause of dementia.
- Causes decline in memory, language, problem-solving, cognitive skills
- Areas of the brain for bodily functions also become affected
- Ultimately fatal

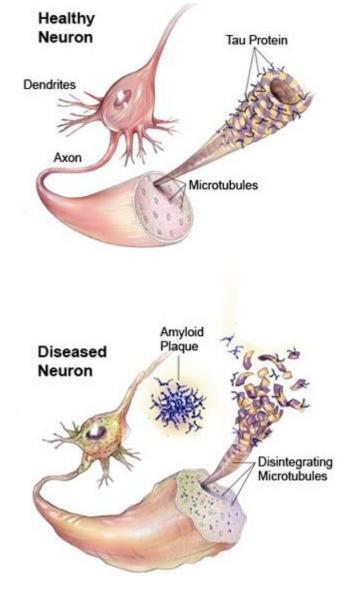




# Alzheimer's Mechanism

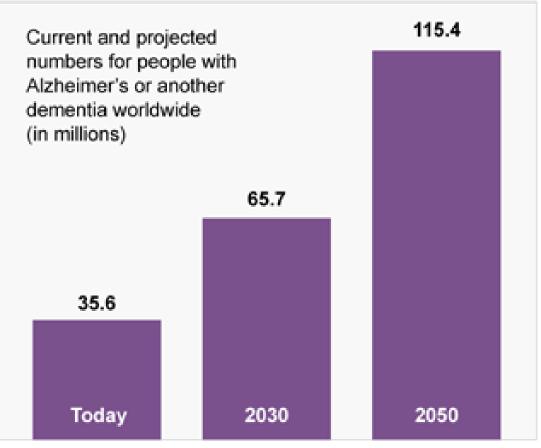
 Nerve cells (neurons) in parts of the brain involved in cognitive function become damaged or destroyed, and the damage spreads rapidly.





## Alzheimer's Statistics

 Alzheimer's will impact more people as human longevity increases

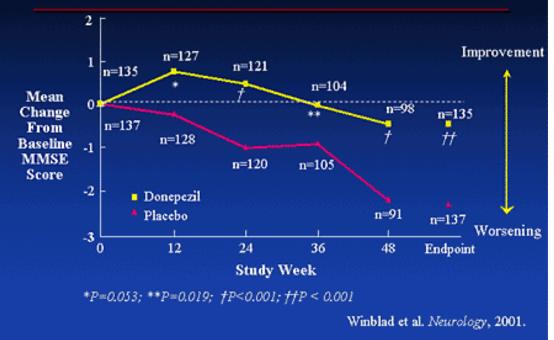


Source: 2009 World Alzheimer Report, from Alzheimer's Disease International (ADI), a London-based nonprofit, international federation of 71 national Alzheimer organizations including the Alzheimer's Association.

## Current treatments are inadequate

- Current treatments (donezepil, known as "Aricept") slow the progression of nerve damage, but degeneration still continues.
- Side effects of the best treatments are numerous and undesirable

#### Donepezil in Mild to Moderate Alzheimer's Disease



- Drowsiness, malaise, loss of appetite, cramps, insomnia, tremor, nausea, diarrhea, vomiting, possible seizures, possible chest pains.

### **Antioxidants as new treatments for AD**

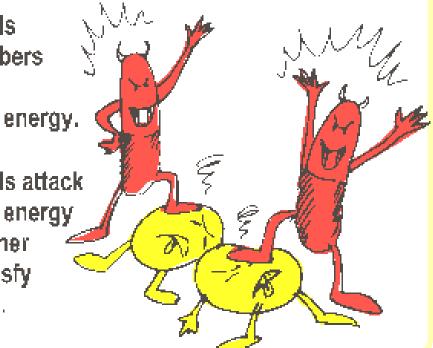
- Antioxidants are believed to play a role in preventing the development of such chronic diseases as Alzheimer's disease (AD)
  - For example, antioxidants emerged as potential AD preventive agents based upon epidemiological evidence and animal studies.\*
- The imbalance between free radicals and antioxidants in neurons plays a key role in the development of AD.
  - This is called oxidative stress.
  - Oxidative stress occurs when the production of harmful molecules called **free radicals** is beyond the protective capability of the antioxidant defenses.
- Free radicals containing oxygen, known as **reactive oxygen species** (ROS), are the most biologically significant free radicals.

\* Zhou et al. Am J Transl Res. 2016;8:246-69.

# **Free Radicals**

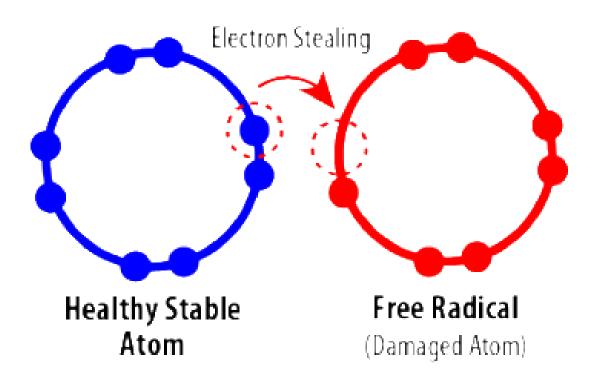
### What are Free radicals ?

- Free radicals are like robbers which are deficient in energy.
- Free radicals attack and snatch energy from the other cells to satisfy themselves.

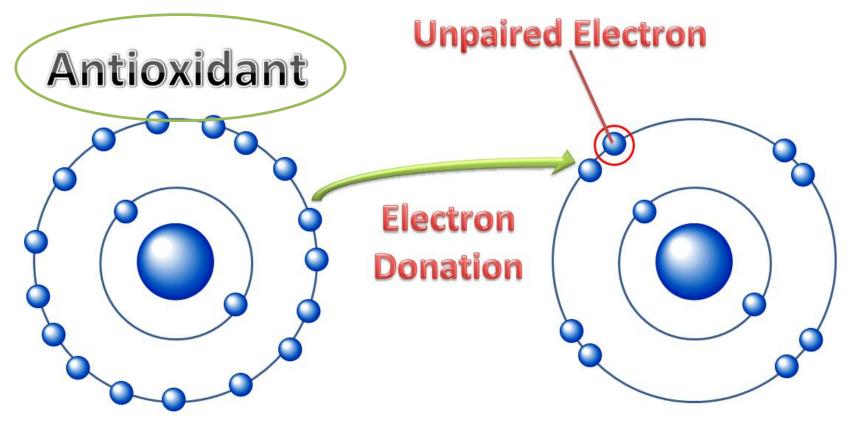


# Free Radicals -Damaging healthy, stable cells

FREE RADICAL EXAMPLE



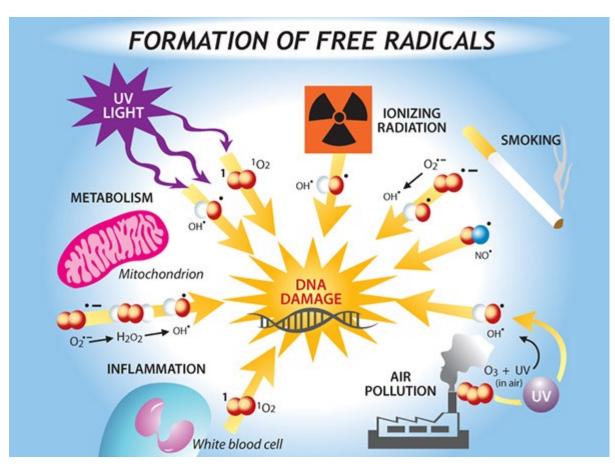
## **Free Radicals**



**Free Radical** 

### **Free Radical: Environmental Factors**

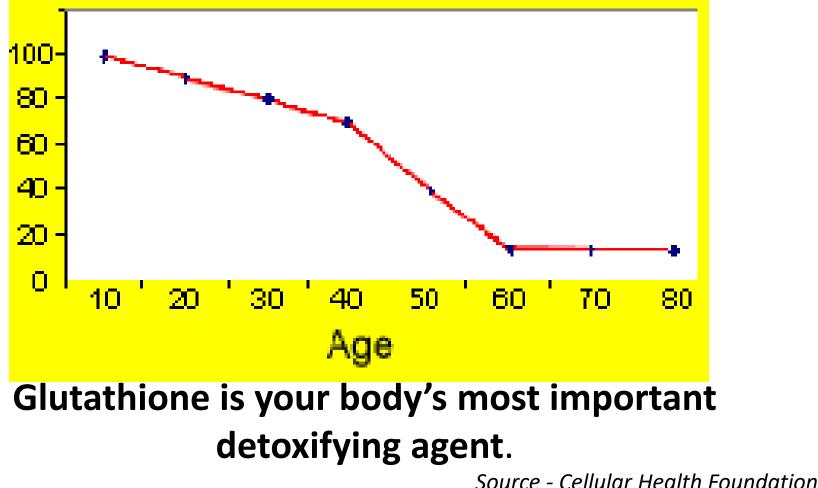
Free radicals can form from environmental factors such as pollution, sunlight, exhausting exercise, X-rays, smoking and alcohol.



## **Free Radical and Aging**

# Our antioxidant systems are not perfect, so as we age, cell parts damaged by oxidation accumulate.

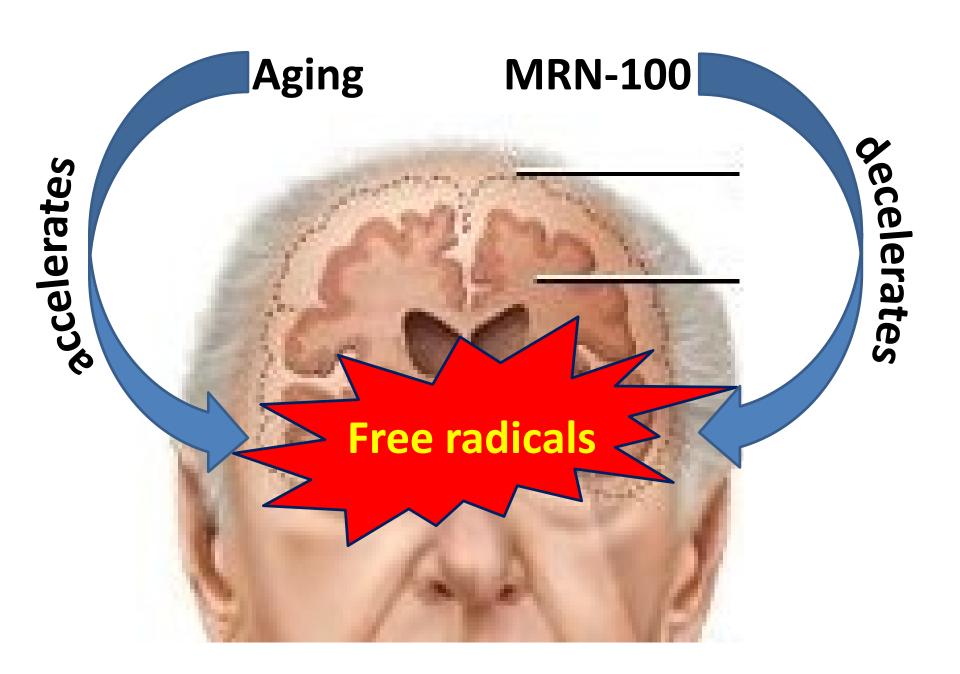




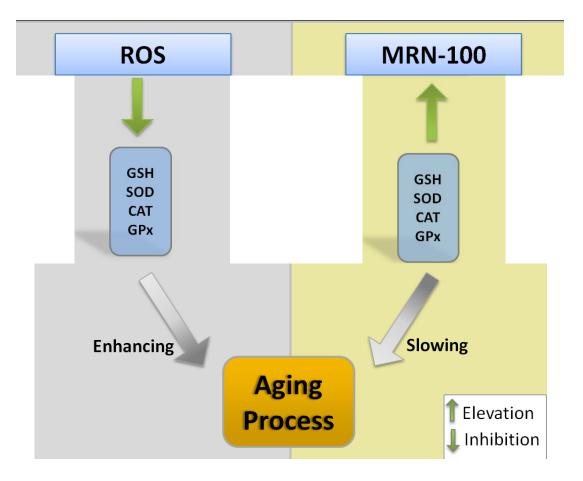
# MRN-100 is a potent Antioxidant agent

# MRN-100 demonstrated its effectiveness as an antioxidant by:

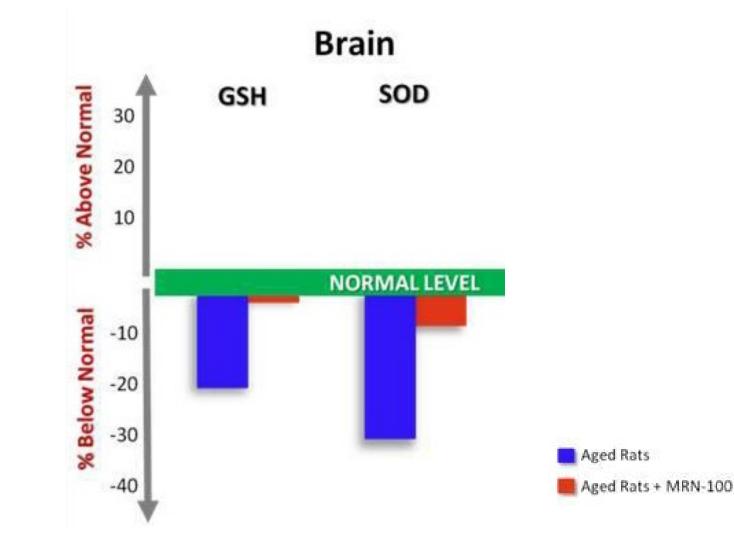
- 1. Increasing the levels of Glutathione (GSH; free radical scavenger)
- 2. Increasing antioxidant scavenger enzymes SOD, CAT and GPx
- **3. Prevention of Free Radicals**



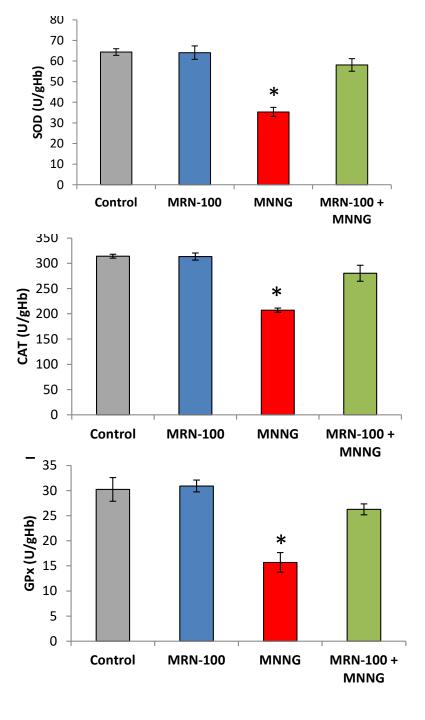
## ROS enhances the aging process while MRN-100 counteracts this effect of ROS



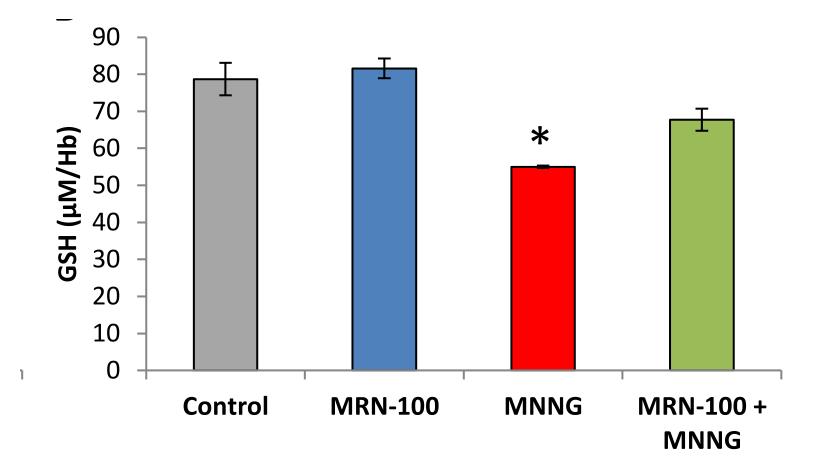
# In aged rats, MRN-100 restores the levels of GSH and SOD to normal levels in the brain



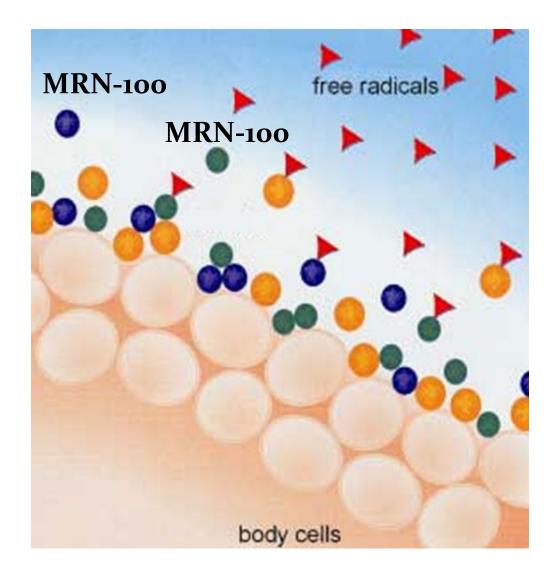
### MRN-100 increases the levels of antioxidant enzymes SOD, CAT and GPx



## MRN-100 increase the level of glutathione (GSH), (ROS quencher/ Free radical scavenger)



# MRN-100 neutralizes free radicals and protects the cells from their damage



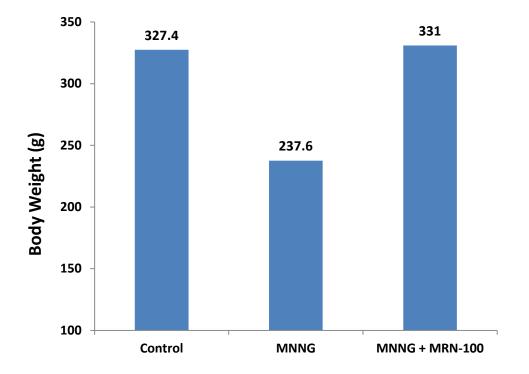


This is Taz, our cat





### MRN-100 Protects Against Cancer-Induced Loss of Body Weight





## MRN-100 Protects Against Cancer-Induced Loss of Body Weight

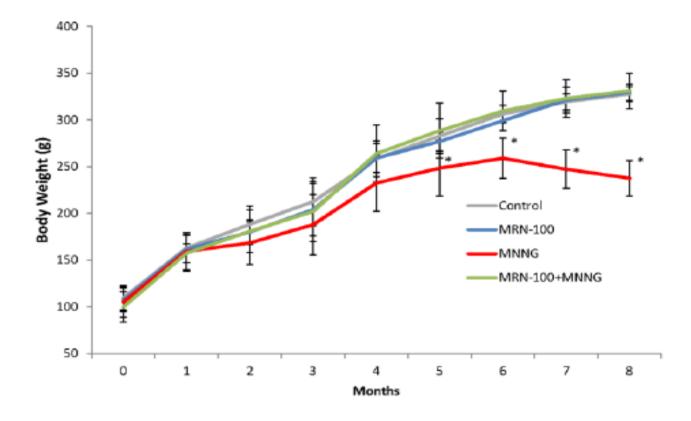


Figure 3. Changes in body weight under different treatment conditions. Rats were given carcinogen MNNG in the presence or absence of MRN-100. Animals in the 4 groups were examined for the changes in their body weight every month for 33 weeks. \*p<0.01 compared to control and MRN-100 plus MNNG group. Each bar represents the mean ± SD of 10 rats/group.

#### MRN-100 Protects Against Cancer-Induced Loss of Organ Weight

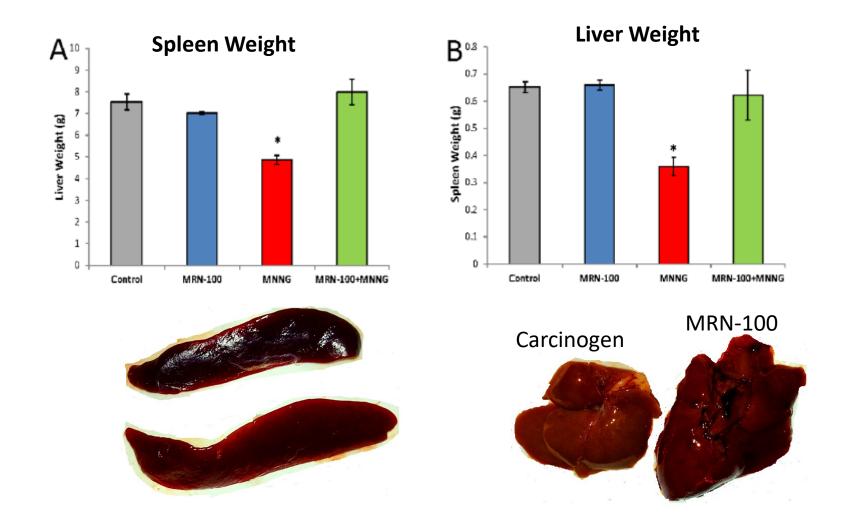


Figure 4. Changes in the liver and spleen weight. Rats were given carcinogen MNNG in the presence or absence of MRN-100 for 33 weeks and were examined for changes in the weight of livers (A) and spleens (B). \*p<0.01 compared to control and other groups. Each bar represents the mean ± SE of 10 rats/group.

# Conclusions

- 1. New data supports that Bedil Ai may be useful for enhancing eye vision.
- 2. MRN-100 exerts anti-cancer activity via immune modulation
- 3. MRN-100 may be a useful for fighting against Alzheimer's disease via its potent antioxidant effect
- 4. MRN-100 is a safe agent



# **Publications and Presentations related to MRN-100**

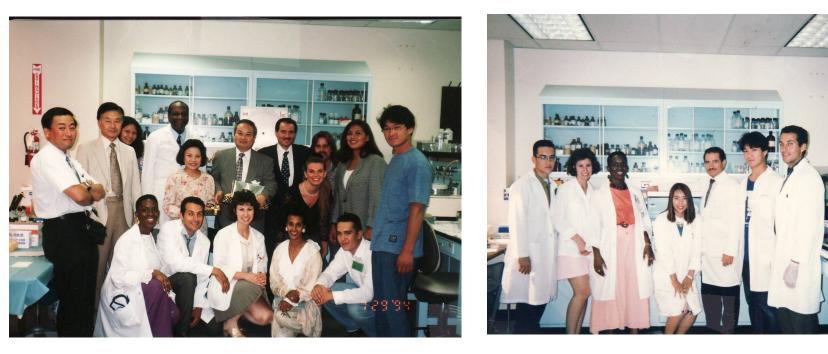
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- Lina Wang, MD. USC, USA
- Motohiro Matsuura, Ph.D. Jichi Medical University, Japan





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



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#### House of Representatives State of Tennessee

NASHVILLE

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,

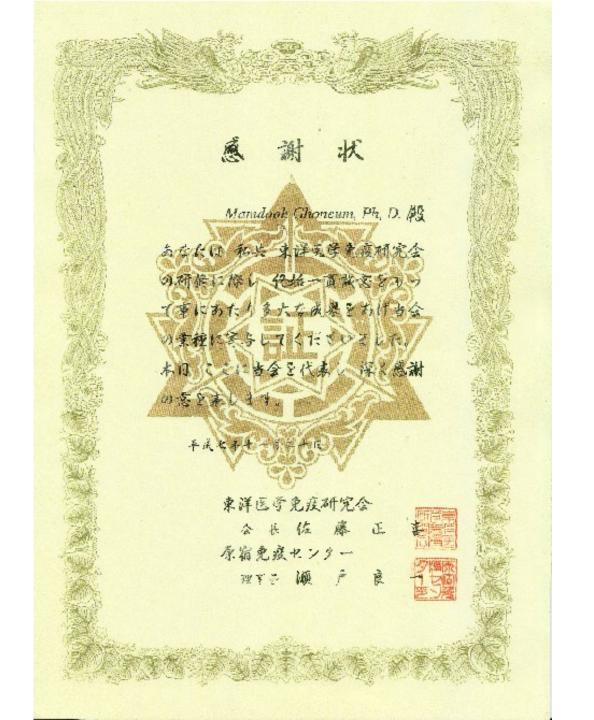
Nathan Valighn\_\_\_\_\_ Nathan Vaughn 2<sup>nd</sup> District State Representative

MEMBER OF COMMITTEES CHILDREN AND FAMILY AFFAIRS FINANCE, WAYS AND MEANS TRANSPORTATION

SUBCOMMITTEES DOMESTIC RELATIONS PUBLIC TRANSPORTATION AND HIGHWAYS

# Japanese Society of Complimentary and Alternative Medicine. Japanese Immunology Society









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>RD</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.

Lange & N.

CARMENCITA LO, M.D. President

und du

SUSAN LEE, M.D. Chairman Scientific Committee

NELSON LIM, M.D.

Secretary

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





