



**The Role of MRN-100 in
Improving Vision
&
Fighting Against Cancer**

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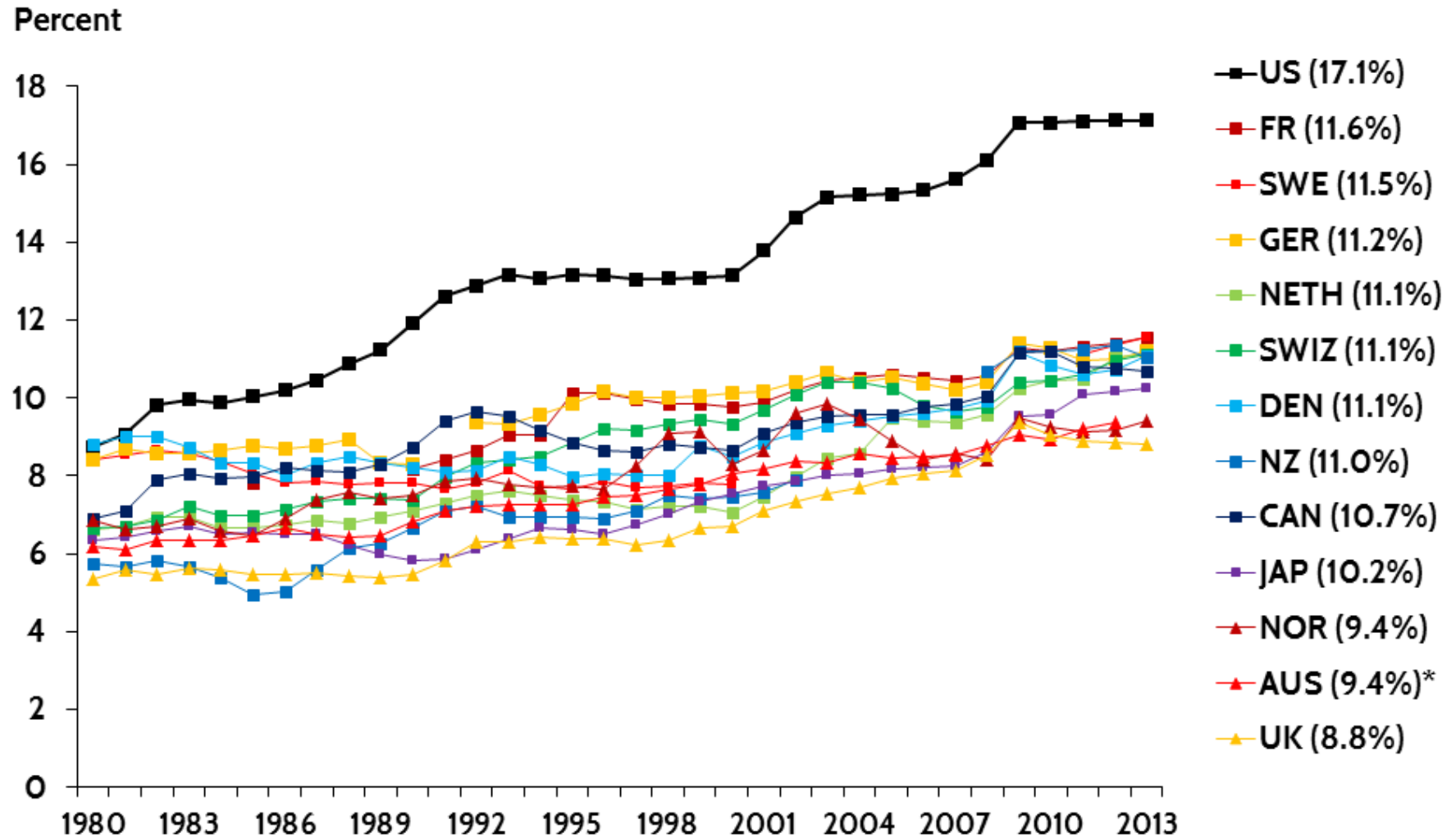
Outline

1. **Healthcare Systems Worldwide**
2. **Bedil Ai Study**
 - A) Eye vision
 - B) Astigmatism
3. **MRN-100 Exerts Anti-Cancer Activity**

Mechanisms of protection against cancer:

 - A) Apoptosis
 - B) Antioxidant Potential
 - C) Immunomodulatory Effect
 - D) Increases susceptibility of cancer cells to NK cells
4. **Conclusion**

Exhibit 1. Health Care Spending as a Percentage of GDP, 1980–2013

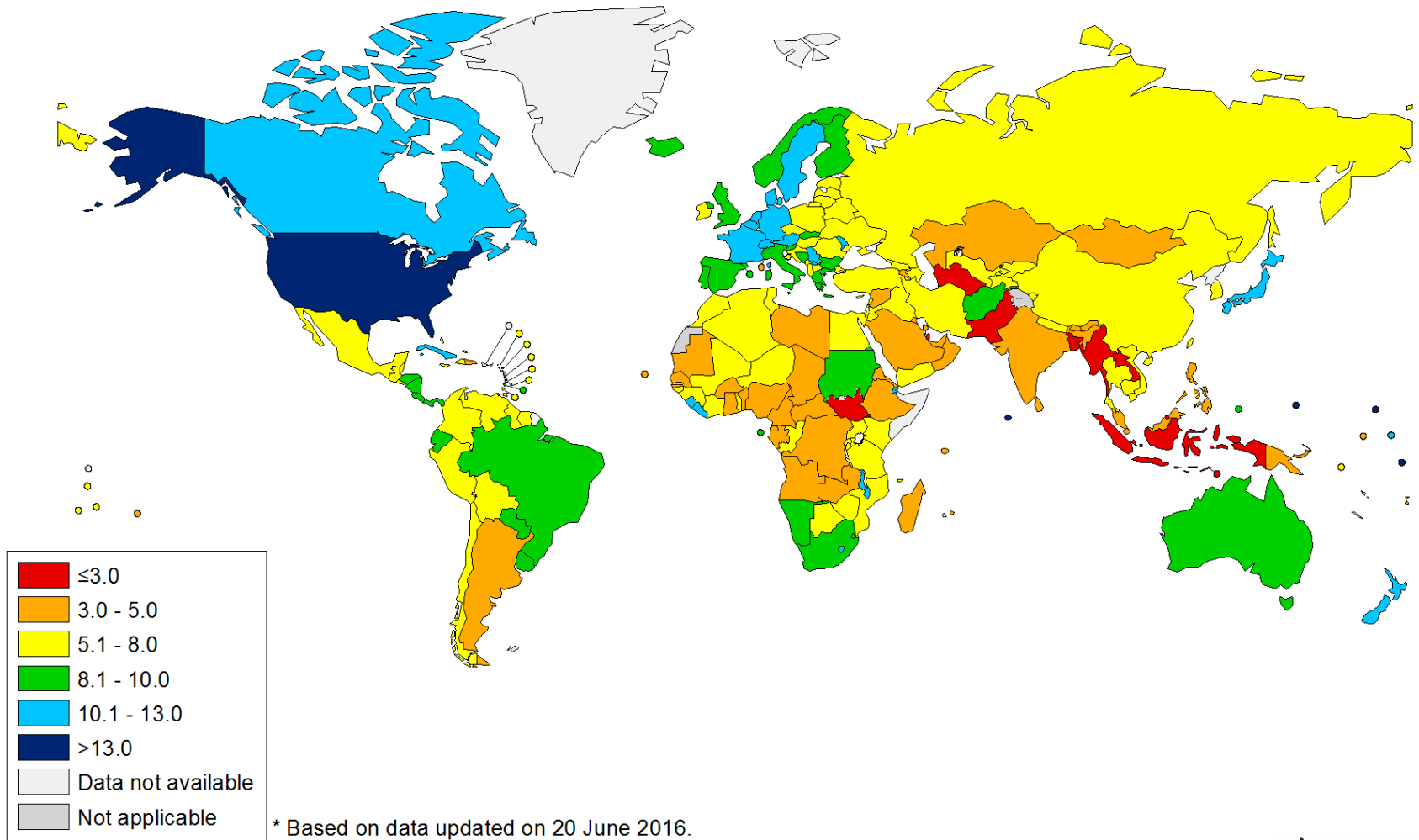


* 2012.

Notes: GDP refers to gross domestic product. Dutch and Swiss data are for current spending only, and exclude spending on capital formation of health care providers.

Source: OECD Health Data 2015.

Total expenditure on health as a percentage of the gross domestic product, 2014 *



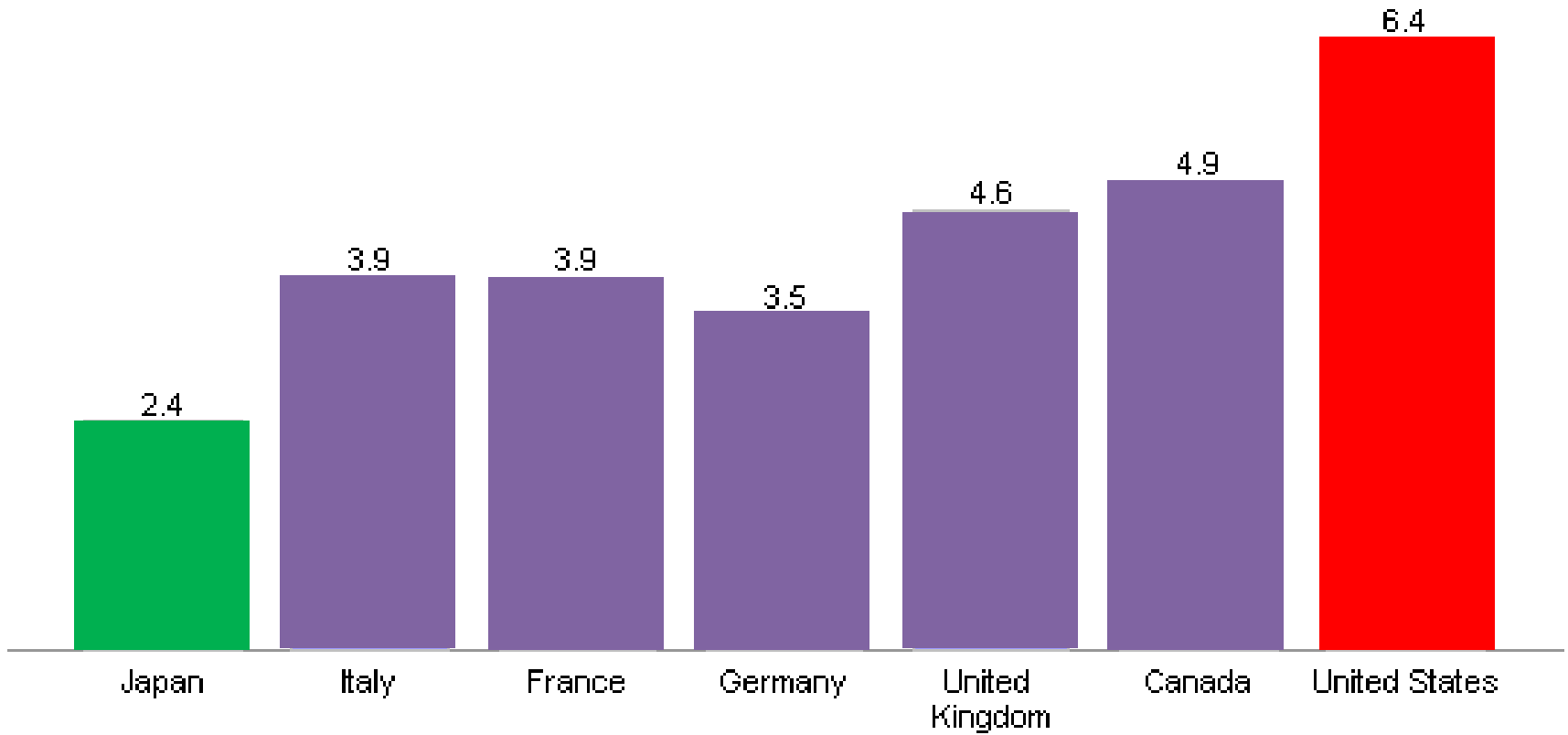
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Health Observatory, WHO
Map Production: Information Evidence and Research (IER)
World Health Organization

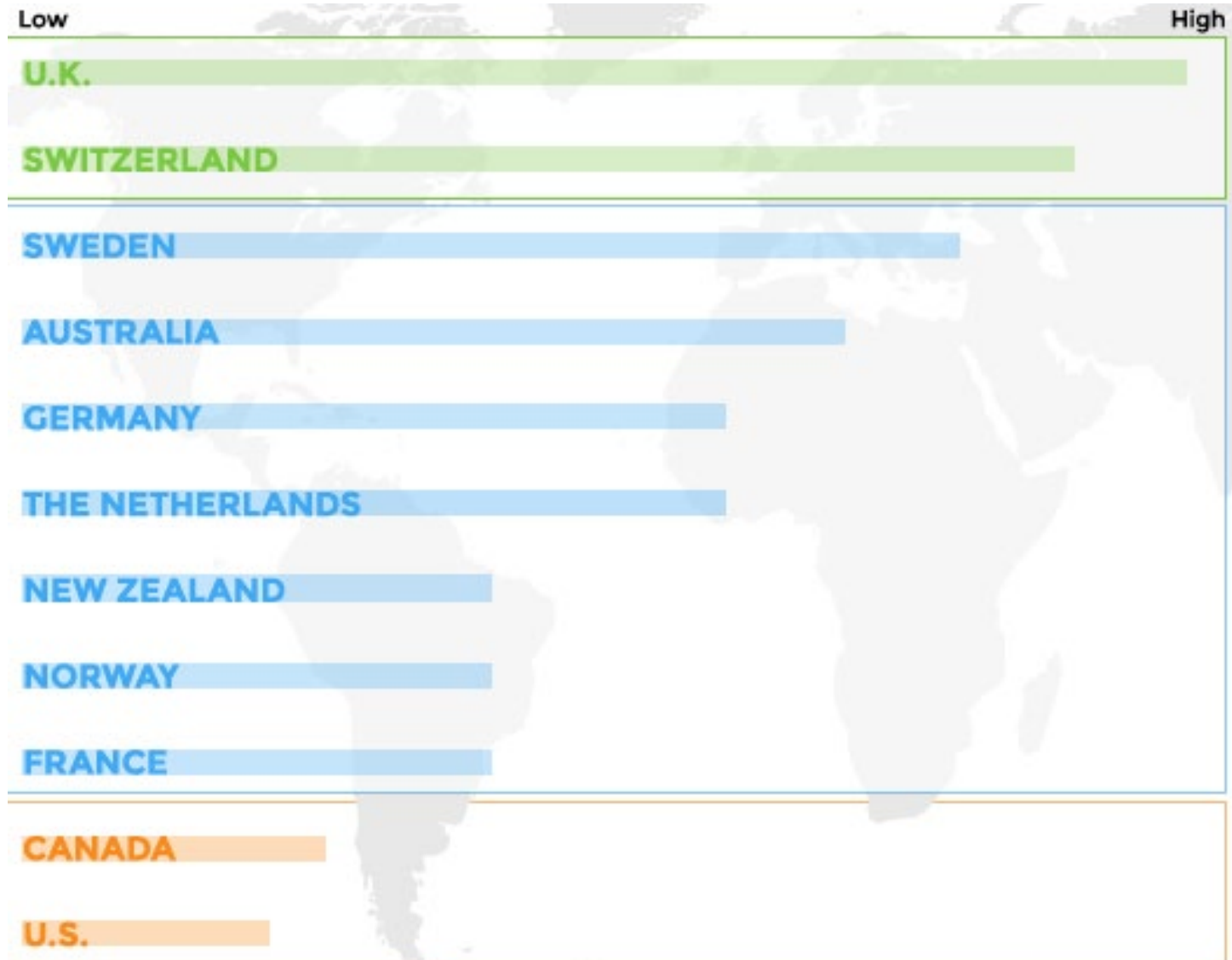


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Infant Mortality 2009 (Per 1,000 Live Births)



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.

Bedil Ai:

Bedil Ai may be a novel product for the improving Eye vision

Bedil Ai is characterized as:

- 1- Safe**
- 2- Low cost**



Bedil Ai

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Did you know that there are some animals that have two differently colored eyes?



Two Different Color Eyes





Two Different Color Eyes



Multiple Eyes



Lizards can have three



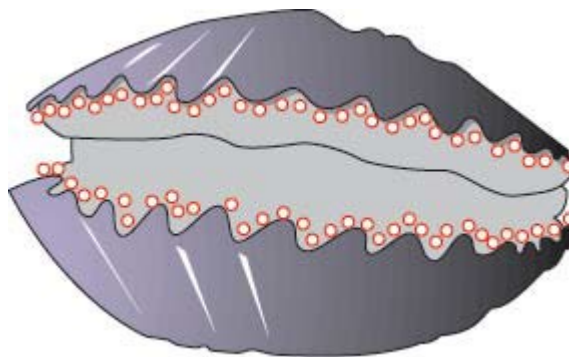
sea stars or **Starfish** have one eye on each arm



Spiders can have eight



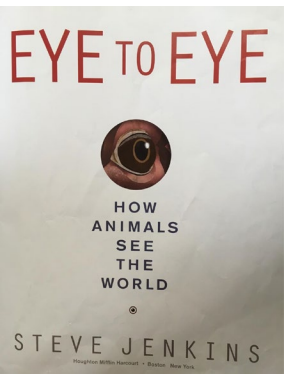
Crab



Scallops have dozens of eyes



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



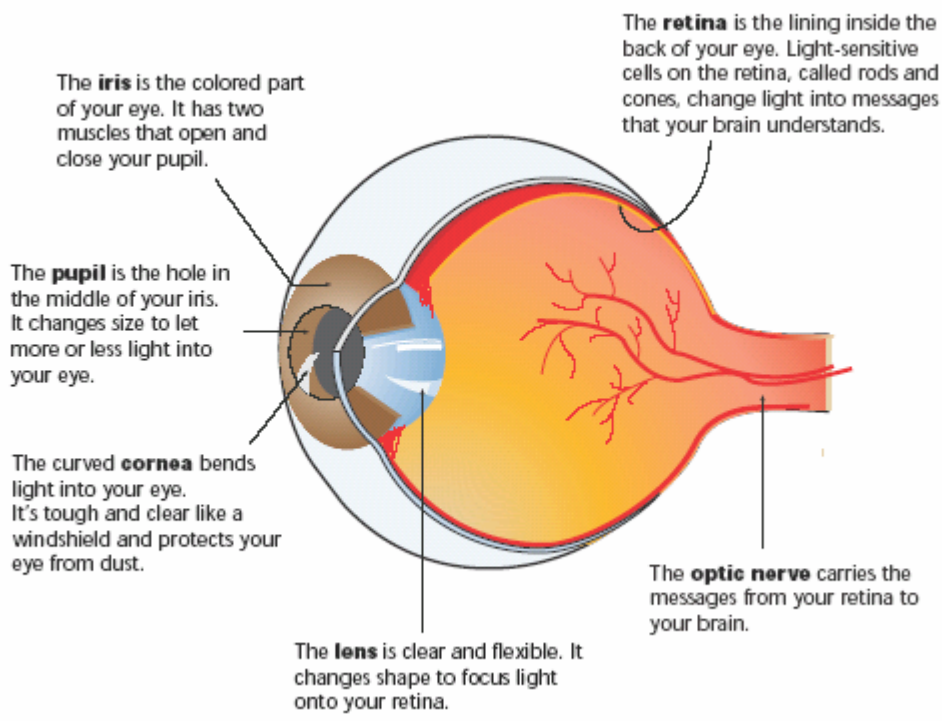
Squid





Presented by Museum of Vision

An educational program of The Foundation of the American Academy of Ophthalmology





The cost and strain of eye vision

- According to the Vision Council of America, over 75 % of adults in the US (>177 million people) require some sort of vision correction
- 1 out of 4 children have an eye problem
- Eyecare is more costly than three of the top seven major chronic illnesses, including heart disease, Alzheimer's, diabetes and cancer.

https://www.mesvision.com/includes/pdf_Broker/MESVision%20Facts%20and%20Statistics.pdf

<http://glassesrafter.com/information/percentage-population-wears-glasses.html>

<http://www.usatoday.com/story/news/nation/2013/06/30/vision-related-diseases-cost/2453119>



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:
 - \$47.4 billion covered by the federal government
 - \$20.8 billion covered by insurance companies in direct medical costs
 - \$1.3 billion in long-term costs
 - \$71.6 billion covered by patients and their families
 - \$238 per person per year

https://www.mesvision.com/includes/pdf_Broker/MESVision%20Facts%20and%20Statistics.pdf

<http://glassesrafter.com/information/percentage-population-wears-glasses.html>

<http://www.usatoday.com/story/news/nation/2013/06/30/vision-related-diseases-cost/2453119>

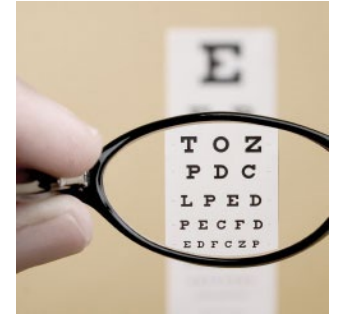
Study Design



Autorefractor



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



Bedil Ai for 1 month

2nd Eye Exam

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

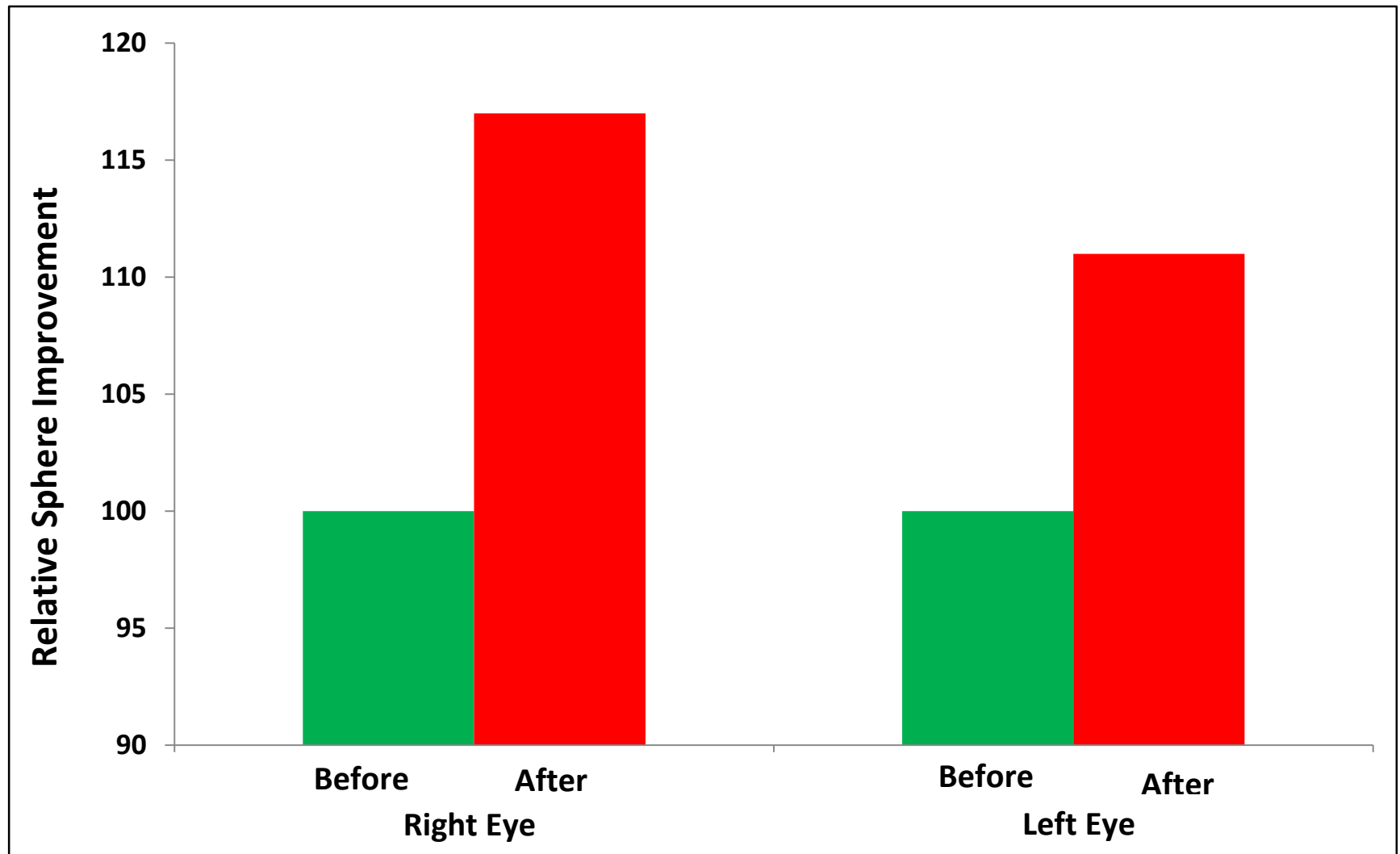


RESULTS

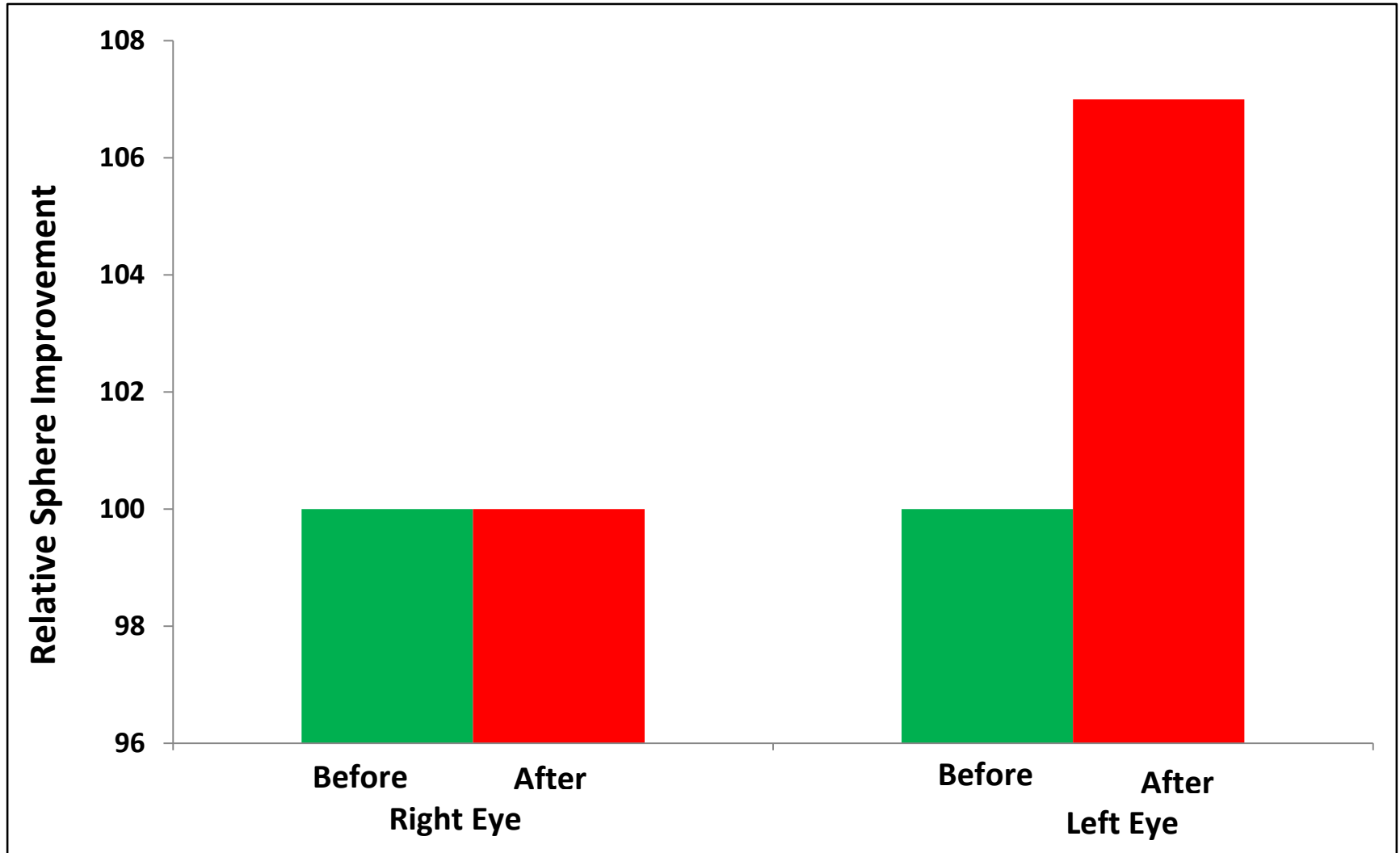


VISION

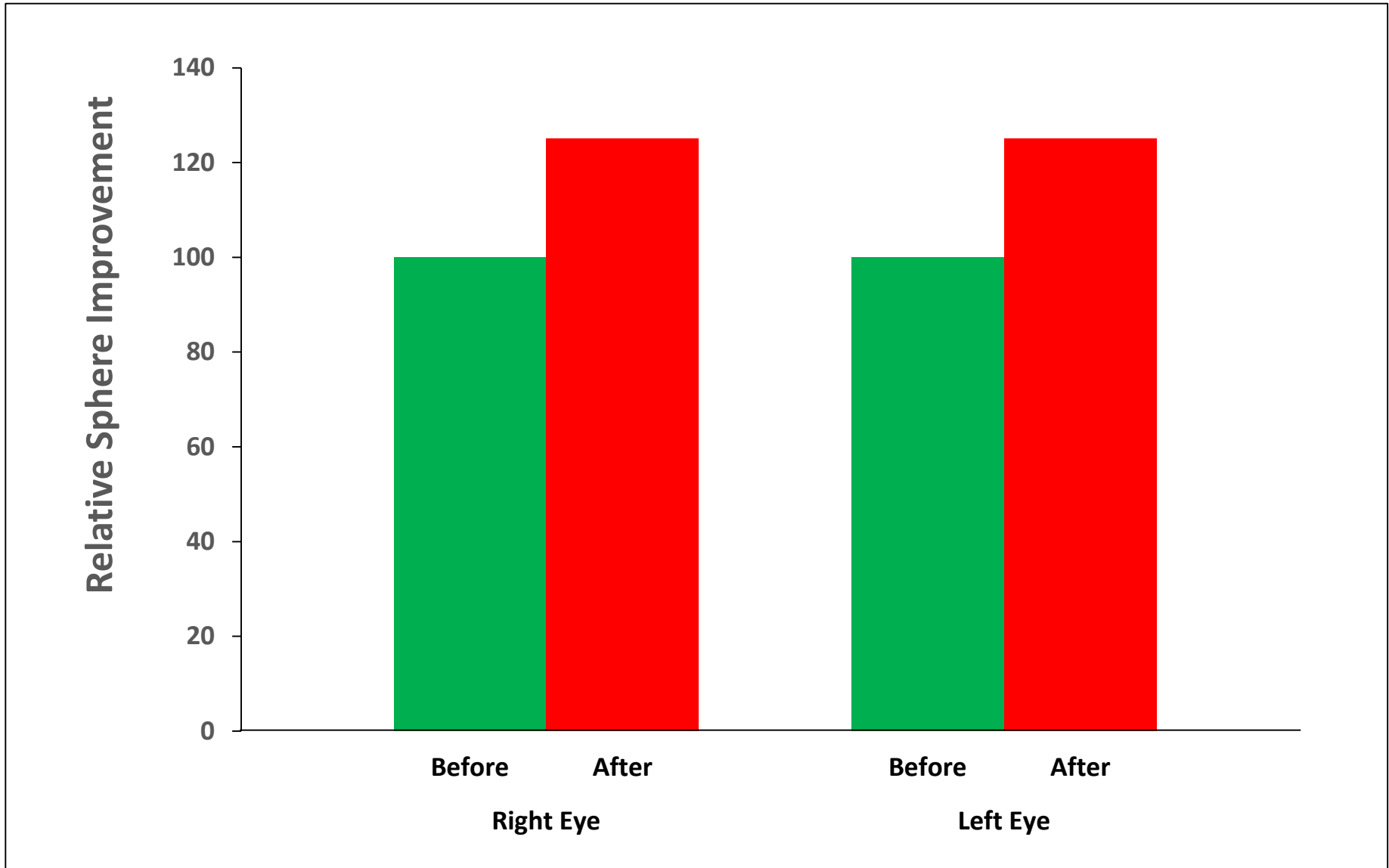
Patient #1- Female, 18 Years Old



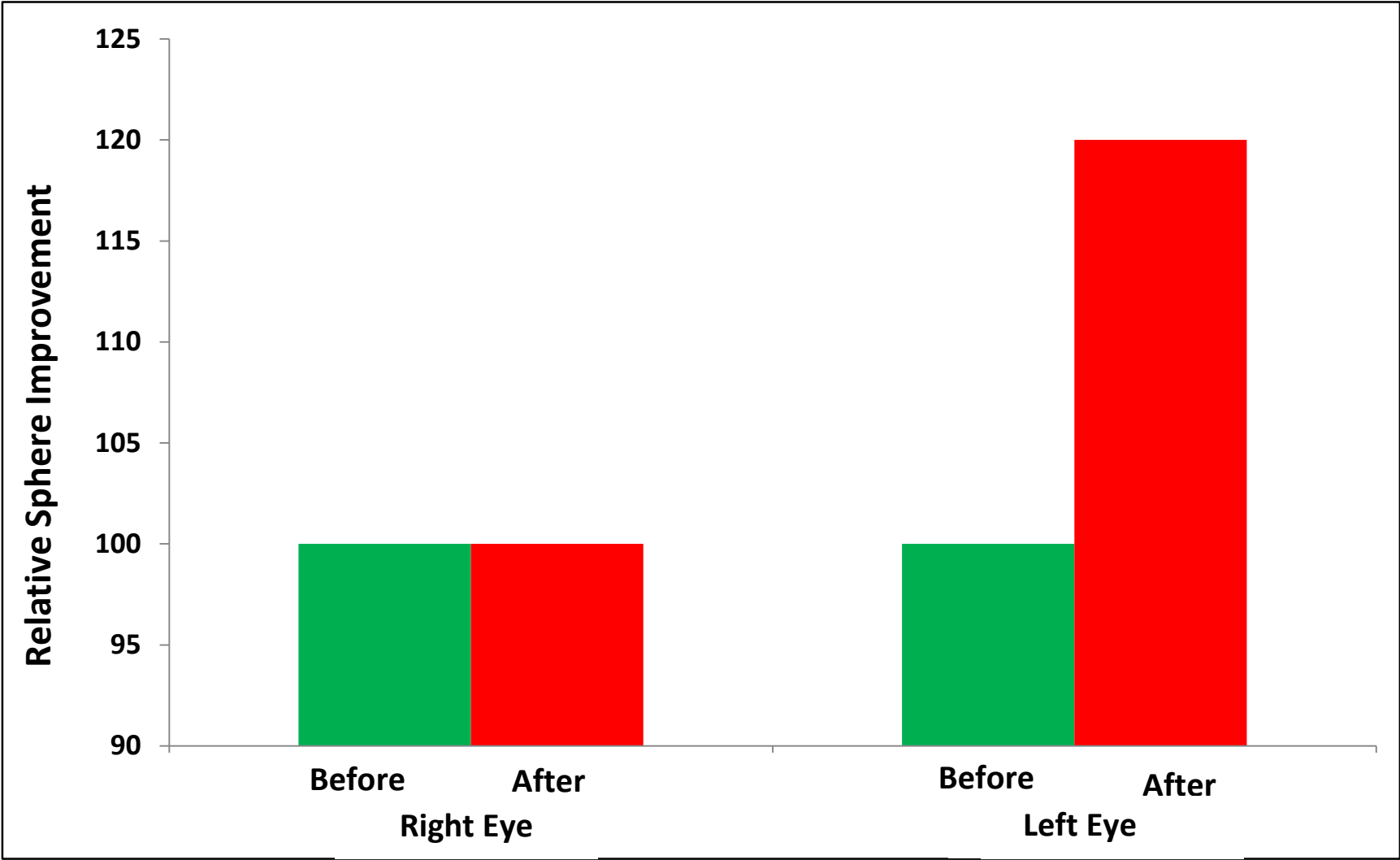
Patient #2- Female, 26 Yrs Old



Patient #3- Male, 71 Yrs Old

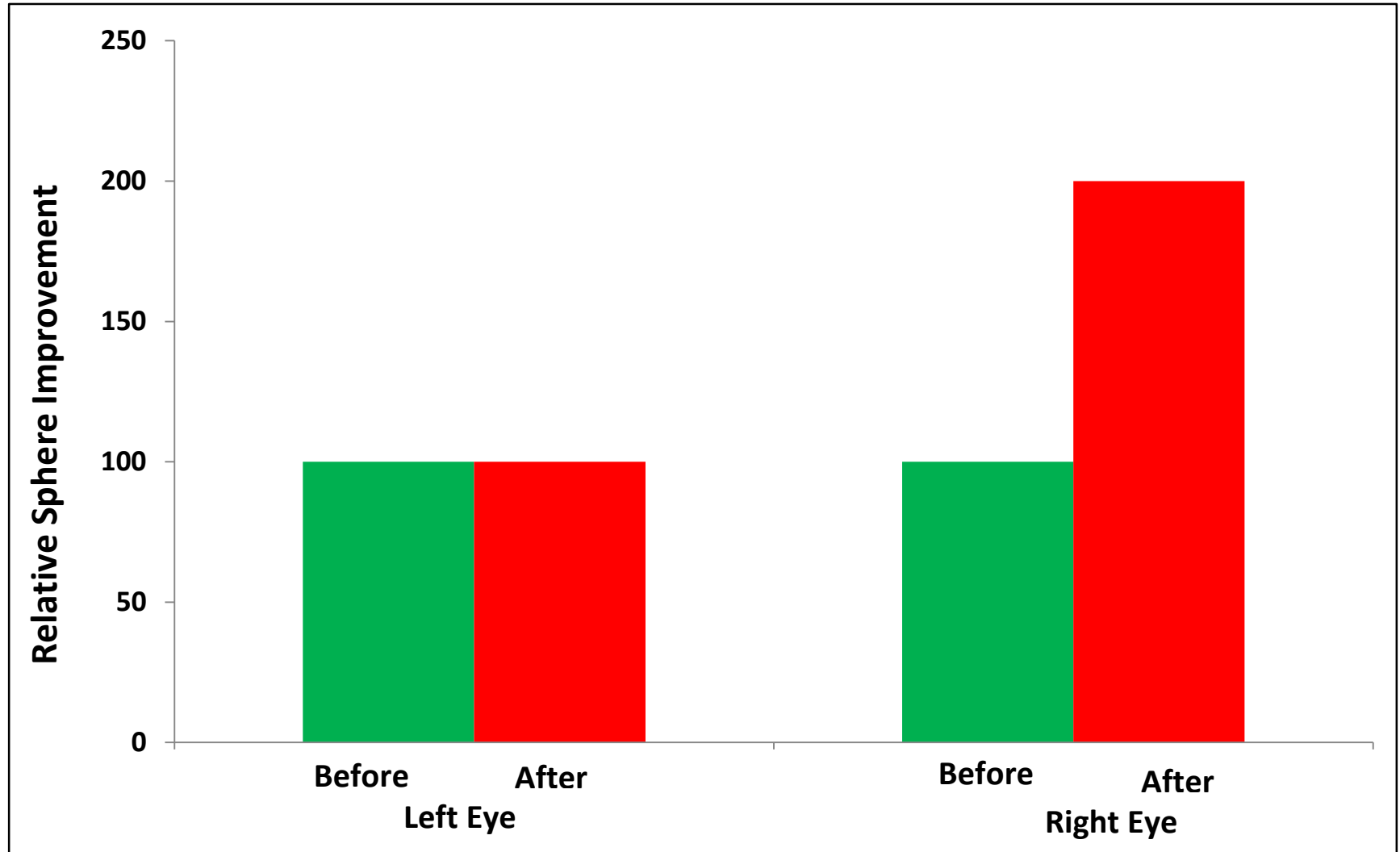


Patient #8- Female, 69 Years Old

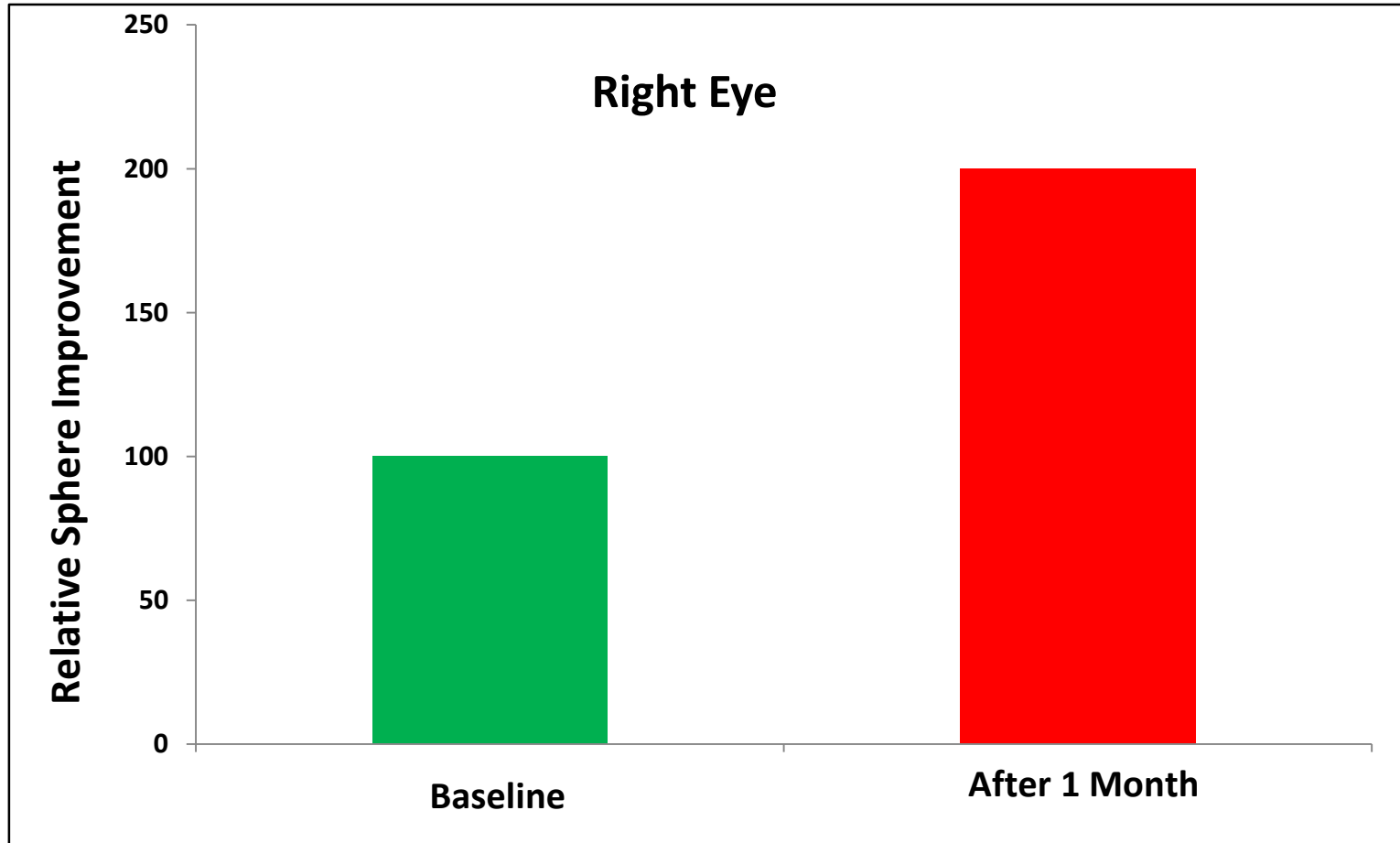




Patient #9- Male, 66 Yrs Old

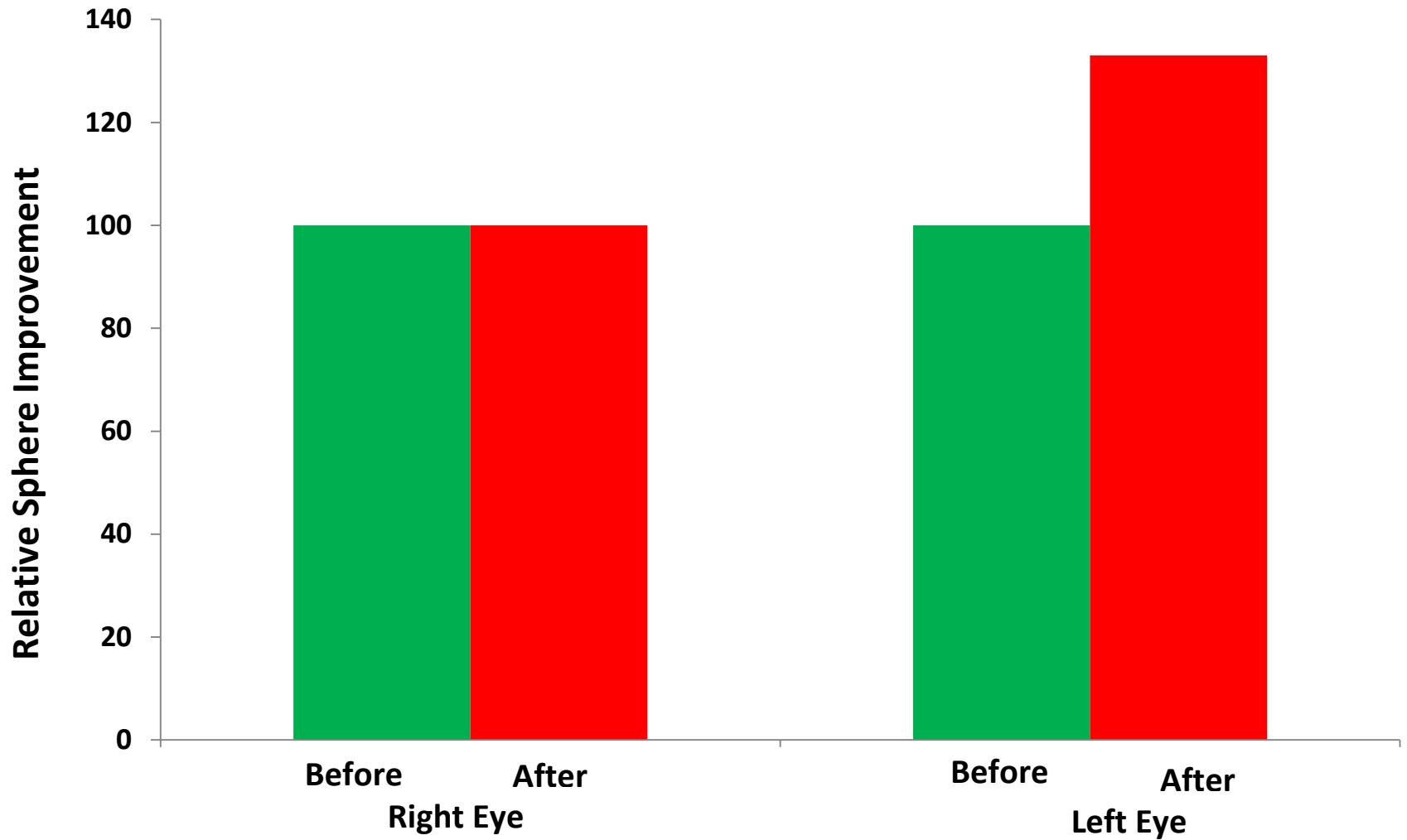


Patient #10- Female, 65Yrs Old

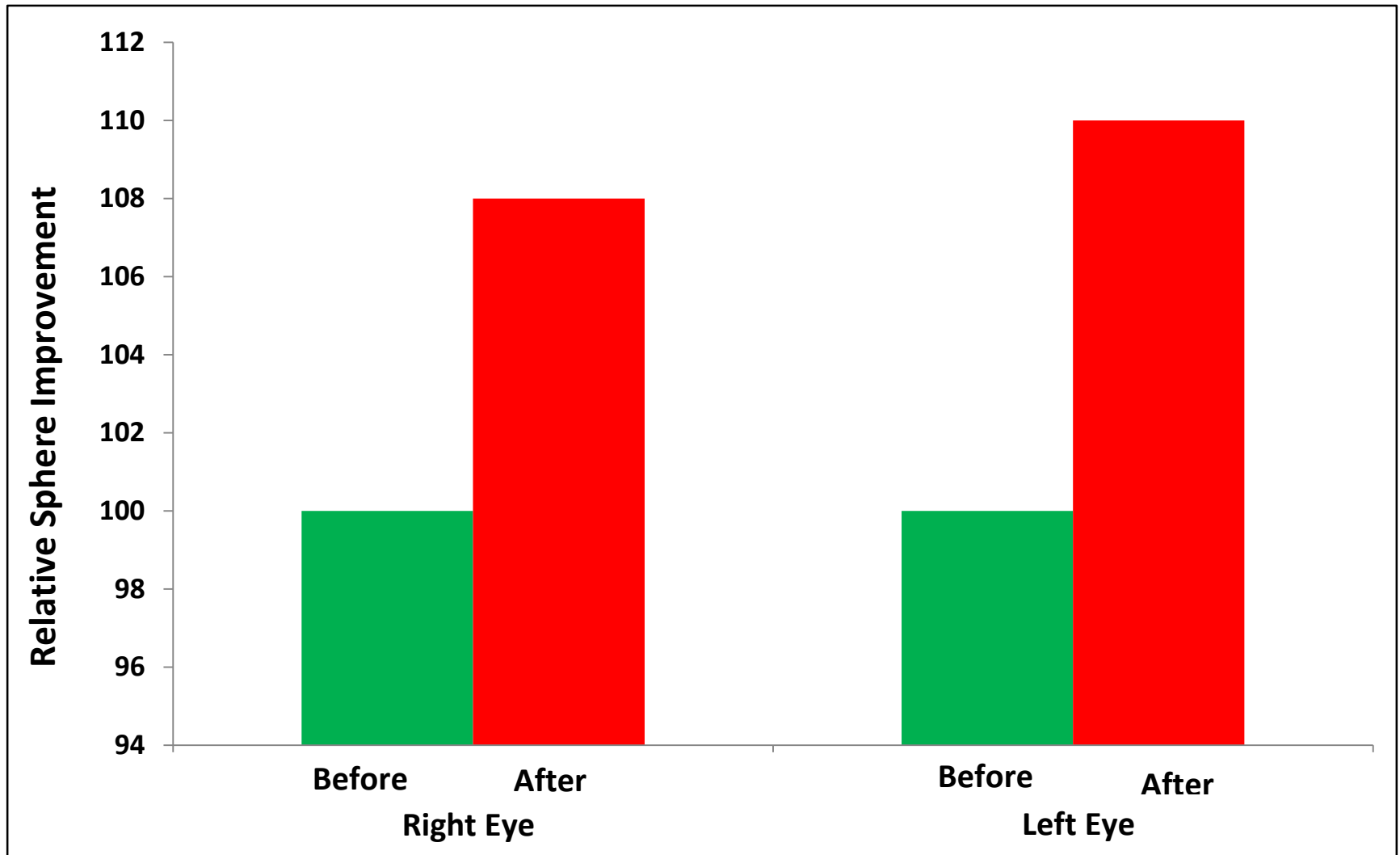


*Left Eye Under Medication

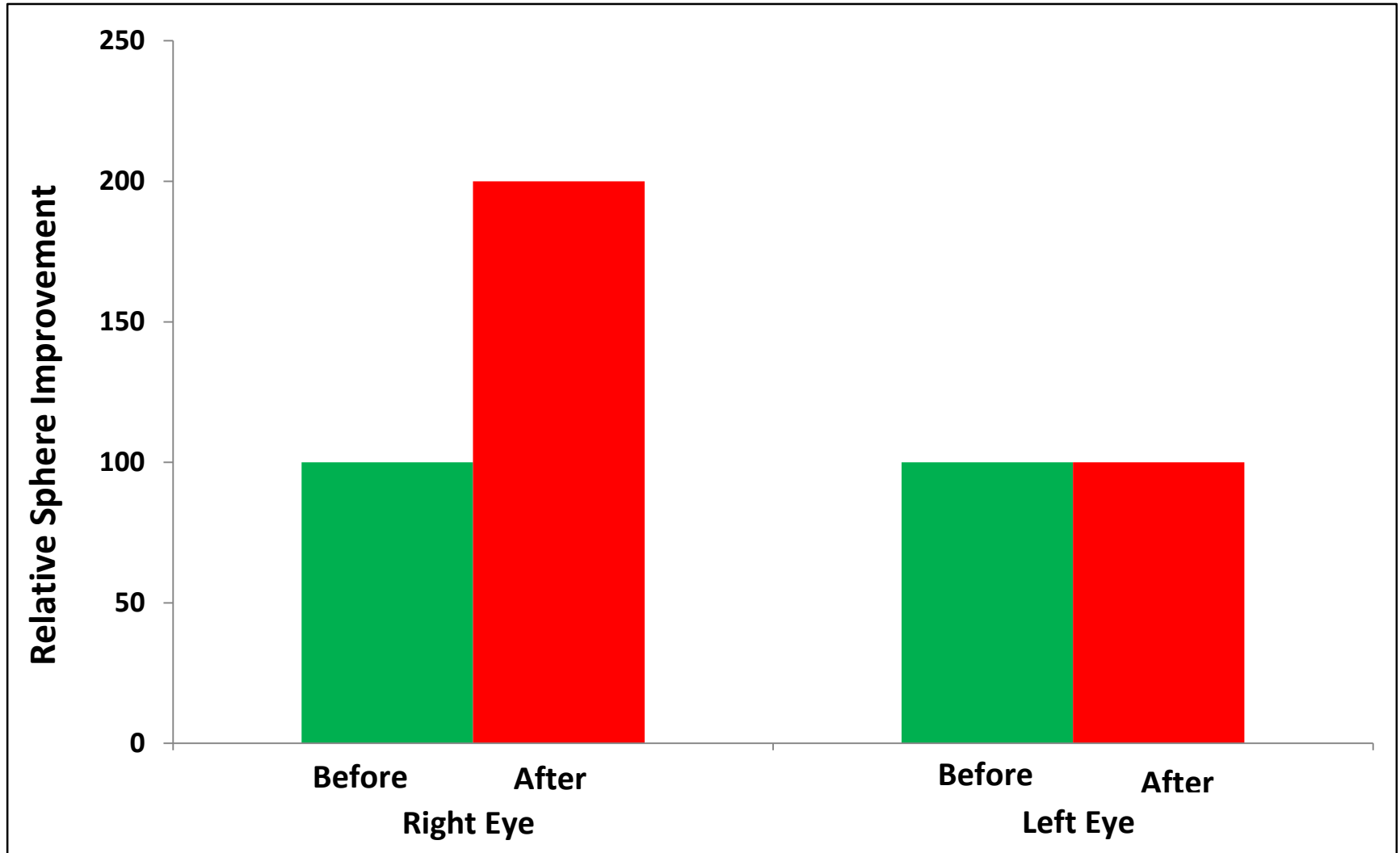
Patient #16- Female, 55 Yrs Old



Patient #18- Male, 70 Years Old



Patient #19 - Female, 57 Yrs Old





2.

Astigmatism



What is Astigmatism?

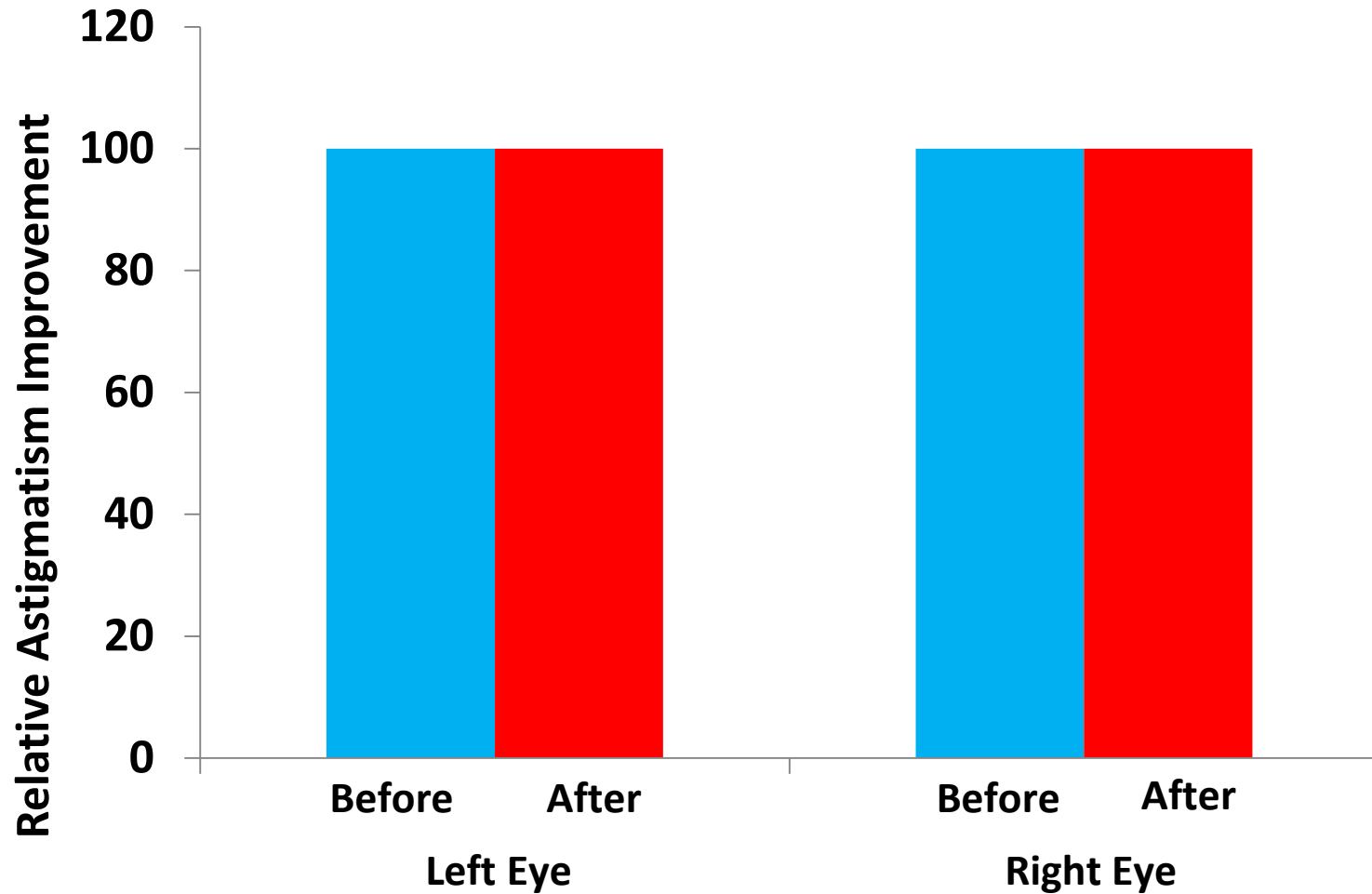
Astigmatism is a condition where the cornea is irregularly shaped causing blurred or distorted vision.

FOCUS

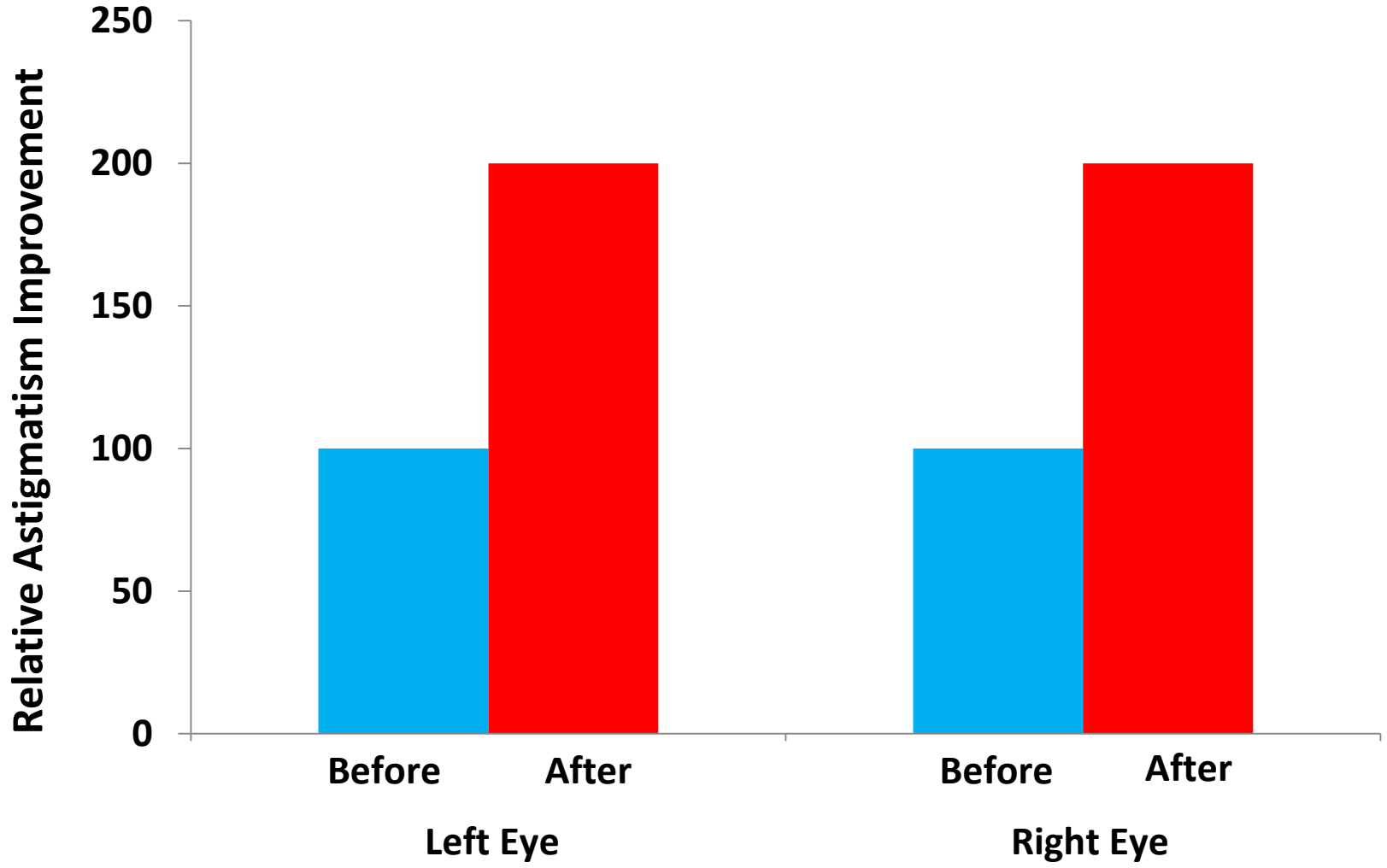
FOCUS

FOCUS

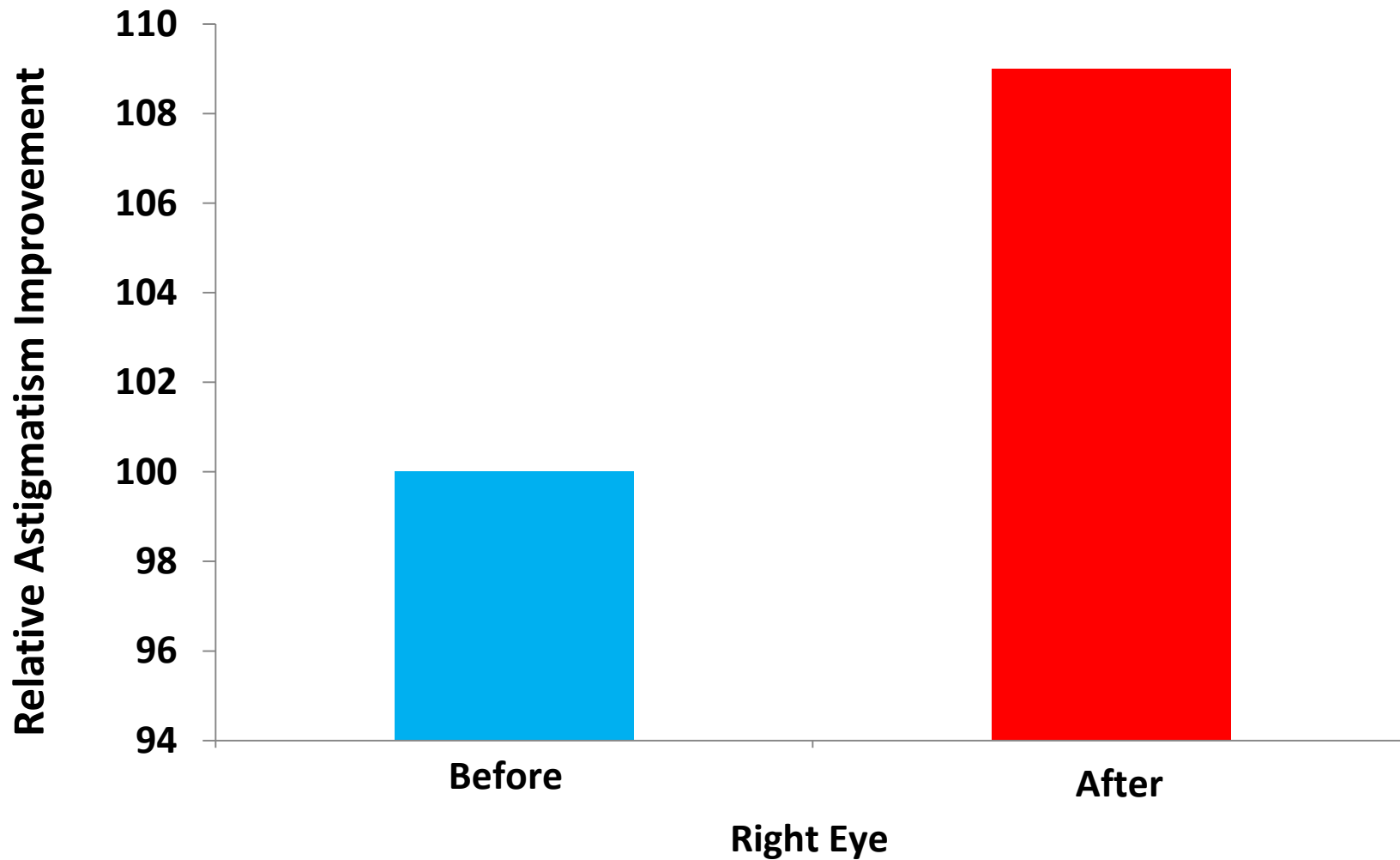
Patient #1- Female, 18 Yrs Old



Patient #2- Female, 26 Yrs Old

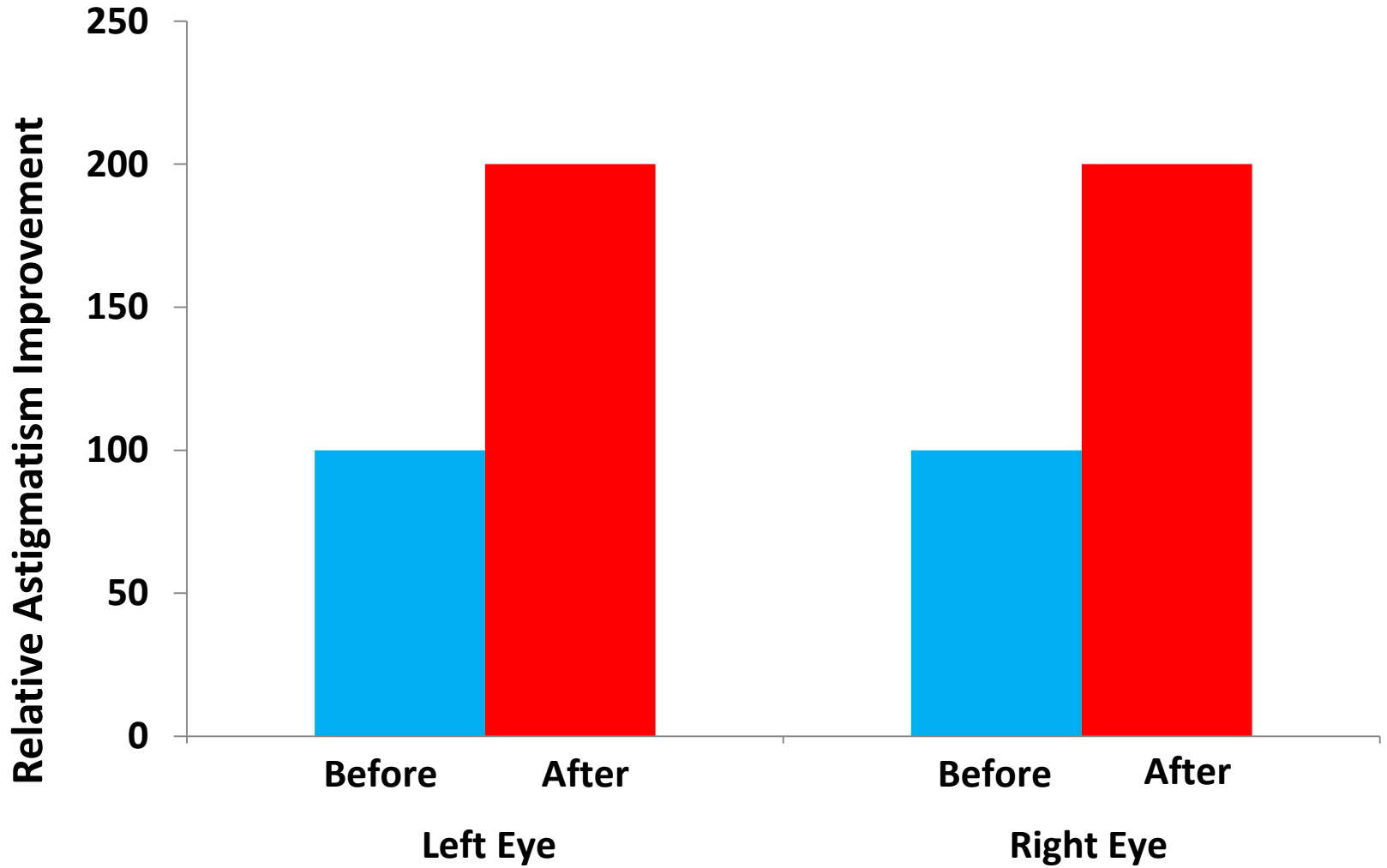


Patient #3- Male, 71 Yrs Old

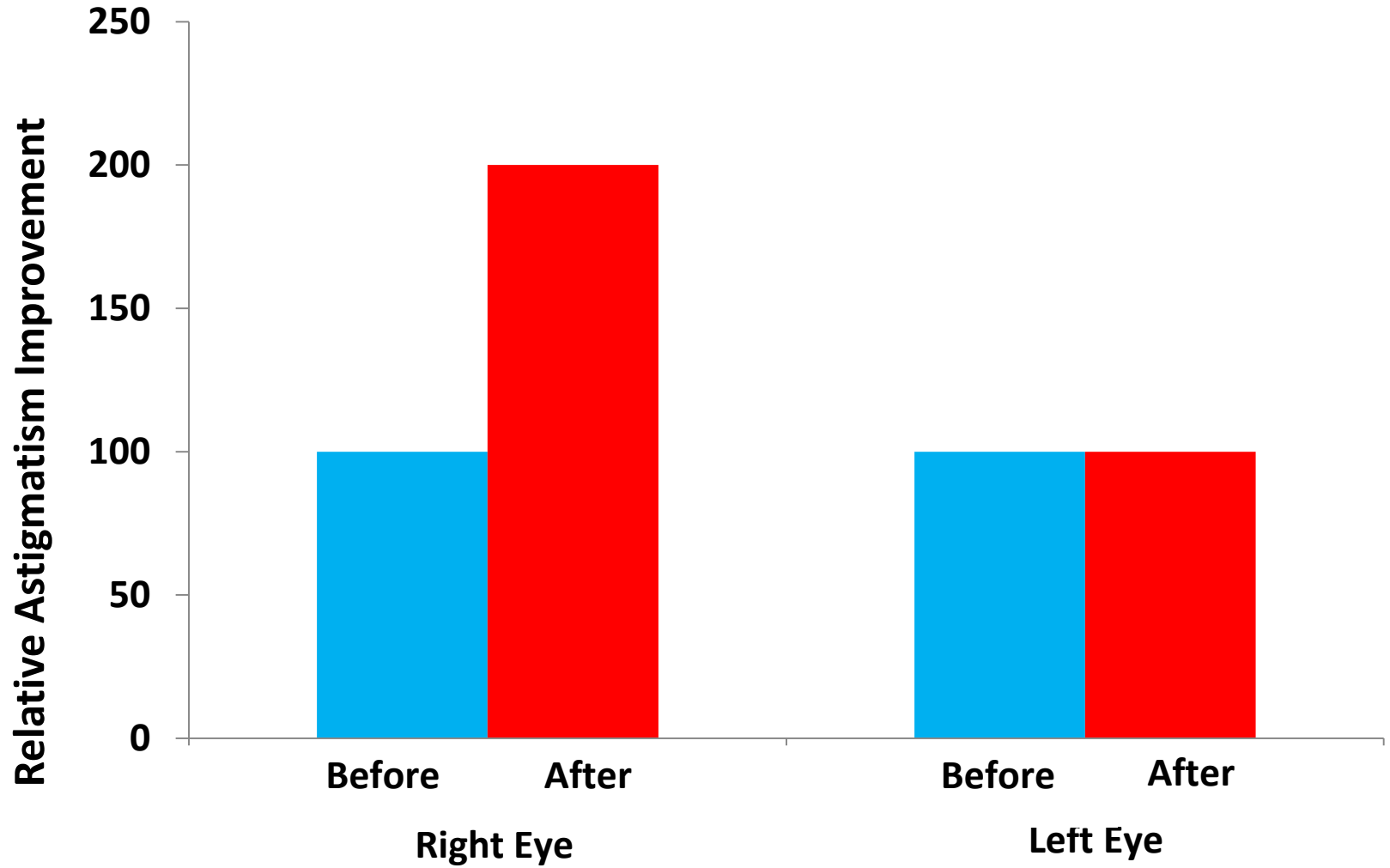


*Left Eye Under Medication

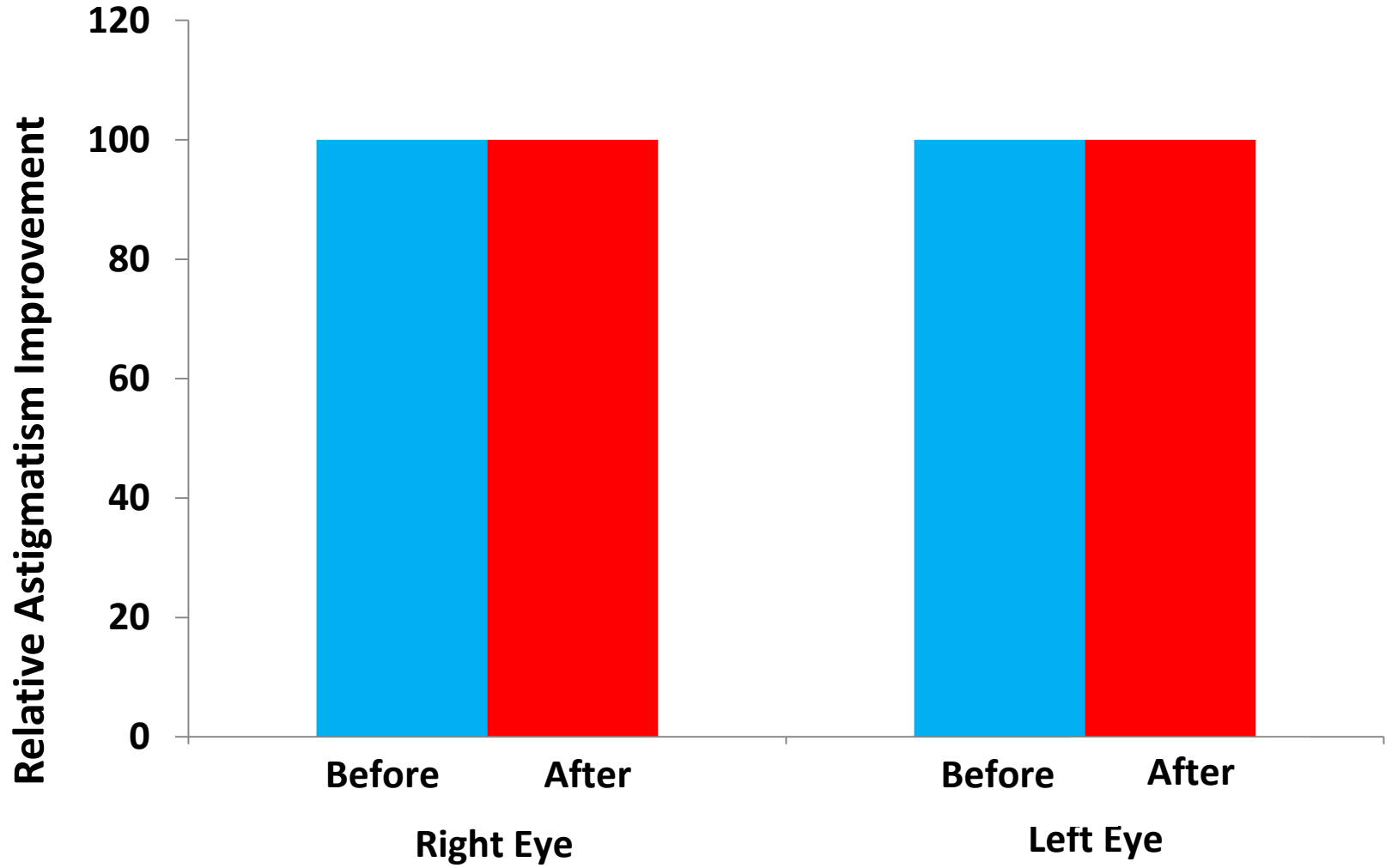
Patient #4- Male, 78 Yrs Old



Patient #5- Female, 58 Yrs Old

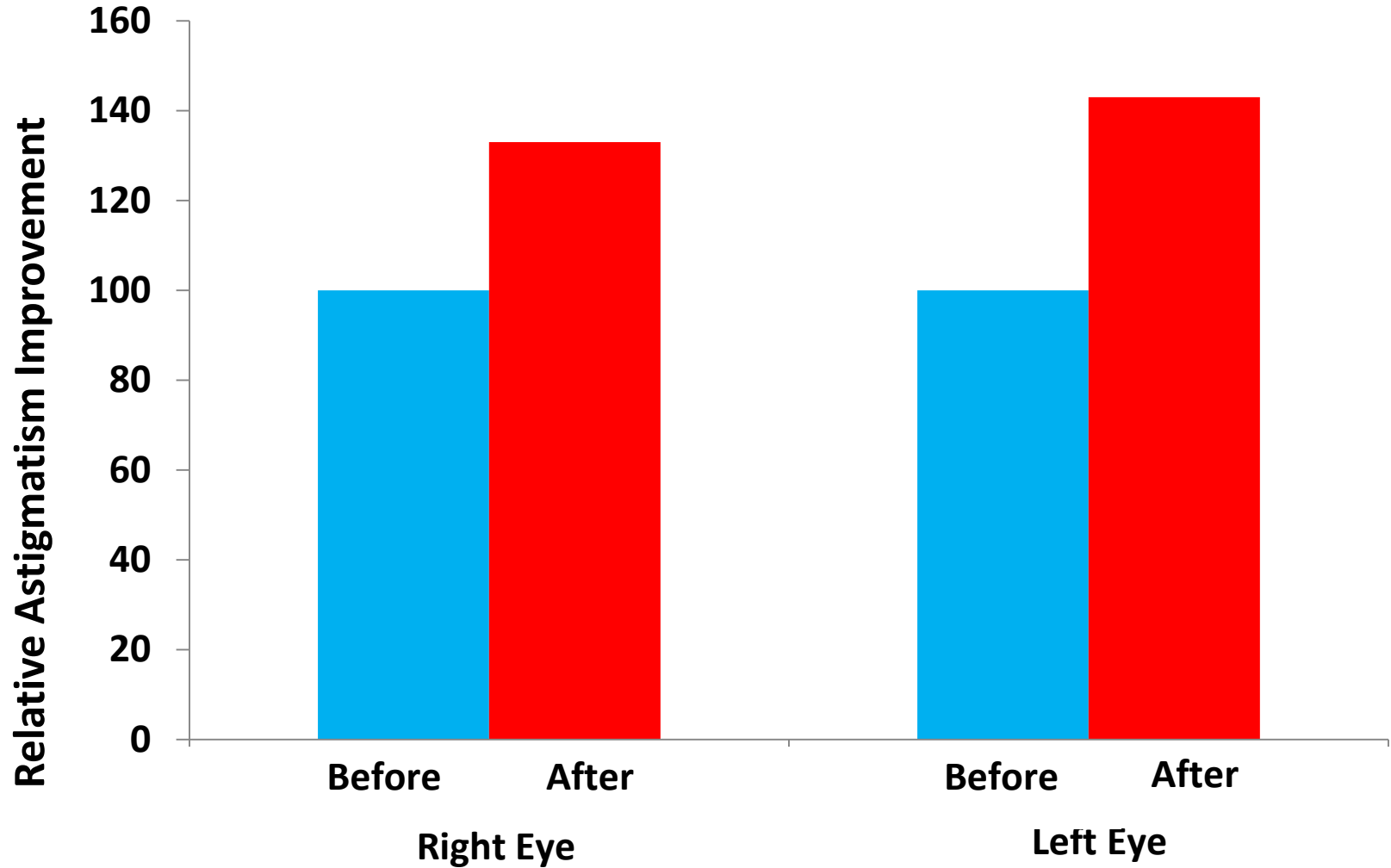


Patient #8- Female, 69 Yrs Old

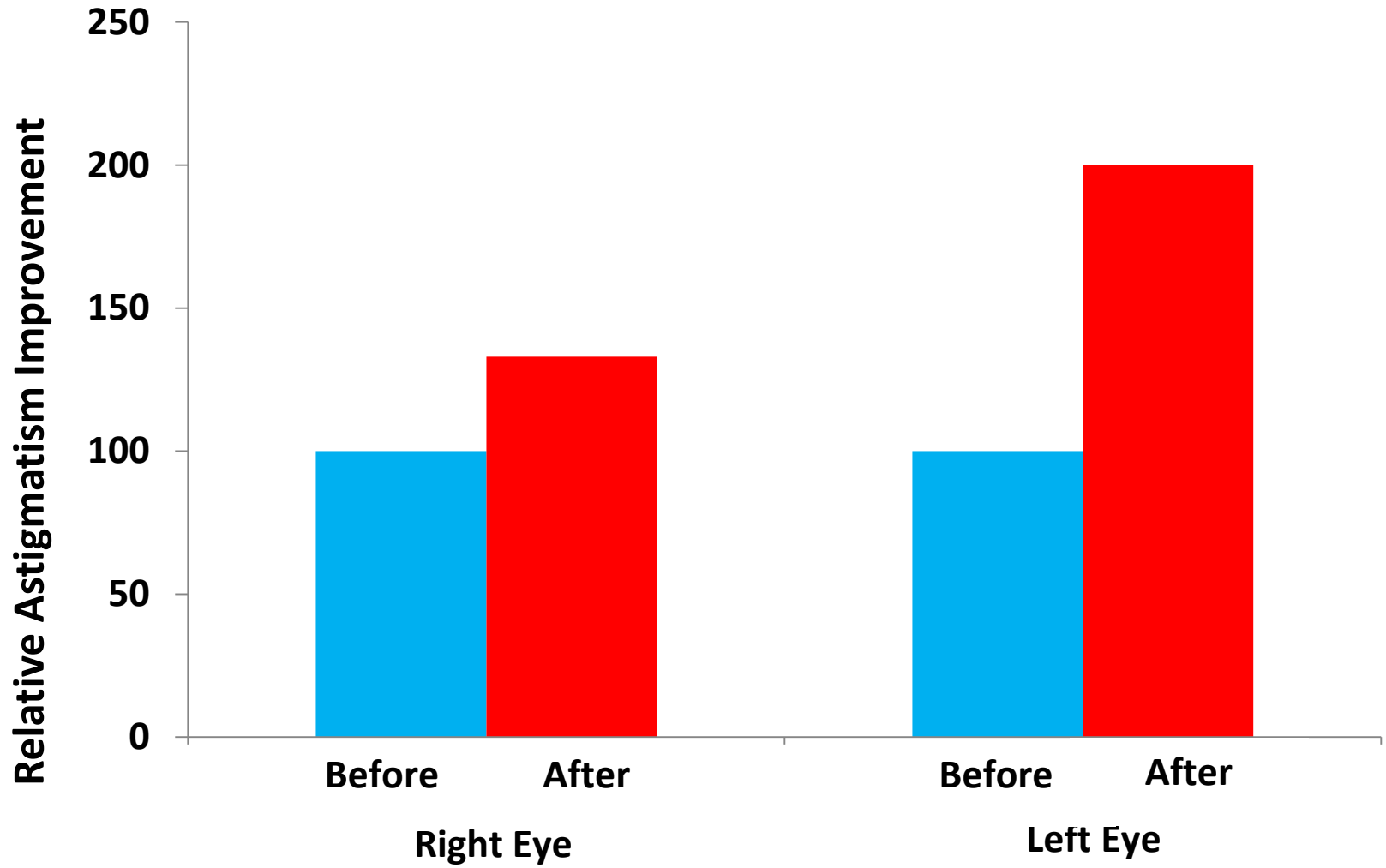


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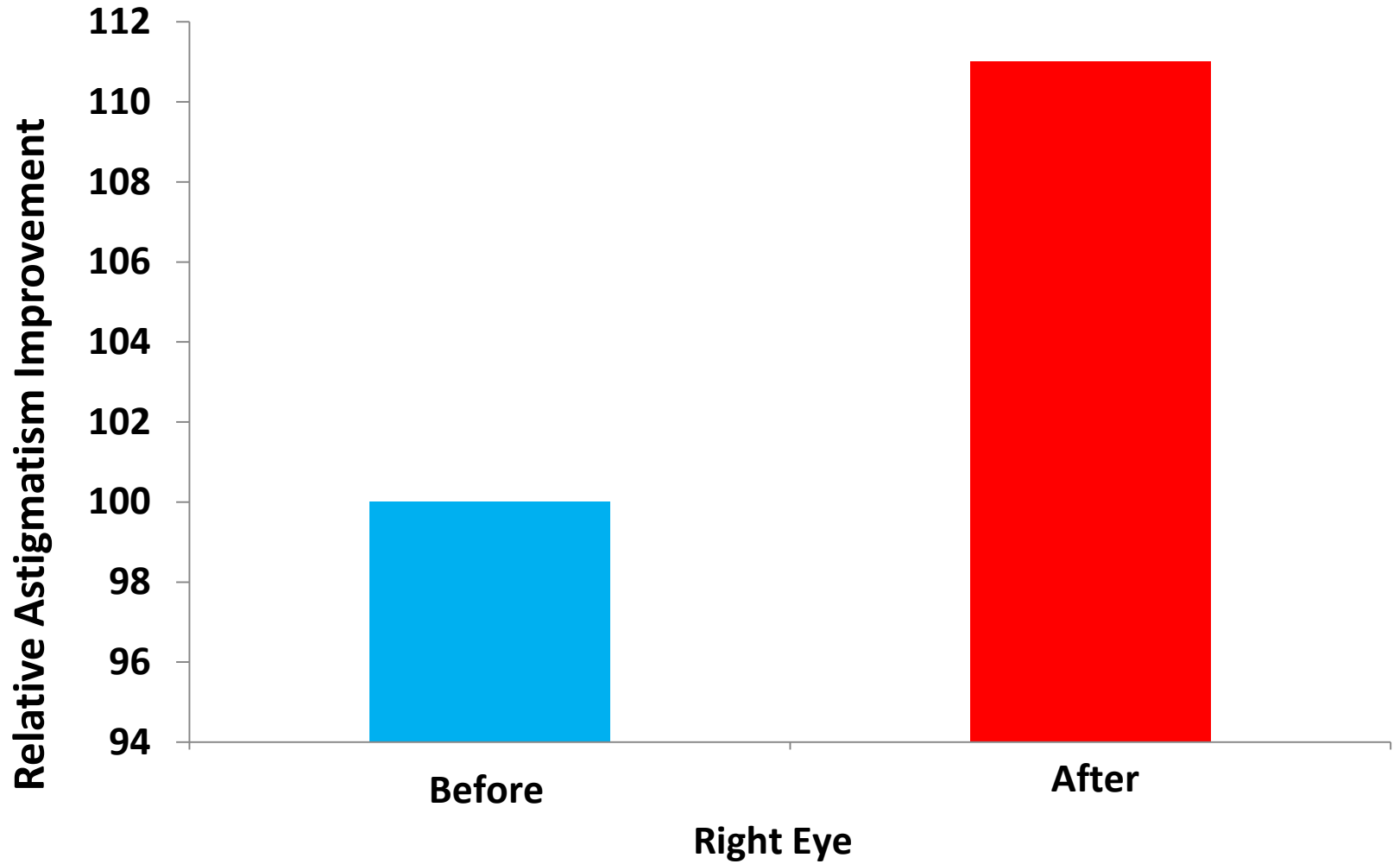
Patient #9- Male, 66 Yrs Old



Patient #10- Female, 65 Yrs Old

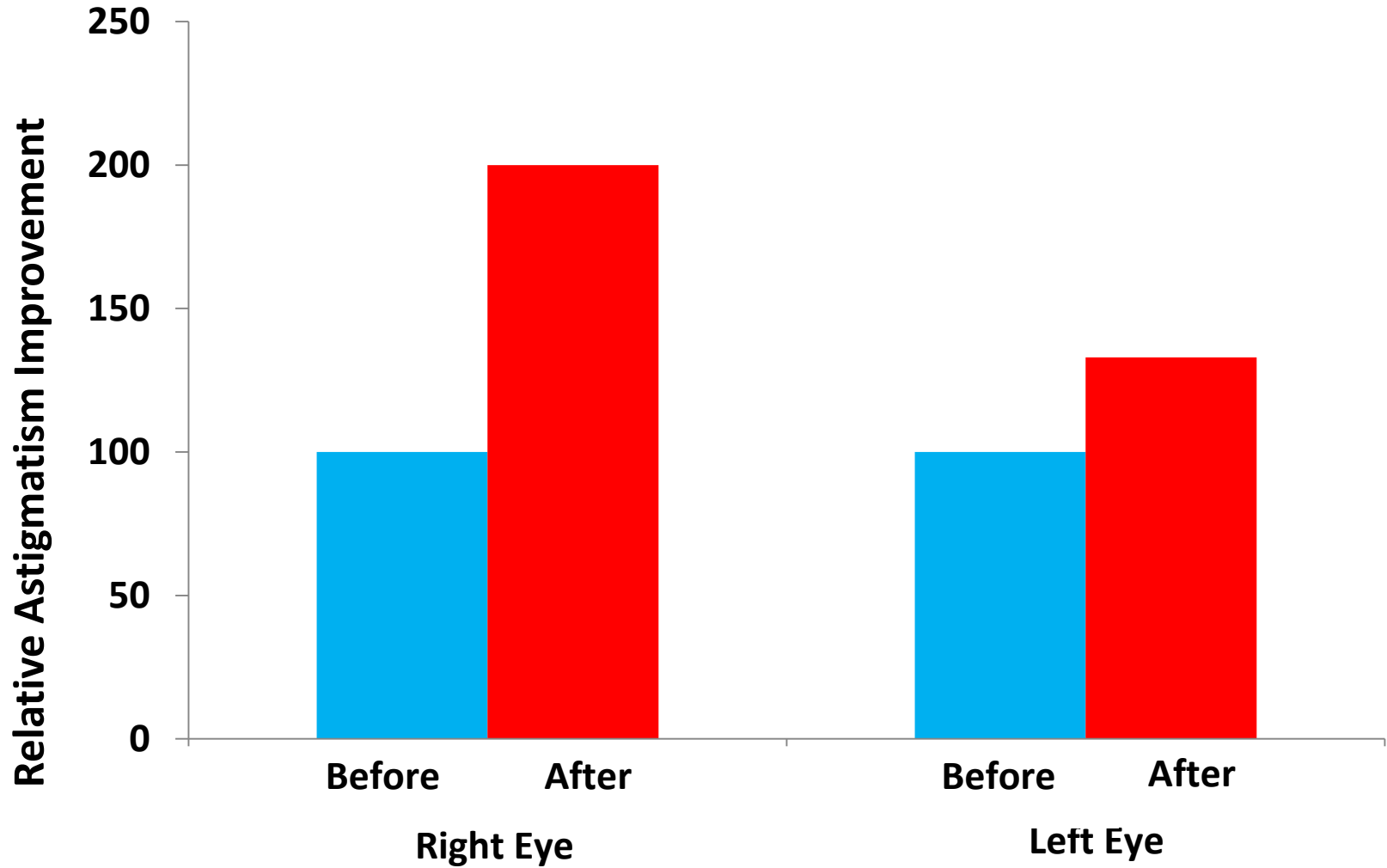


Patient #11- Male, 73 Yrs Old

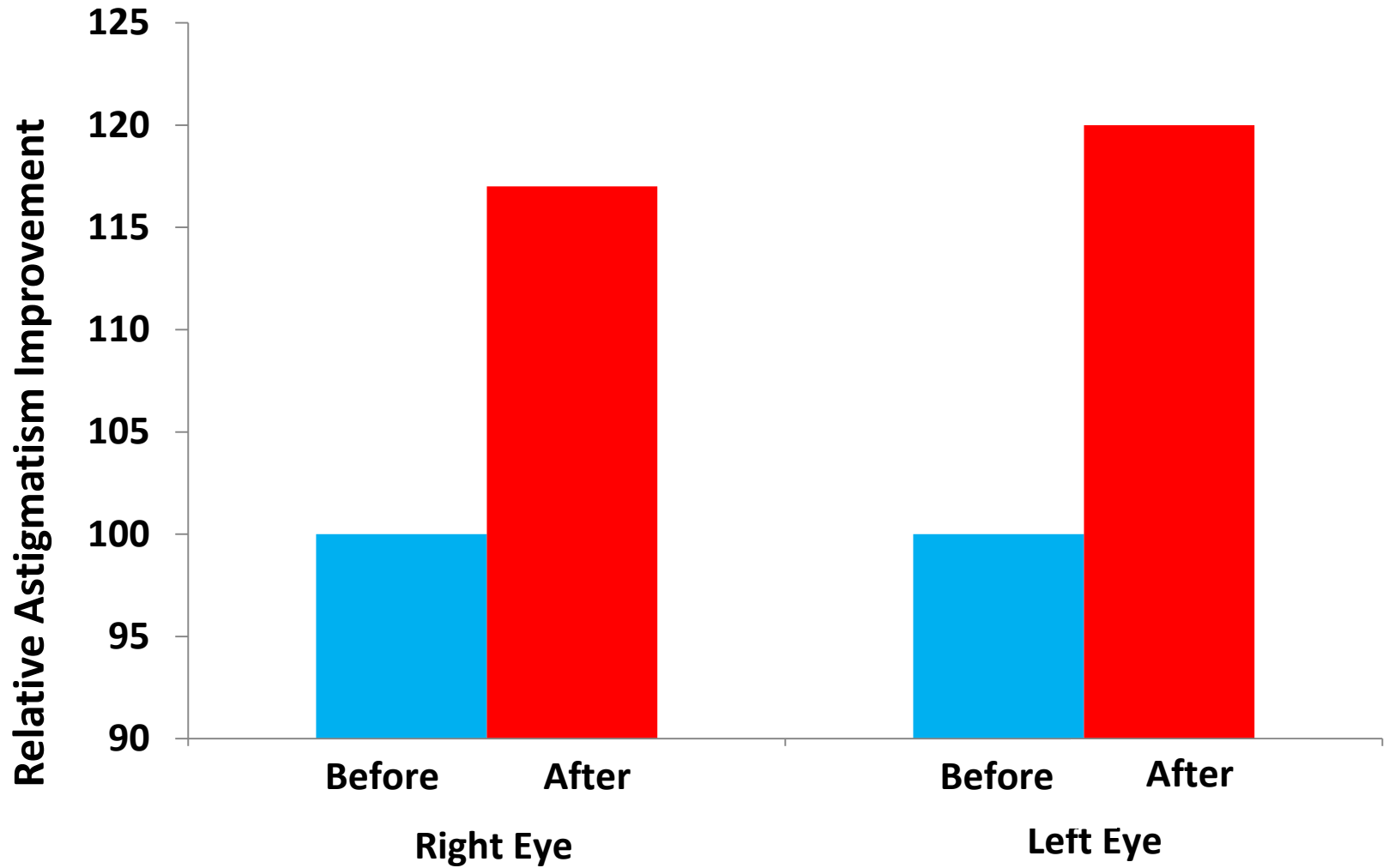


***Left Eye Under Medication**

Patient #12- Female, 68 Yrs Old



Patient #19- Female, 57 Yrs Old





Comments From Doctors & Patients

Patient 10 Personal Comments:

After one month of using spray, could read tiny text on personal check.

Patient 17 Personal Comments:

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

Patient 18 Personal Comments:

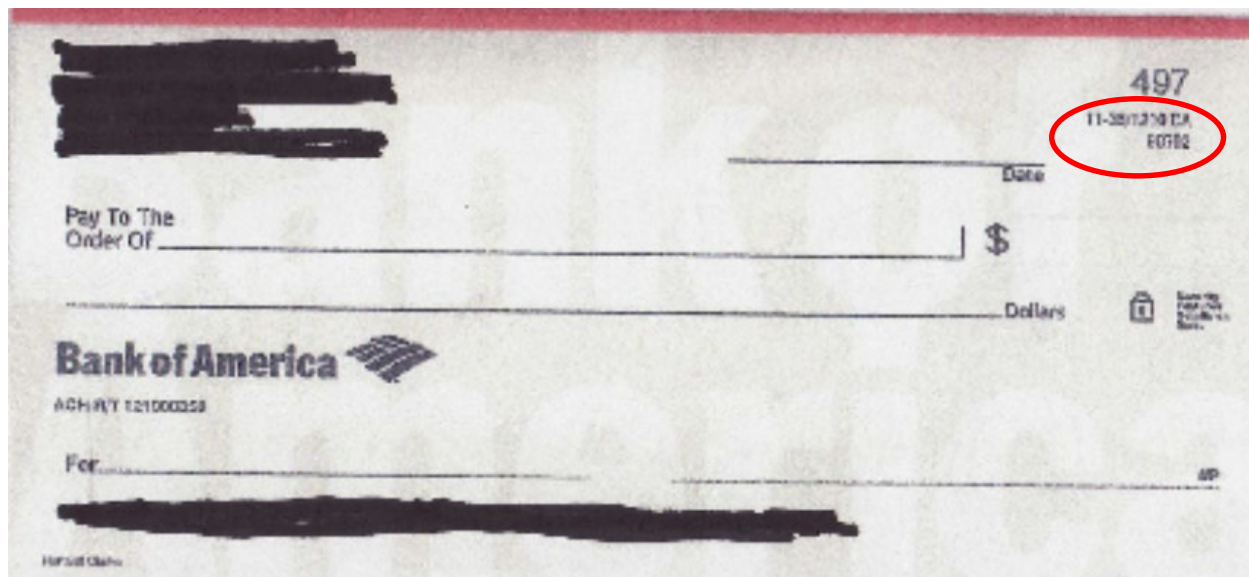
Dr. said glasses need to be changed (glasses too strong).

Patient 19 Personal Comments:

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

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:



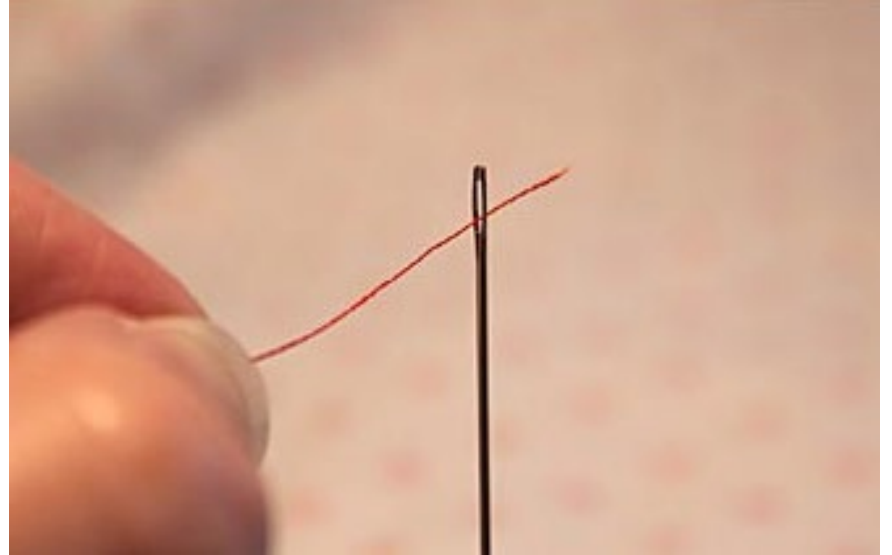
After using spray, tears stopped running and was able to see golf ball more clearly.

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).



Conclusion

Bedil Ai may be useful agent for improving:

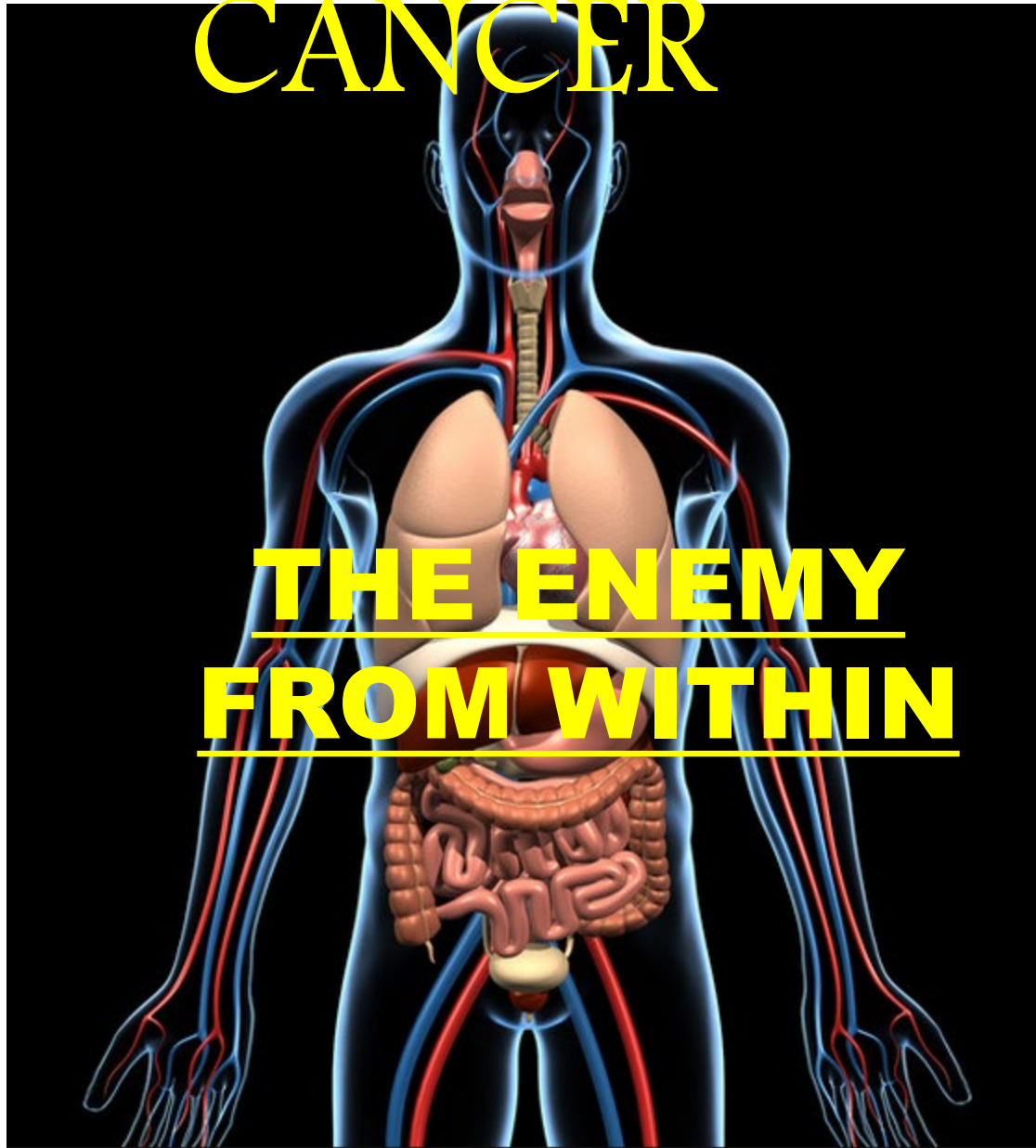
- **eye vision**
- **astigmatism**



Break

CANCER

THE ENEMY
FROM WITHIN



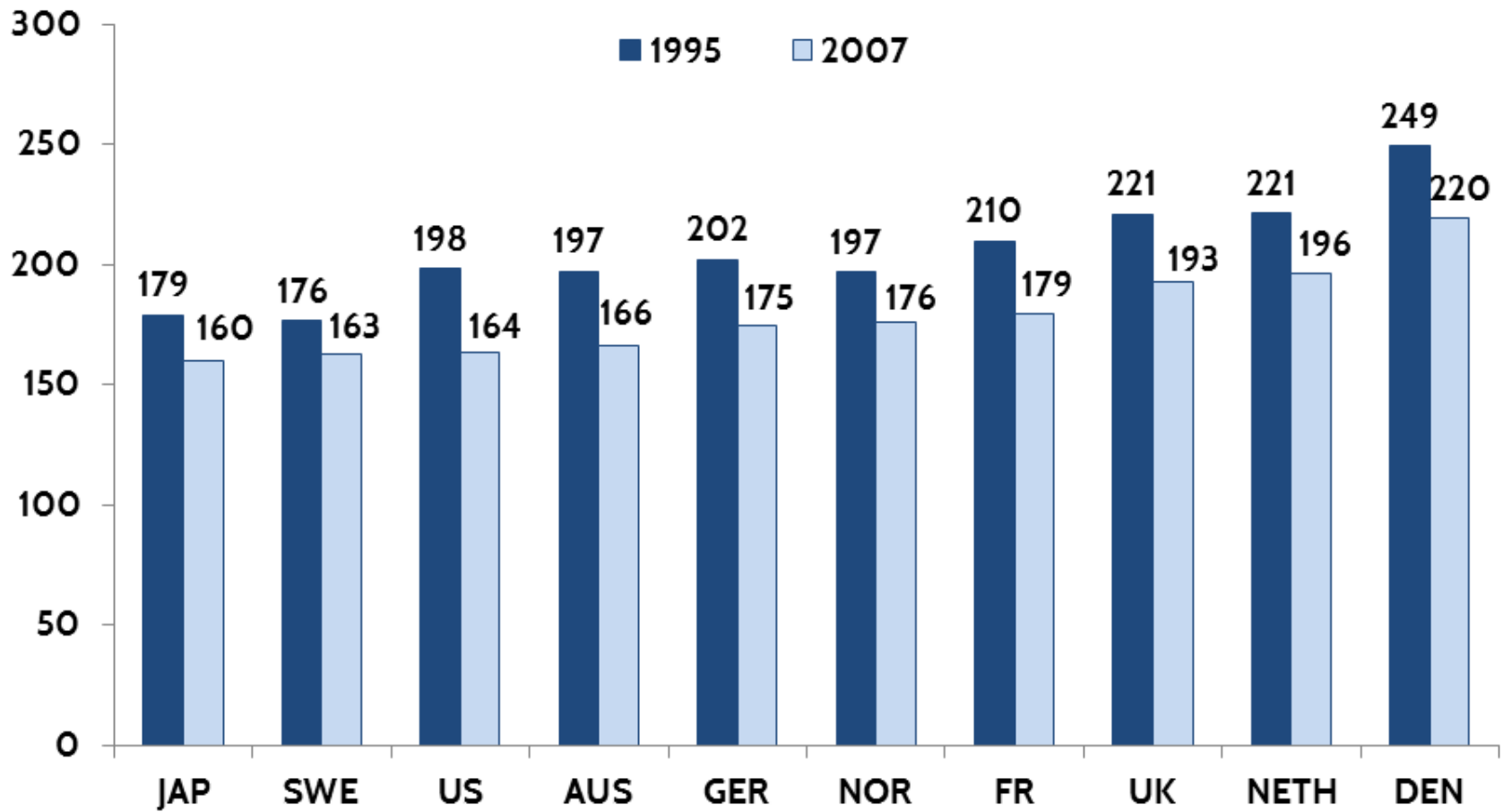
U.S. Cancer Deaths

	2005	2013
Daily	1560	1590
Yearly	570,280	580,350

The decrease in cancer mortality over 22 years was only slight in many major countries

Exhibit 10. Mortality as a Result of Cancer, 1995 to 2007

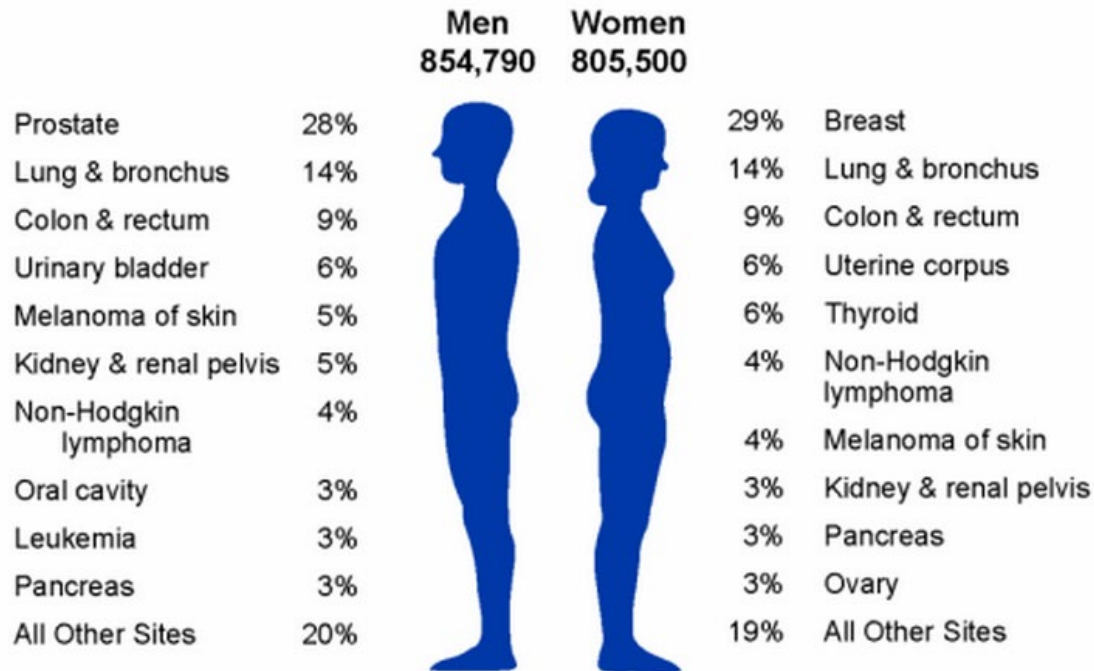
Deaths per 100,000 population (adjusted)*



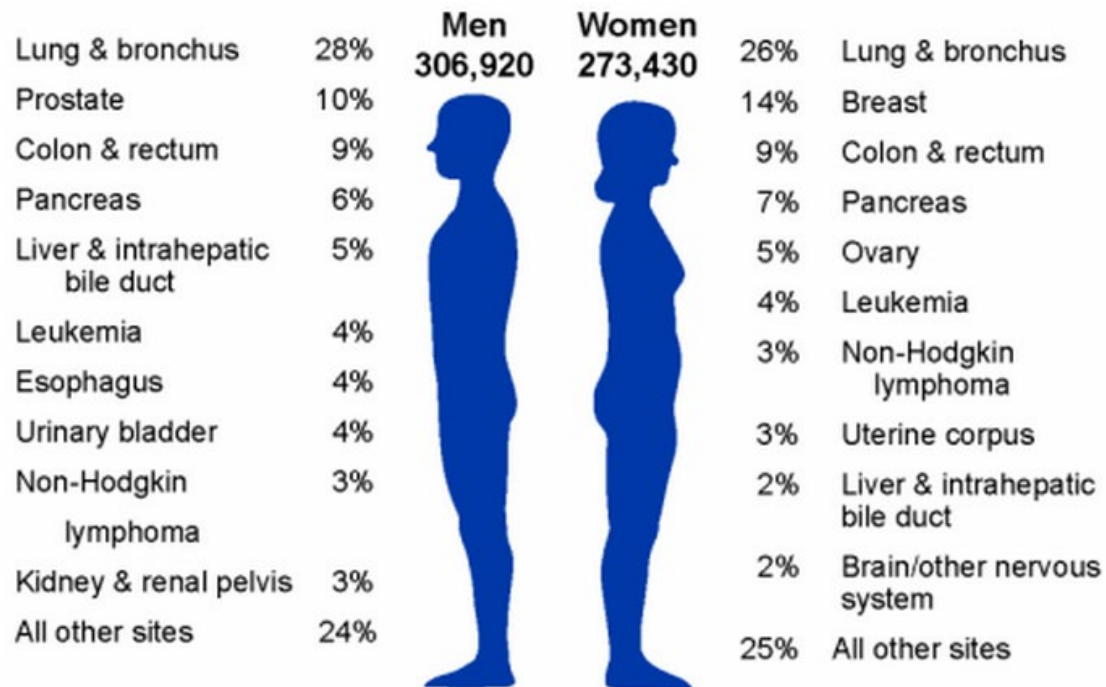
* Mortality rates are adjusted for likelihood of death from other causes.

Source: W. Stevens et al., "Cancer Mortality Reductions Were Greatest Among Countries Where Cancer Care Spending Rose the Most, 1995-2007," *Health Affairs*, April 2015 34(4):562-70.

Estimated New Cancer Cases in the US in 2013



Estimated Cancer Deaths in the US in 2013





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



Preventive Care

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



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

Anticancer by MRN-100

Mechanisms of action



Antioxidant



Immune modulator

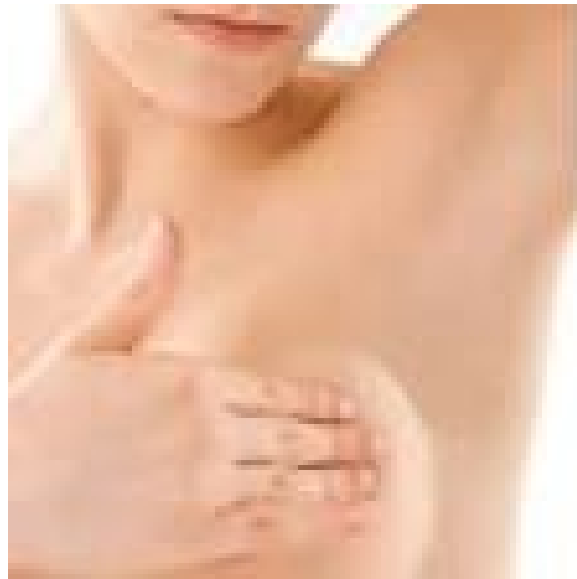
increases
susceptibility of
cancer cells
to NK cells

Apoptosis



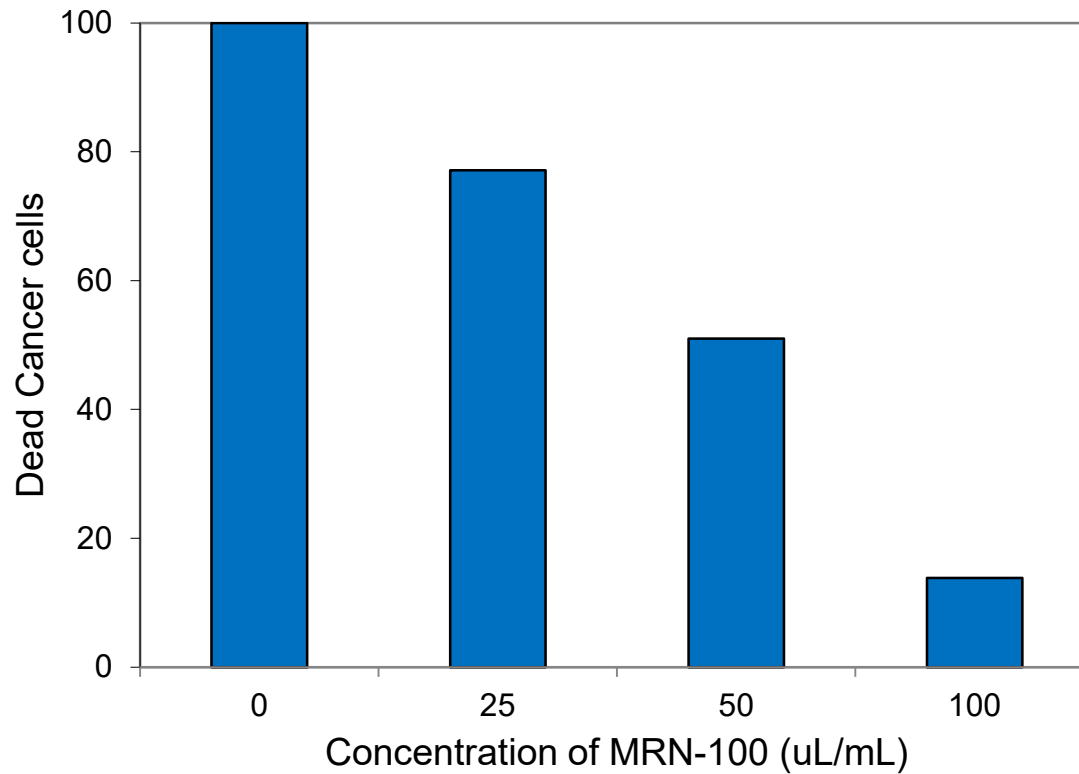
1.

Apoptosis





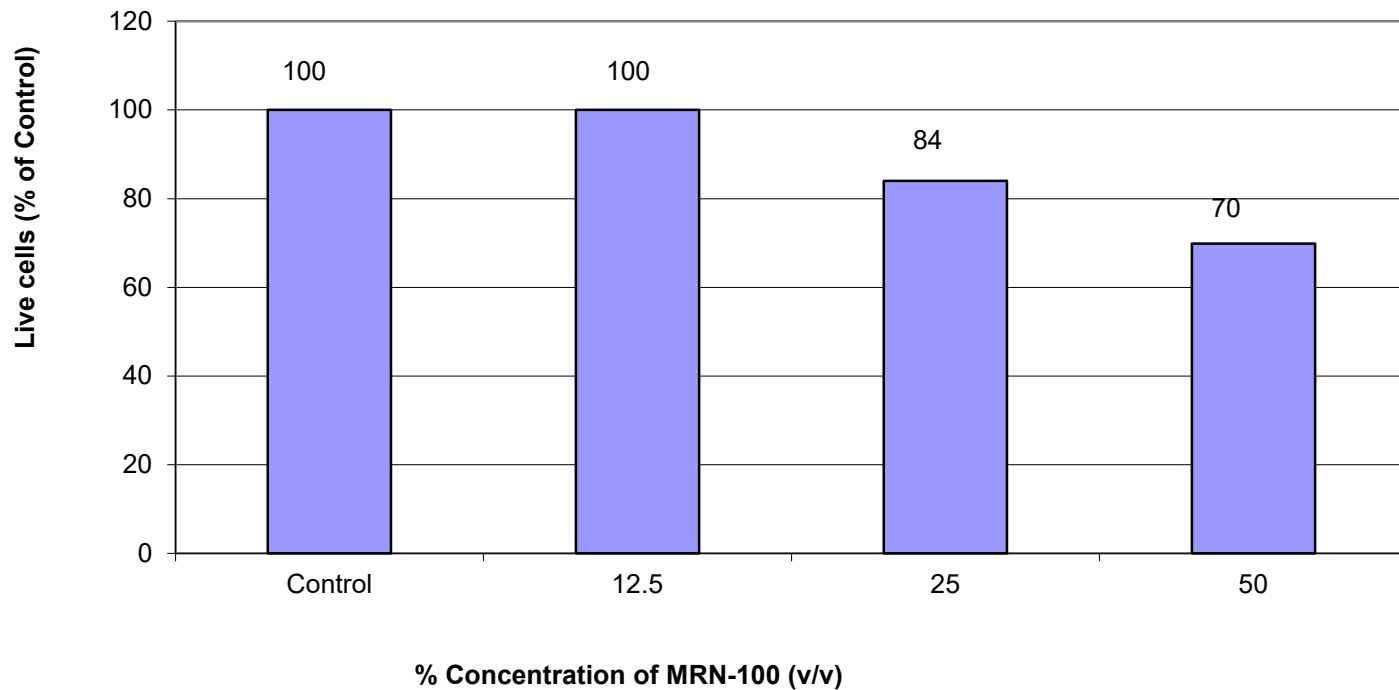
Effect of MRN-100 on Human Breast Cancer Cell Survival (MCF-7)



MTT Assay (24 Hours)

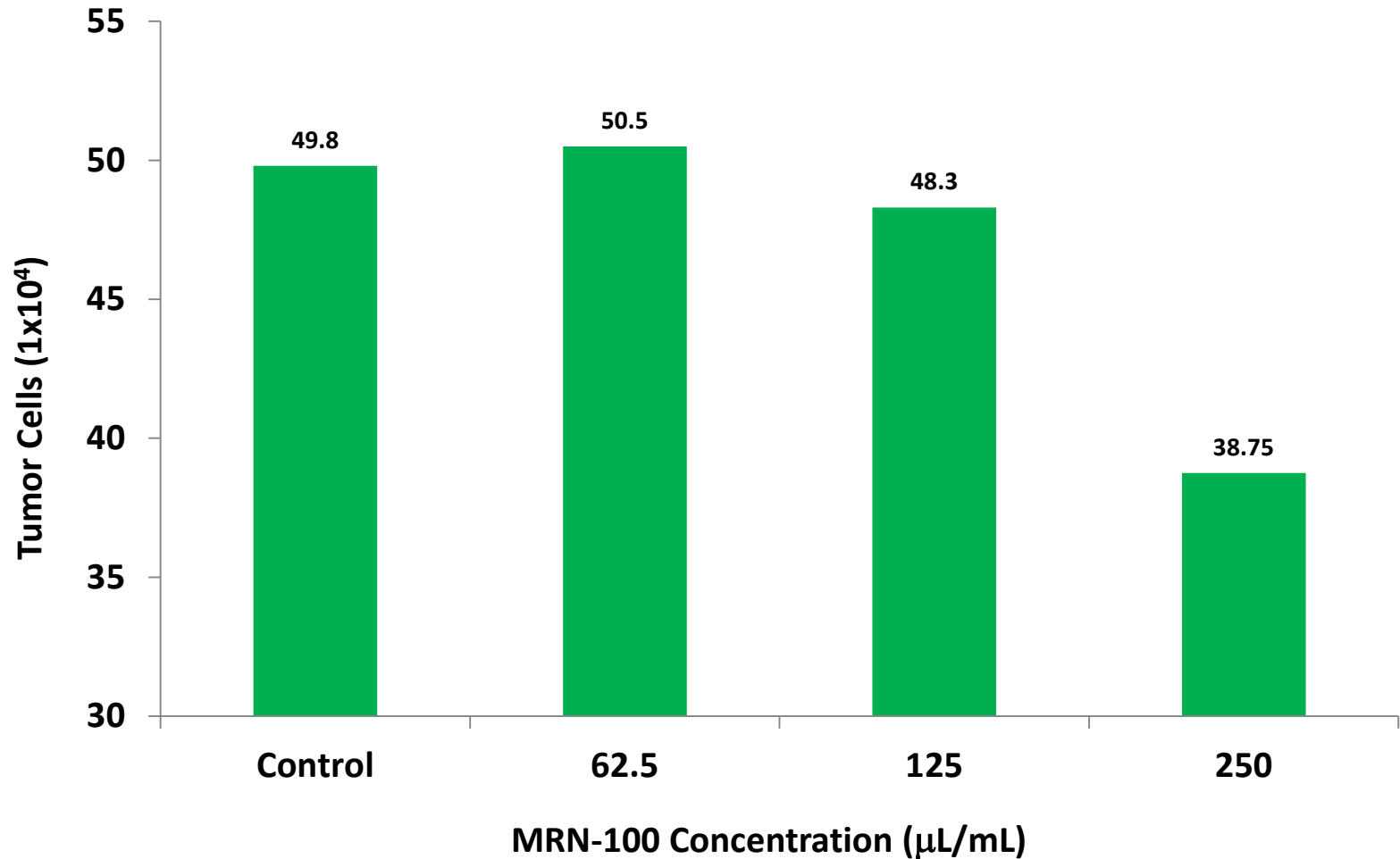


Effect of MRN-100 on Human Breast Cancer Cell Survival (ZR-75)



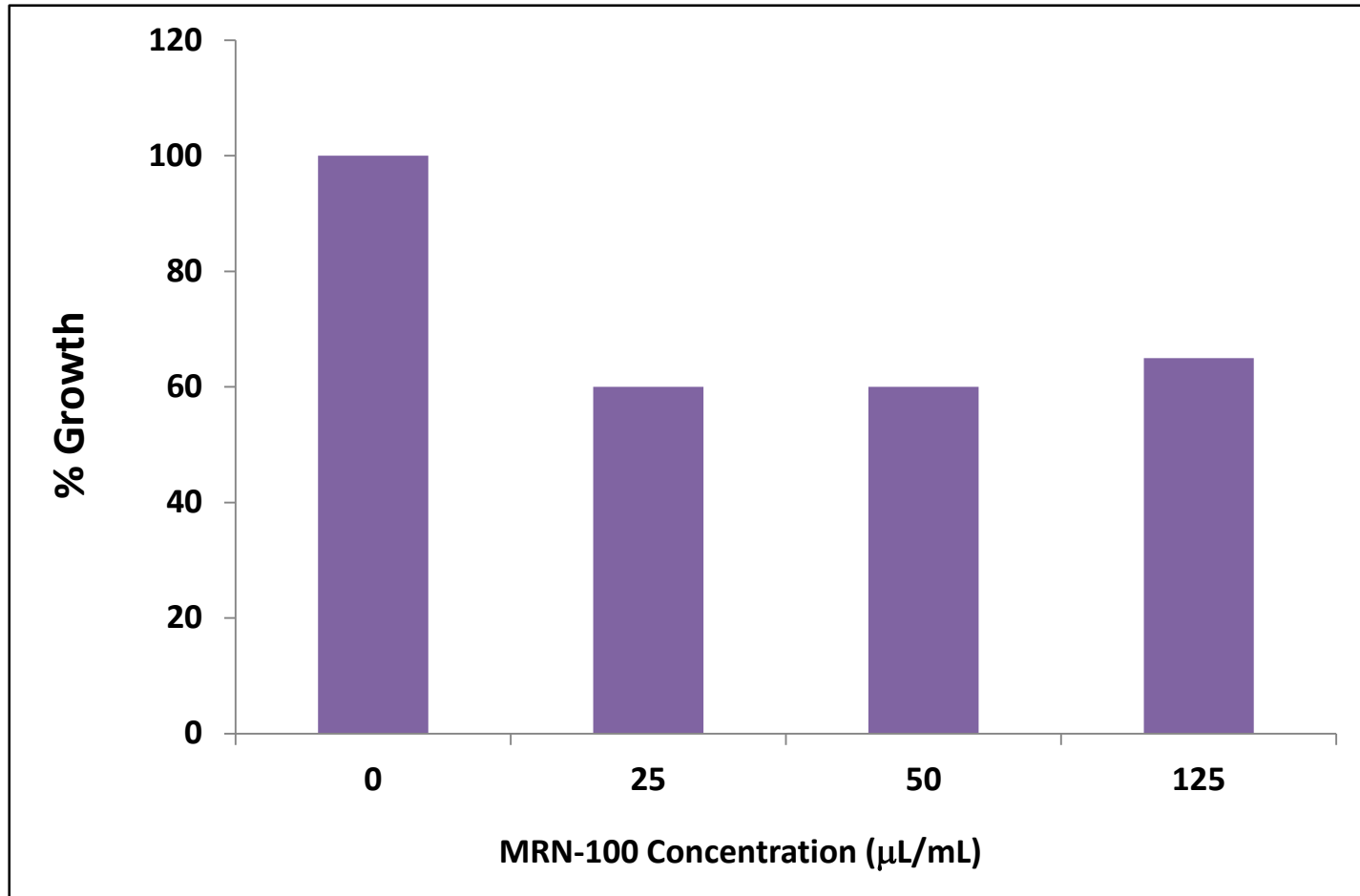
MTT Assay (24 Hours)

Apoptotic Effect of MRN-100 on Erythroleukemic Tumor Cell (K562)



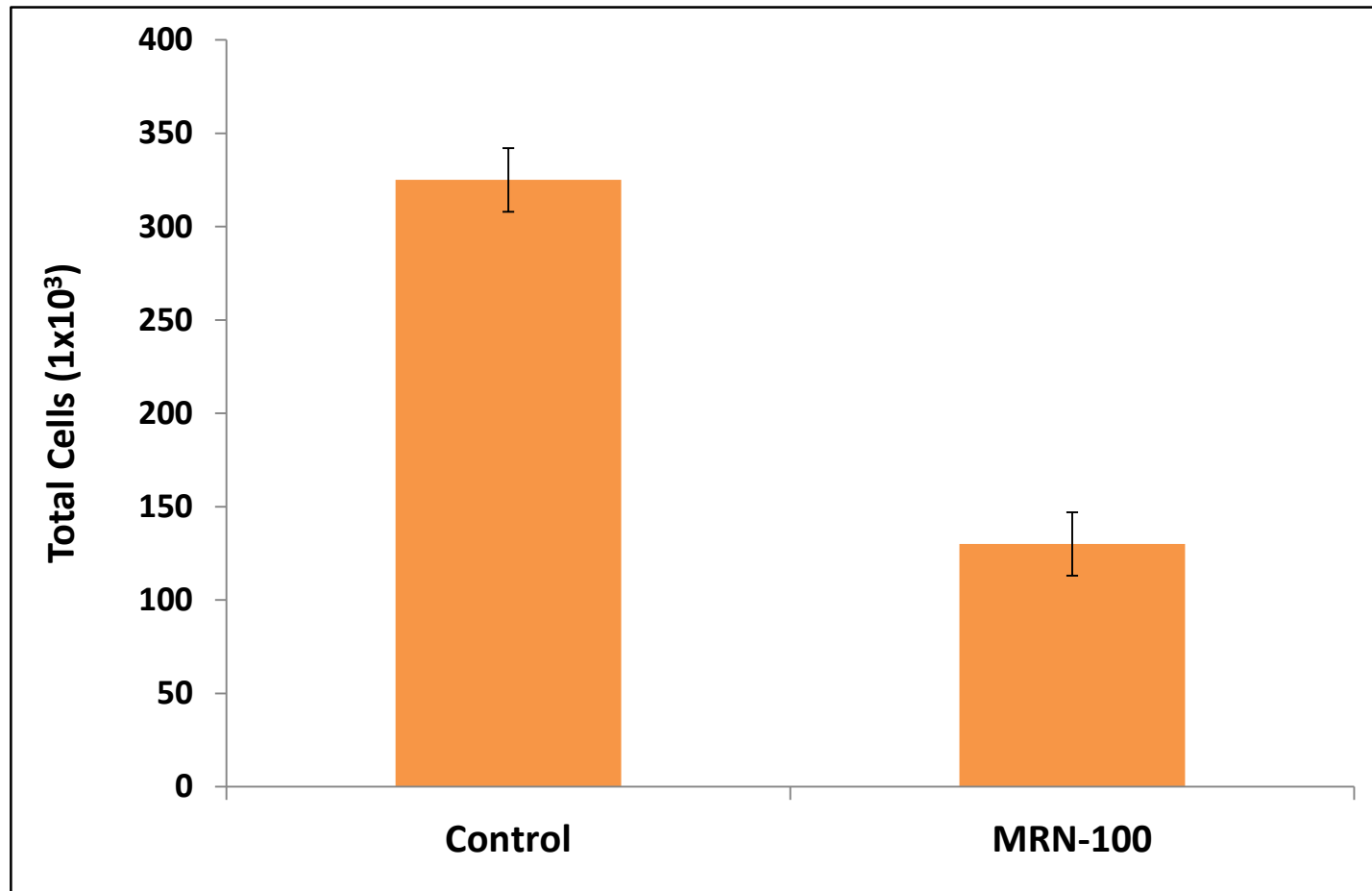
MTT Assay (48 Hours)

Effect of MRN-100 on Murine Leukemia P388 Cell Proliferation



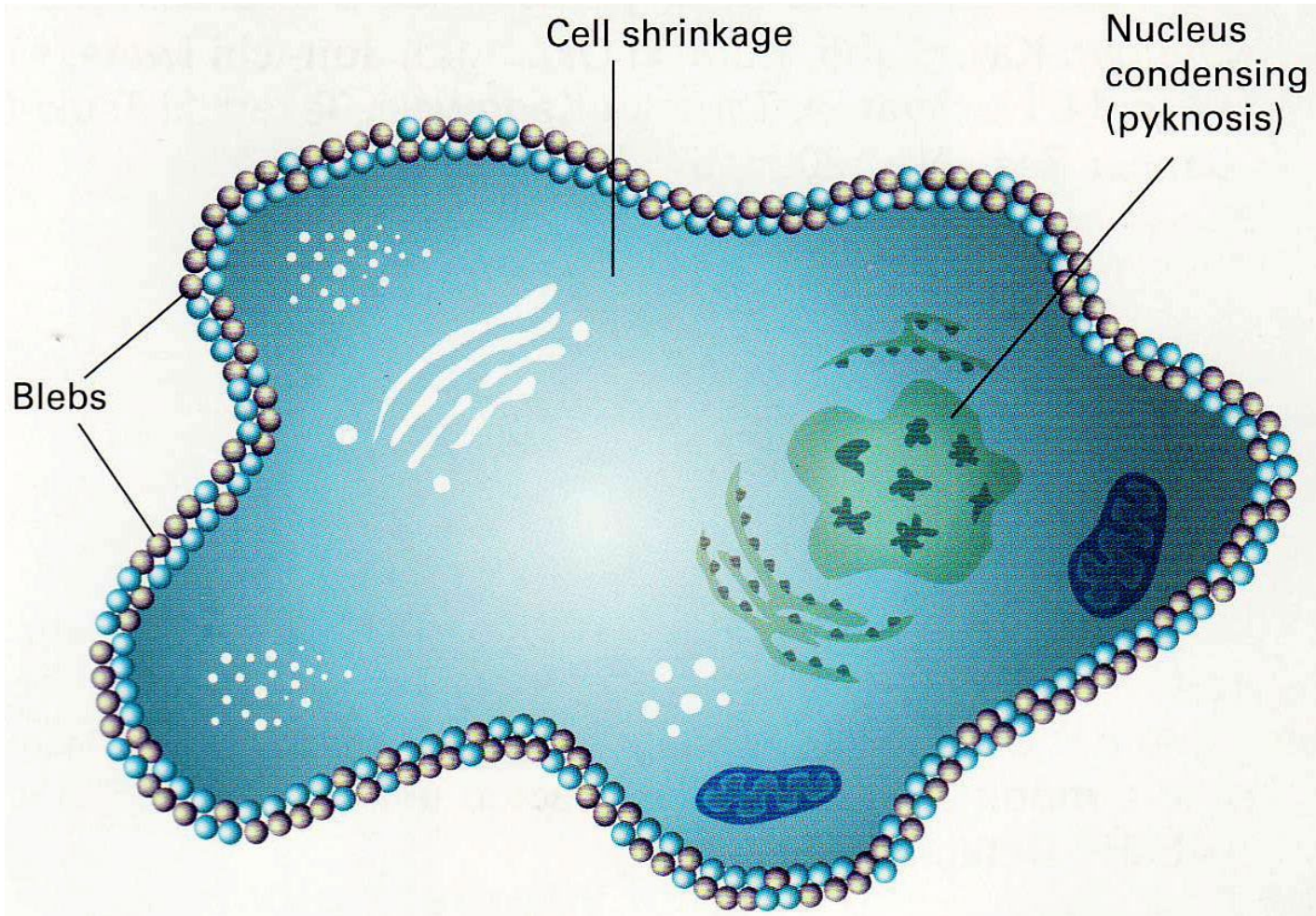
MTT Assay (24 Hours)

Apoptotic Effect of MRN-100 on Squamous Cell Carcinoma of the Skin (SCC13) Treated Cells



MTT Assay (24 Hours)

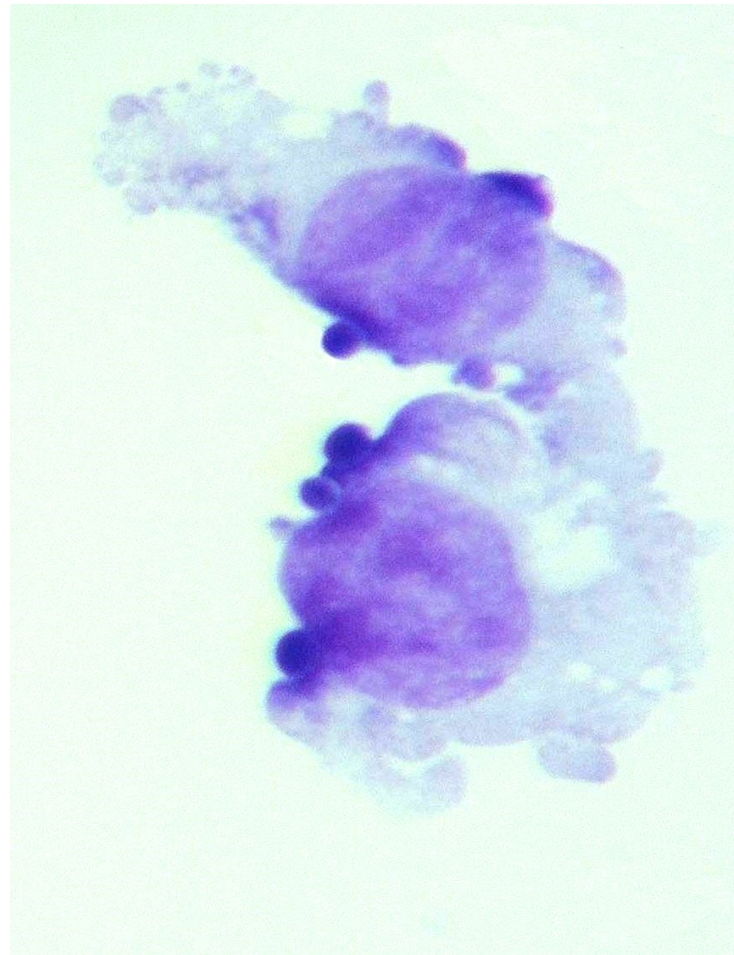
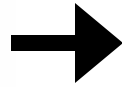
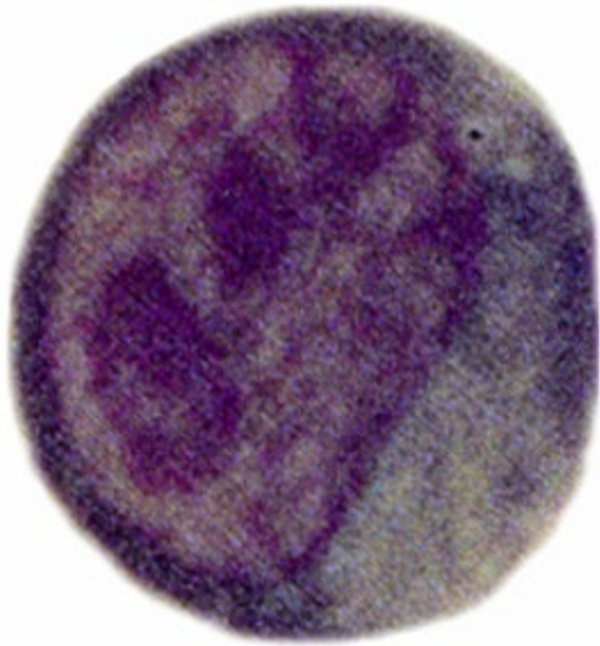
Apoptosis





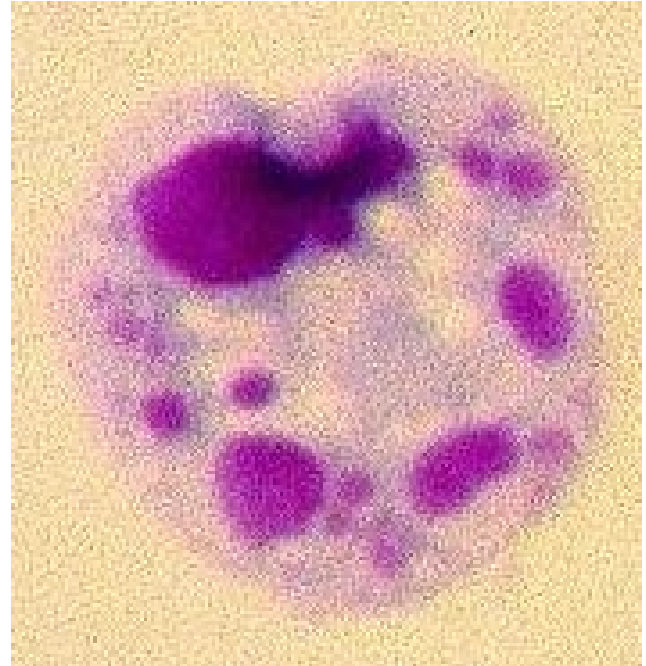
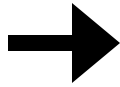
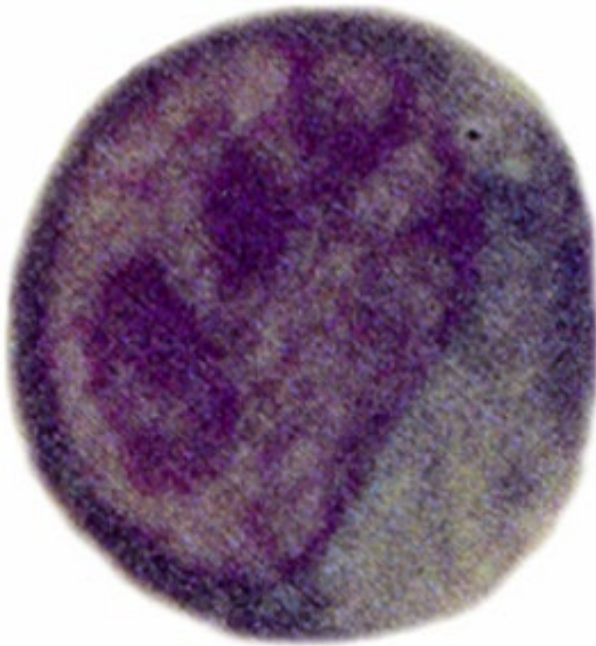
Apoptosis

A- Membrane Blebbing

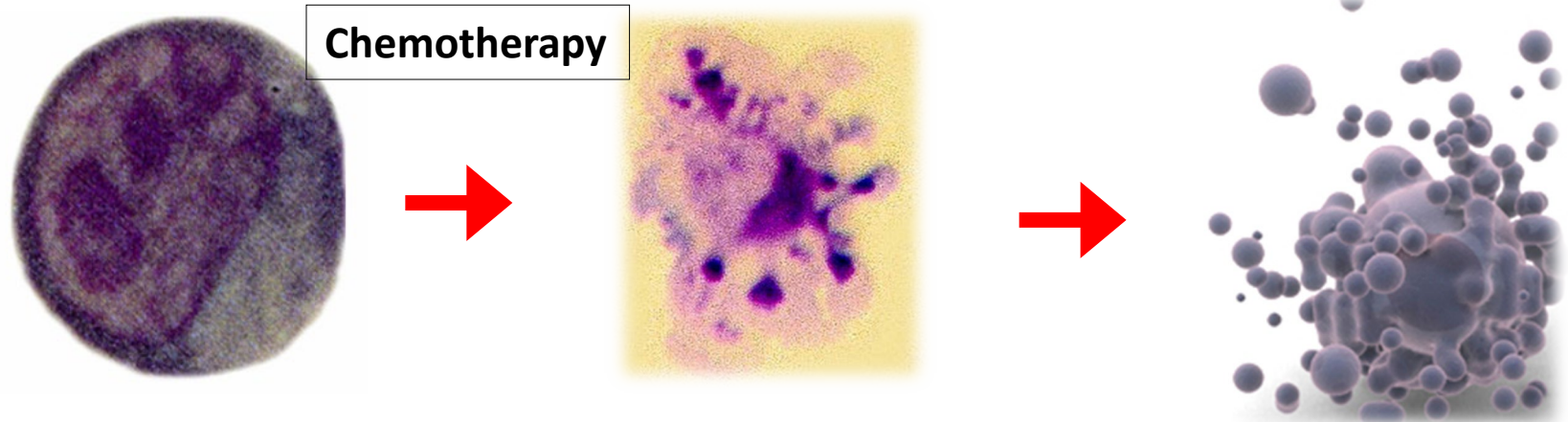


Apoptosis

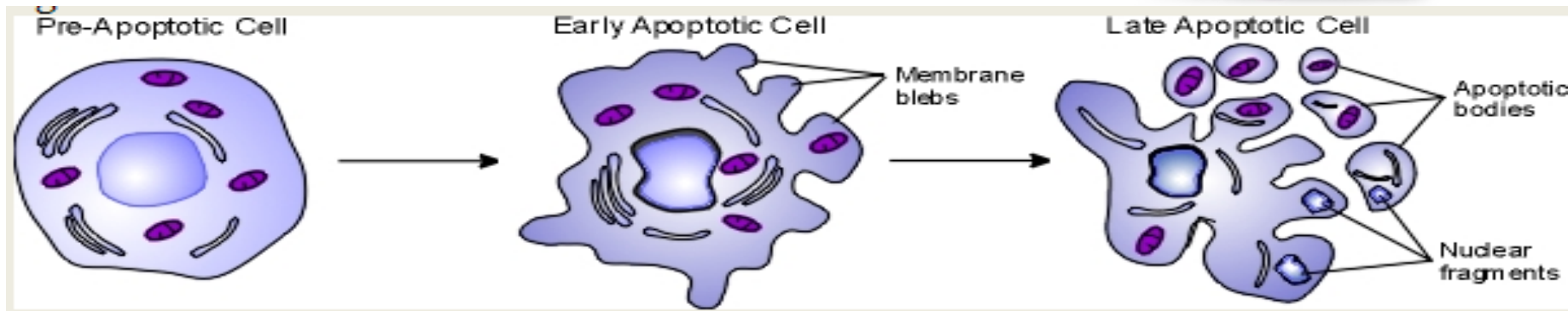
B- Nuclear Fragmentation

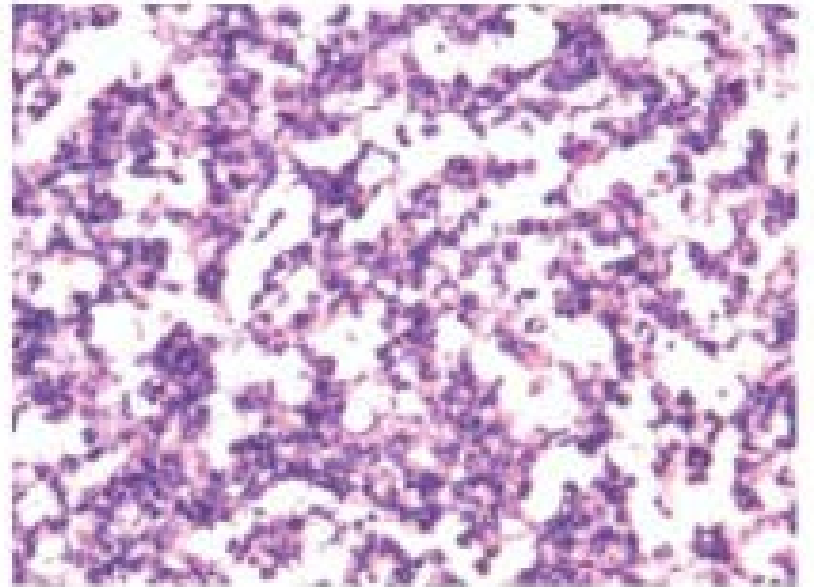
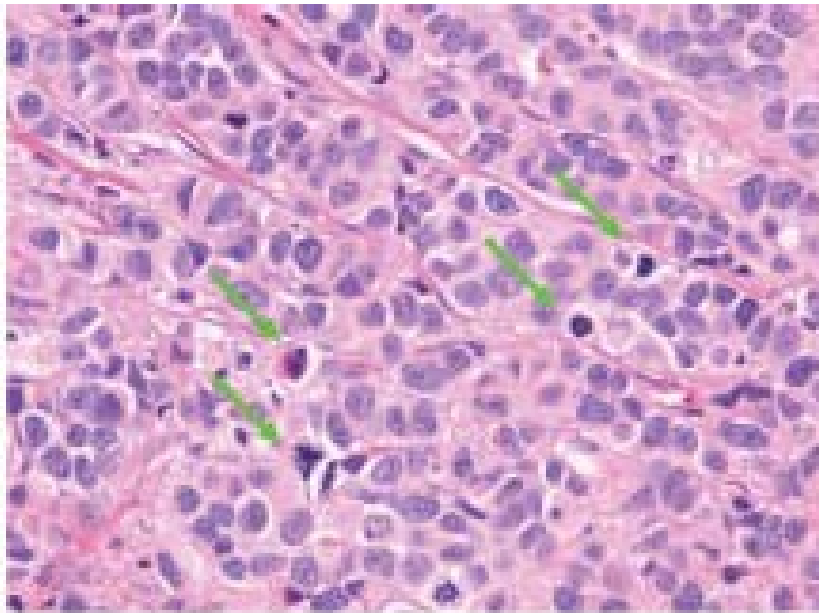


Chemotherapy kills cancer cells



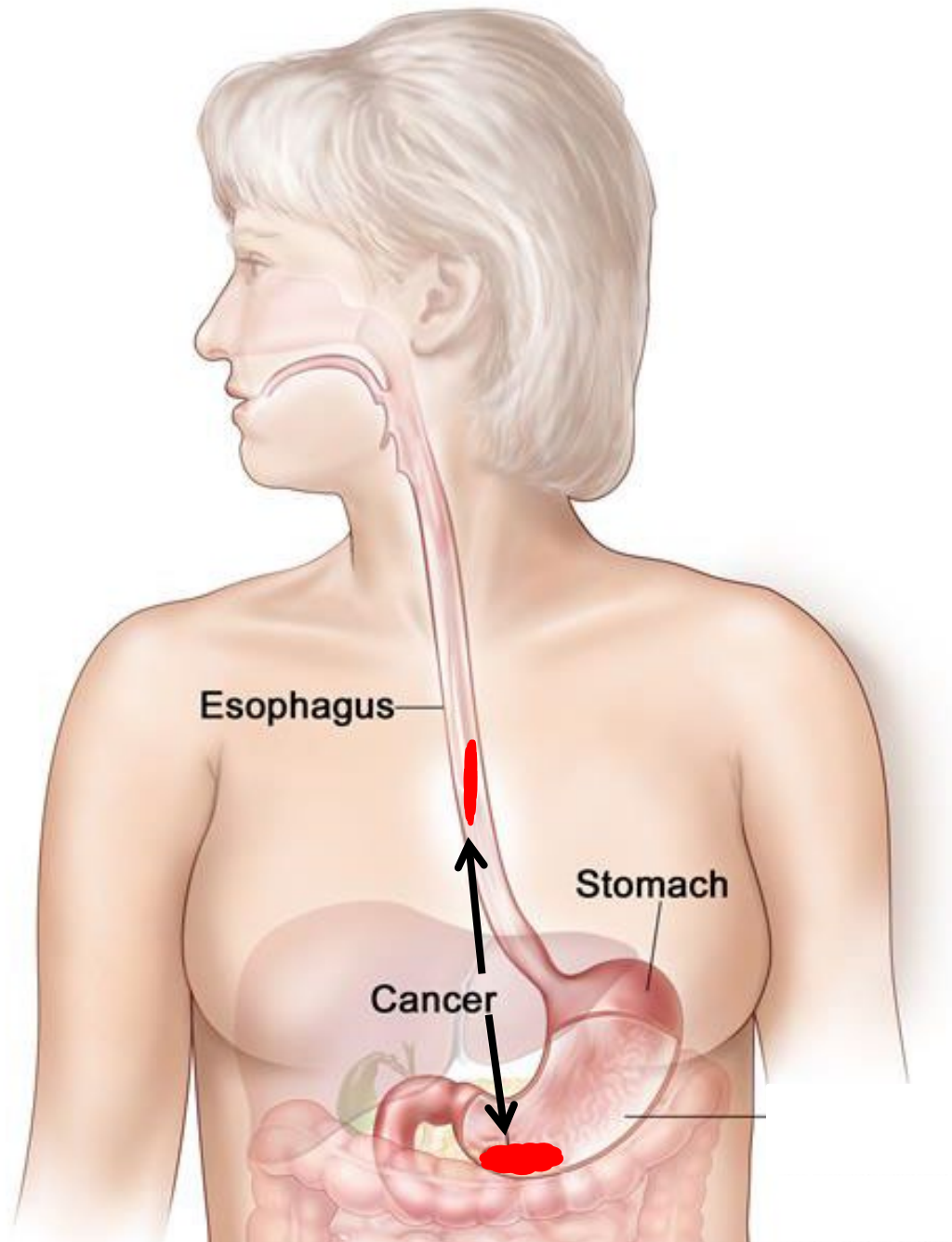
Chemotherapy





2.

**Antioxidant
Potential**



Esophagus

Stomach

Cancer



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



Research Paper

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

Mamdooh H. Ghoneum^{1✉}, Nariman K. Badr El-Din², Salma M. Abdel Fattah³, Deyu Pan⁴, and Lucilene Tolentino⁵

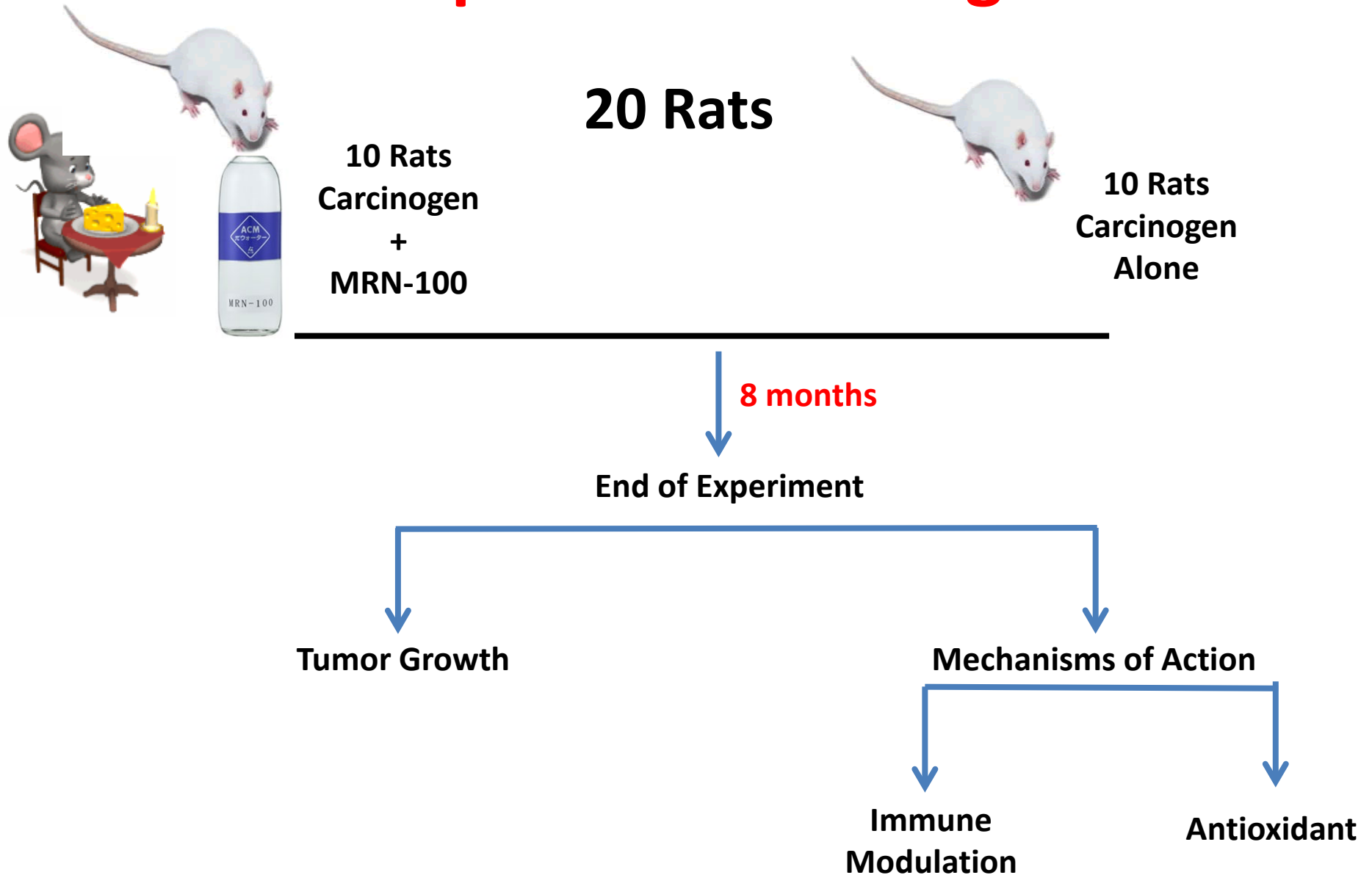
1. Department of Otolaryngology, Charles Drew University of Medicine and Science, 1731 E. 120th Street, Los Angeles, CA 90059, USA.
2. Department of Zoology, Faculty of Science, University of Mansoura, Mansoura 35516, Egypt.
3. Drug and Radiation Research Department, National Center for Radiation and Research Technology, P.O. Box 29 Nasr City, Cairo, Egypt.
4. Department of Internal Medicine, Charles Drew University of Medicine and Science, 1731 E. 120th Street, Los Angeles, CA 90059, USA.
5. Department of Pathology, Charles Drew University of Medicine and Science, 1731 E. 120th Street, Los Angeles, CA 90059, USA.

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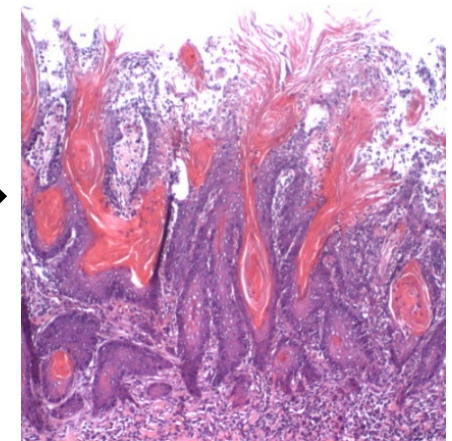
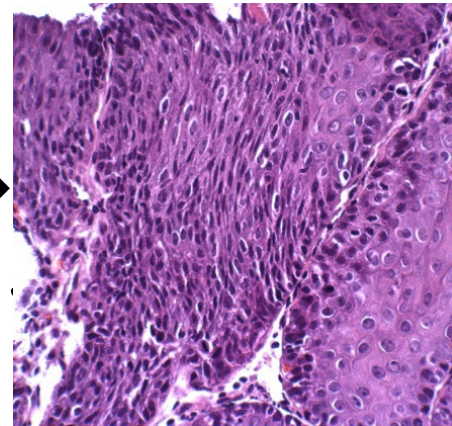
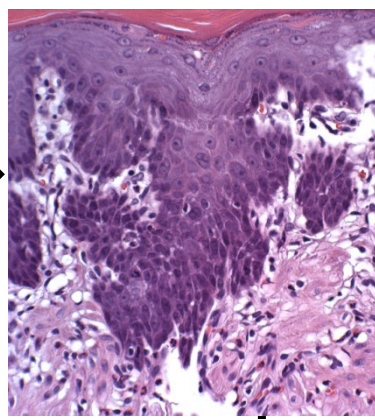
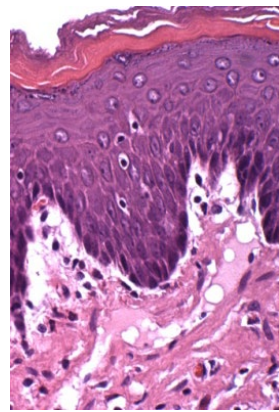
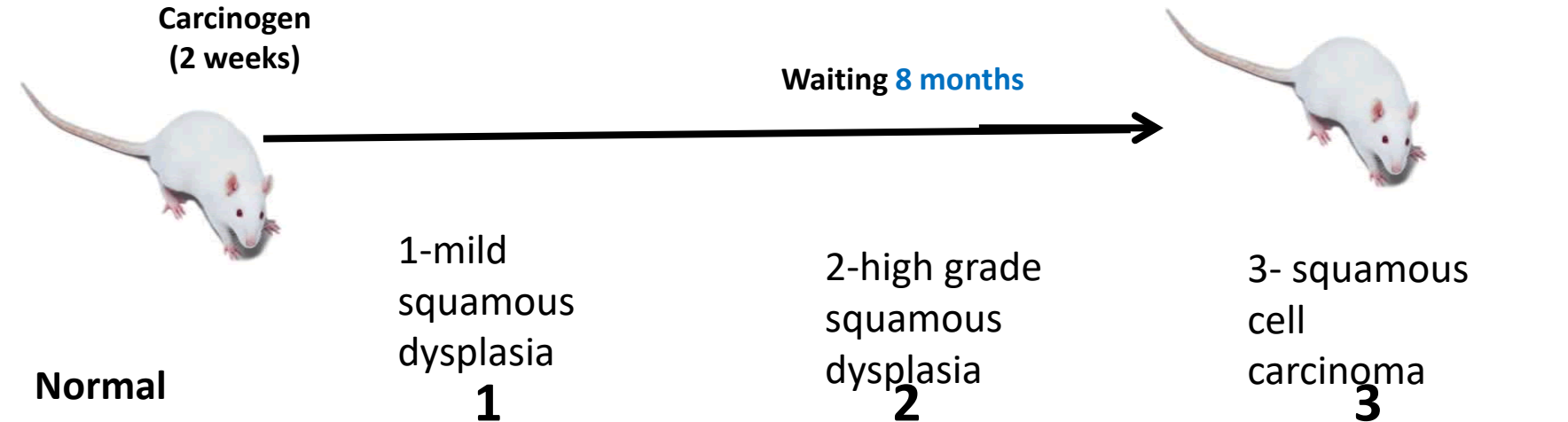
Experimental Design





Experimental Design for Esophageal Cancer

Control Group



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

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

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

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



Carcinogen MNNG (N-methyl-N'-nitro-N-nitrosoguanidine) 200 mg/kg daily

Sodium Chloride 1mL/rat every 3 days

Experimental Design

Control Group

Carcinogen
(2 weeks)



Waiting
8 months



10 rats

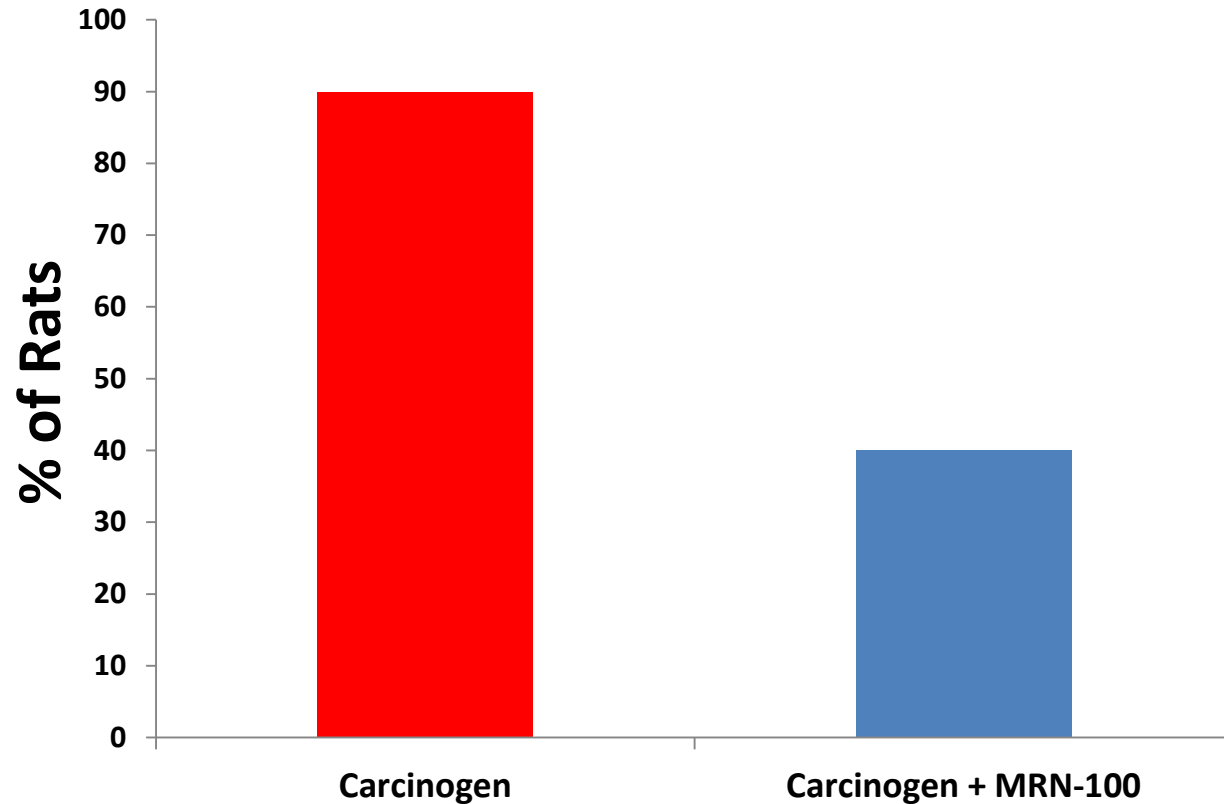
Waiting
8 months

MRN-100 Group



Carcinogen MNNG (N-methyl-N'-nitro-N-nitrosoguanidine) 200 mg/kg daily

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

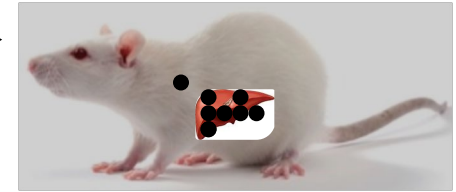


Experimental Design for gastric cancer

Control Group



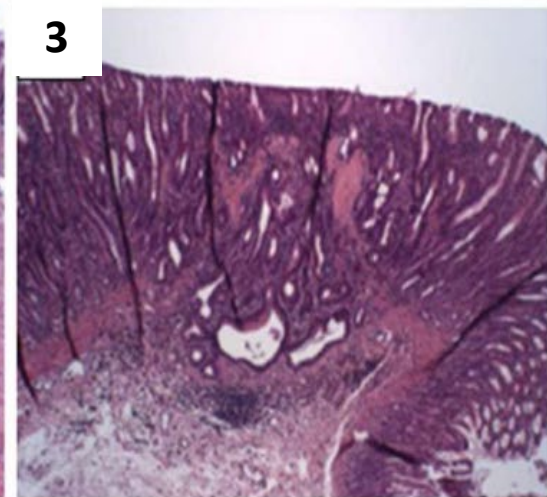
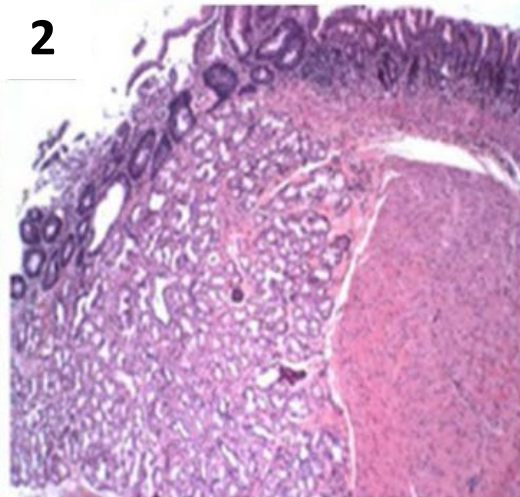
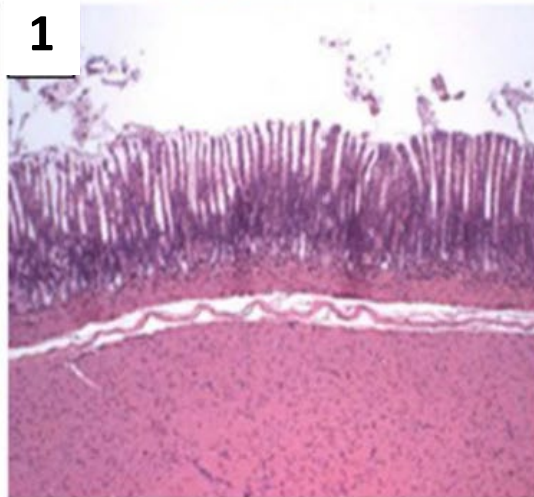
Waiting
8 months



Normal

Mild squamous
dysplasia

High grade squamous
dysplasia



Experimental Design

Control Group

Carcinogen
(2 weeks)



Waiting
8 months



10 rats

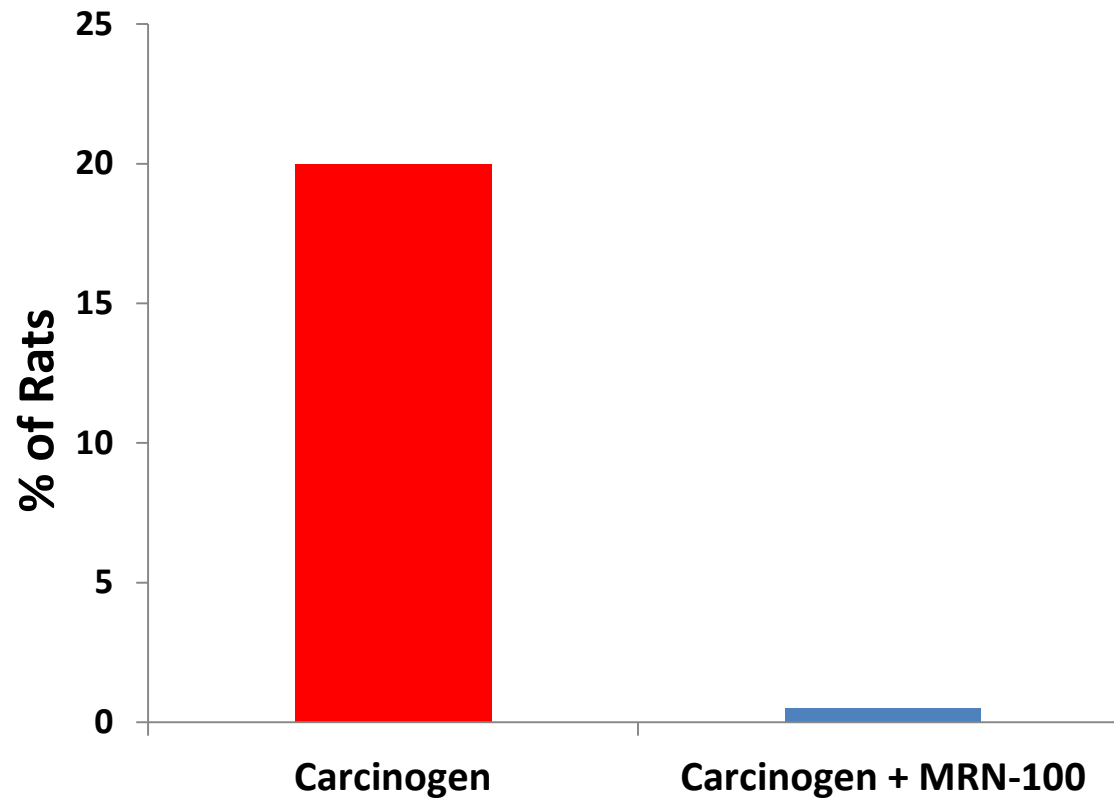
Waiting
8 months

MRN-100 Group

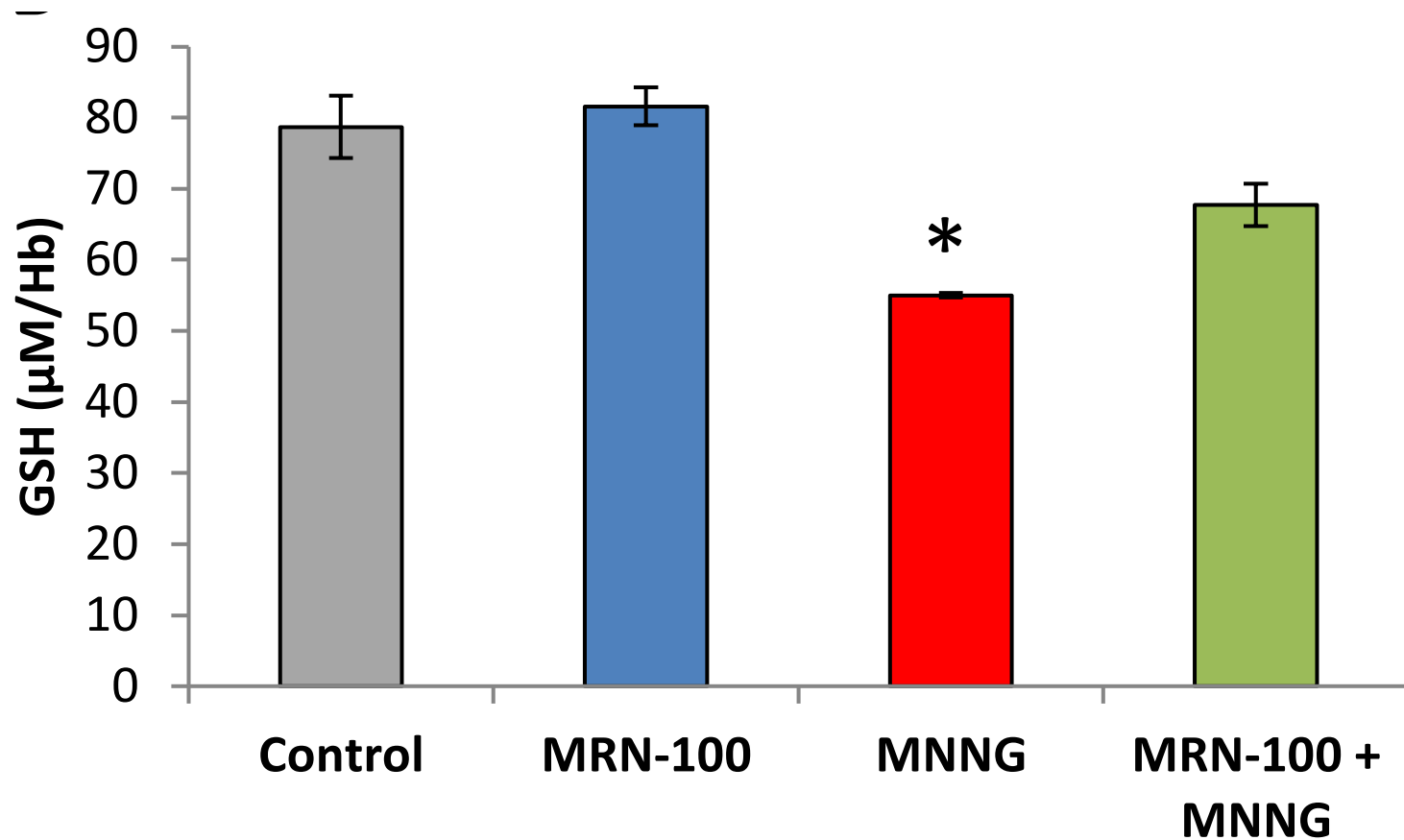


Carcinogen MNNG (N-methyl-N'-nitro-N-nitrosoguanidine) 200 mg/kg daily

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

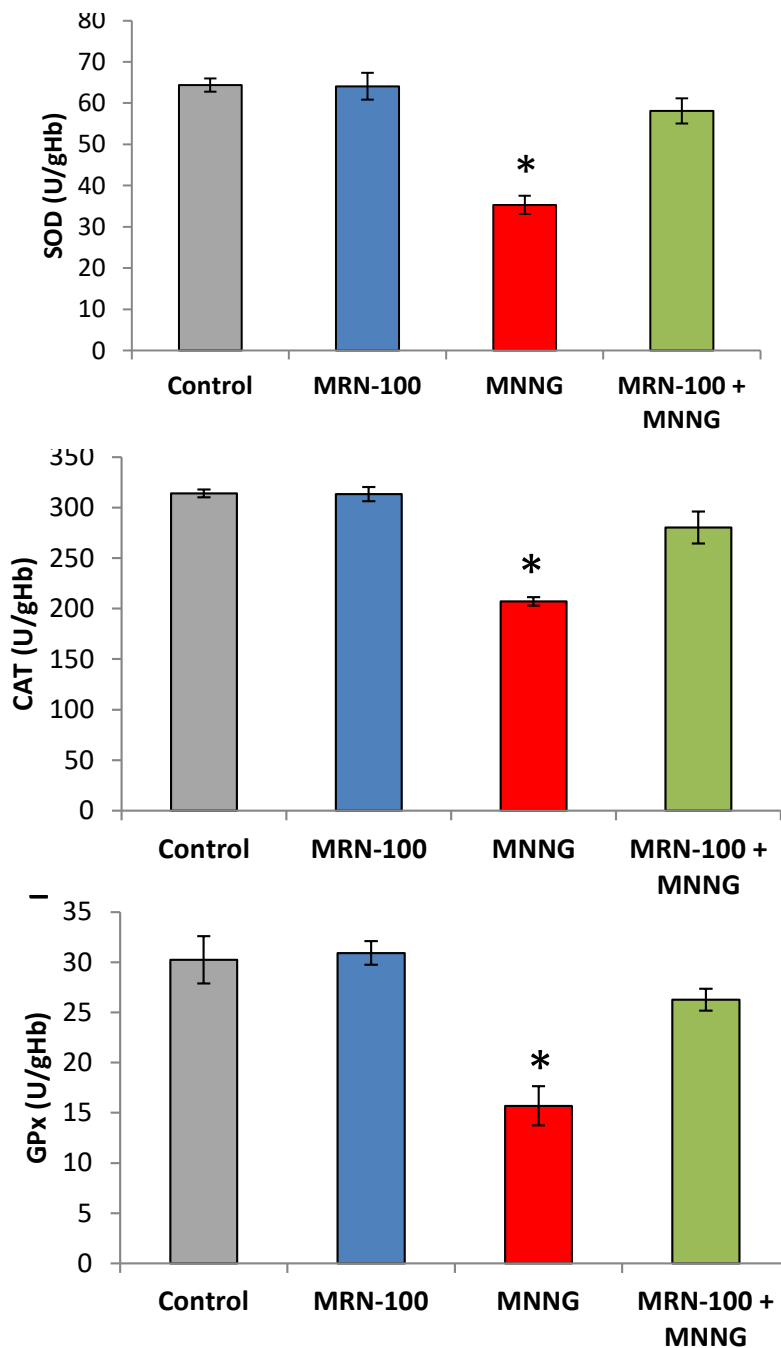


1- MRN-100 increase the level of glutathione (GSH), (ROS quencher/ Free radical scavenger)

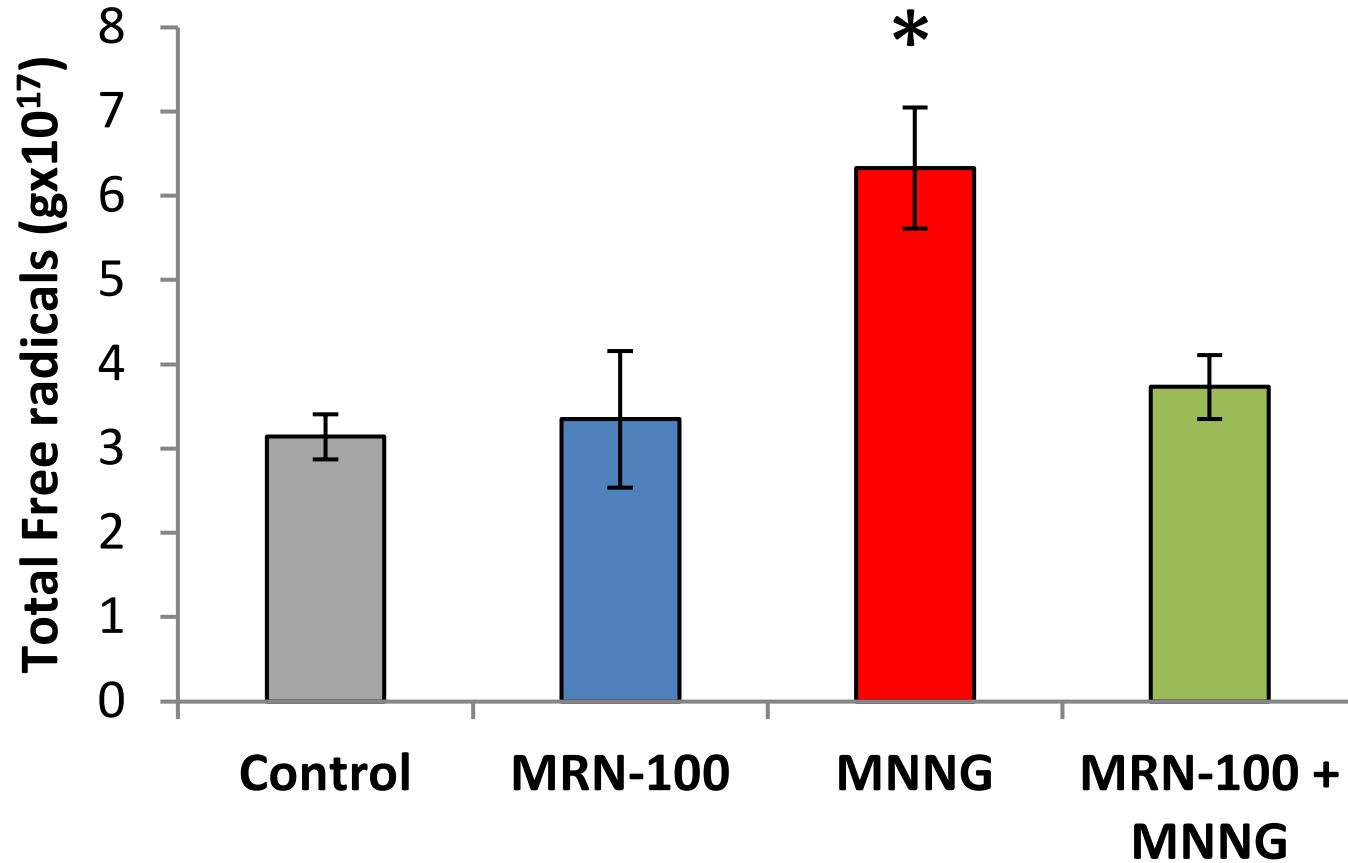




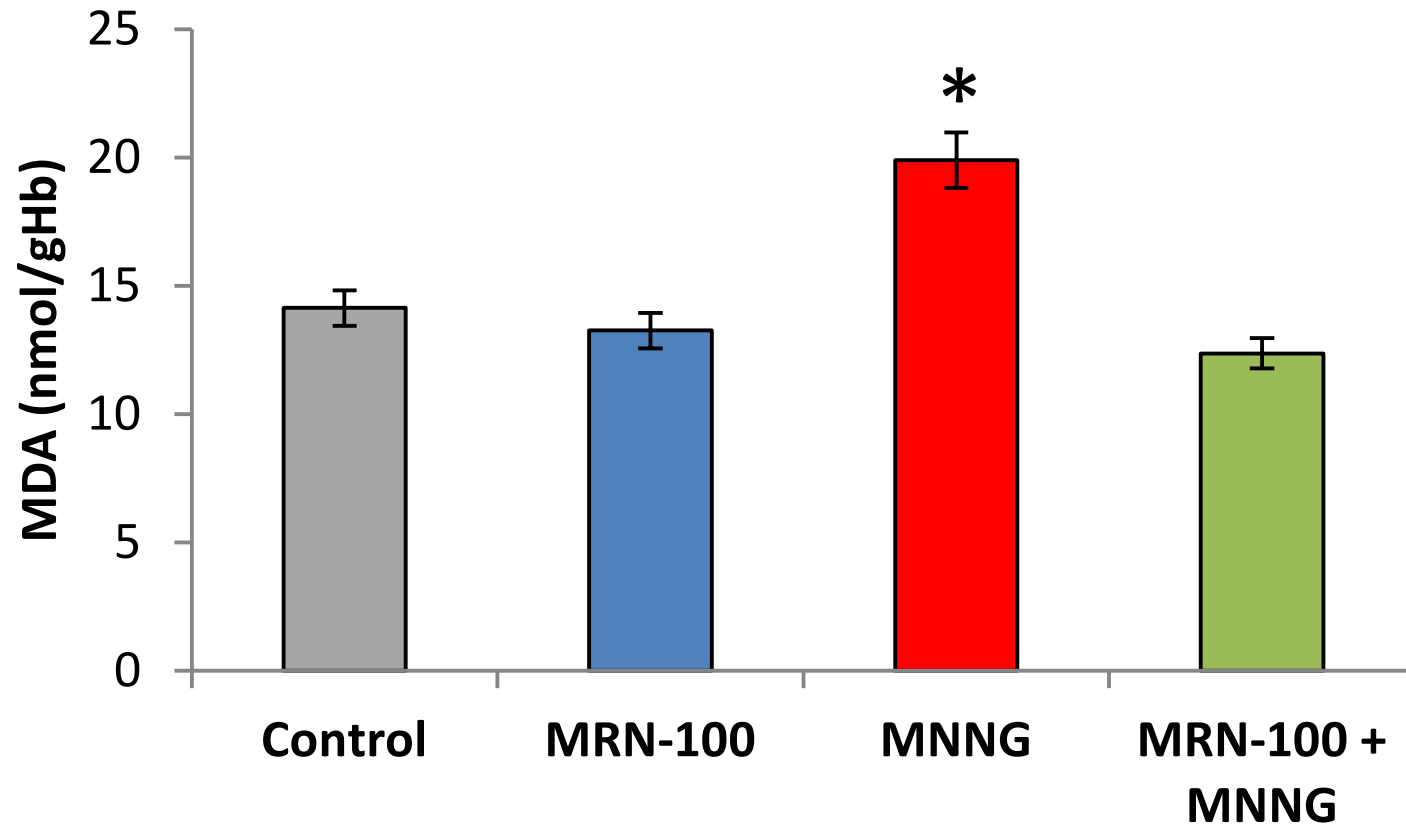
2- MRN-100 increases the levels of antioxidant enzymes SOD, CAT and GPx



3- MRN-100 prevents free radical formation



4- MRN-100 modulates lipid peroxidation (lipid peroxidation biomarker MDA)



3.

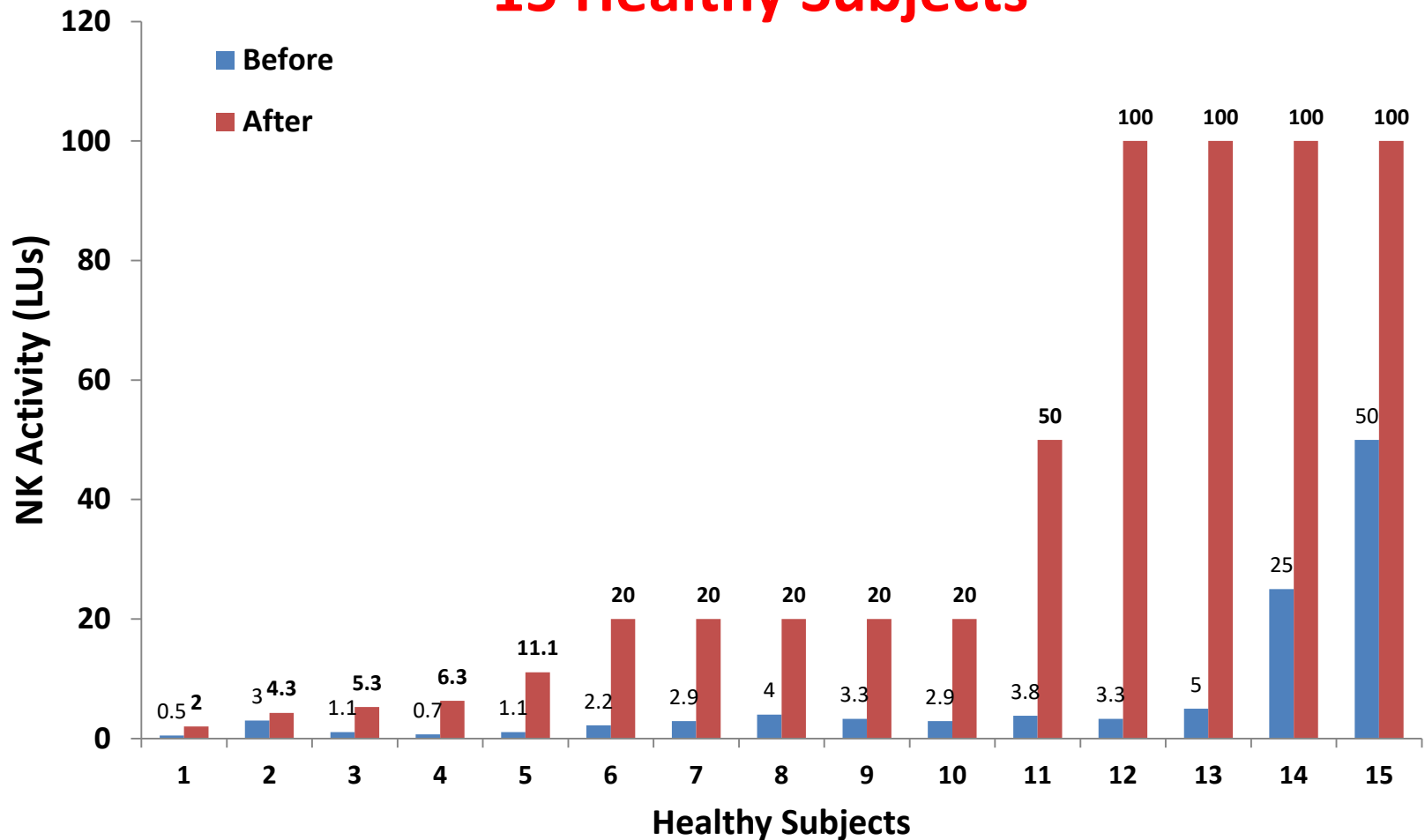
**Immune
Modulation**



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

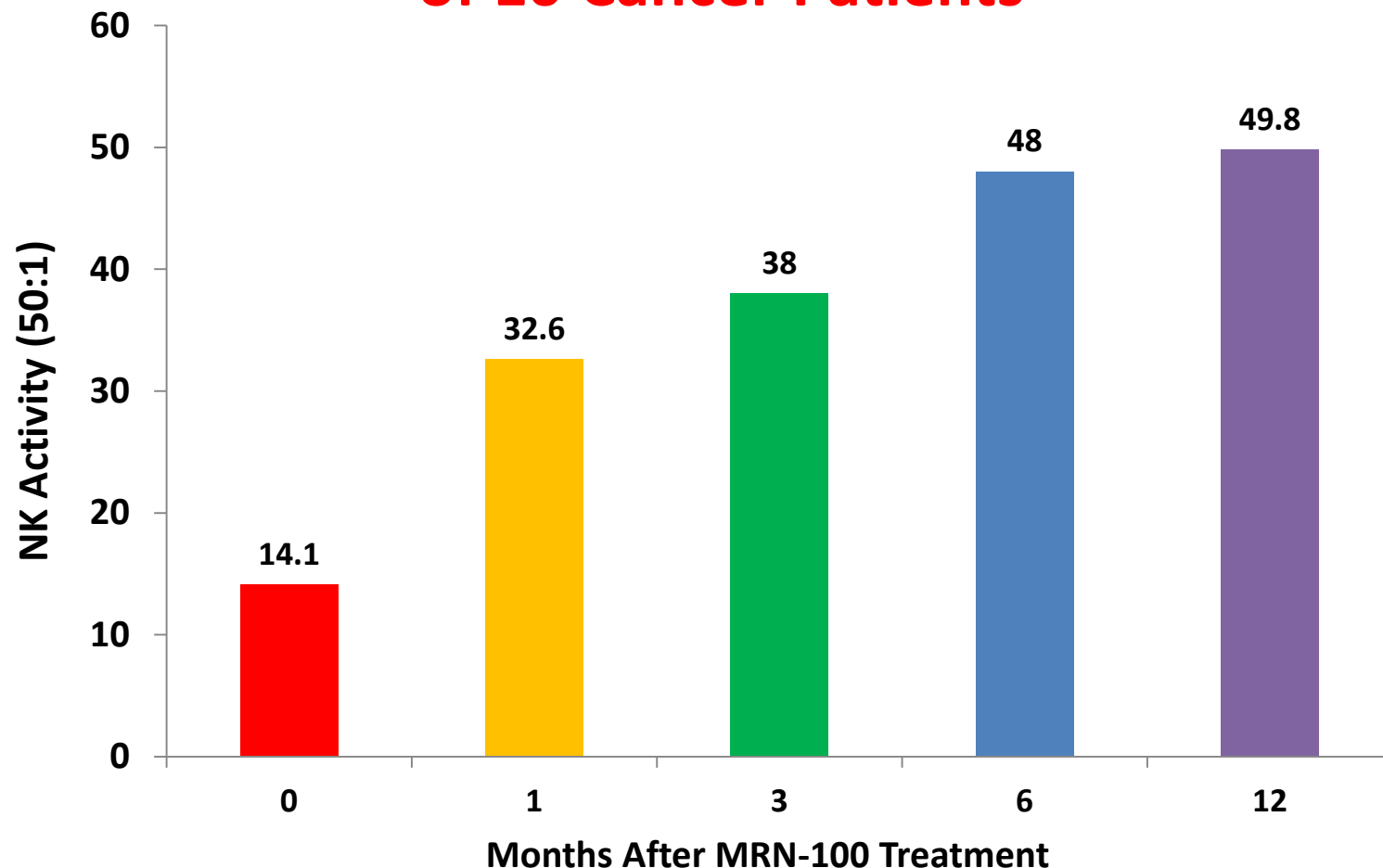
***NK Cells represent the first line of defense
against cancer.***

MRN-100 Enhances NK Cell Activity in 15 Healthy Subjects



- MNC from 15 healthy subjects
- NK cytotoxicity was measured by ^{51}Cr -release assay
- Annual Conference of Clinical Immunology , New Orleans, LA, May 31-June 3, 1996

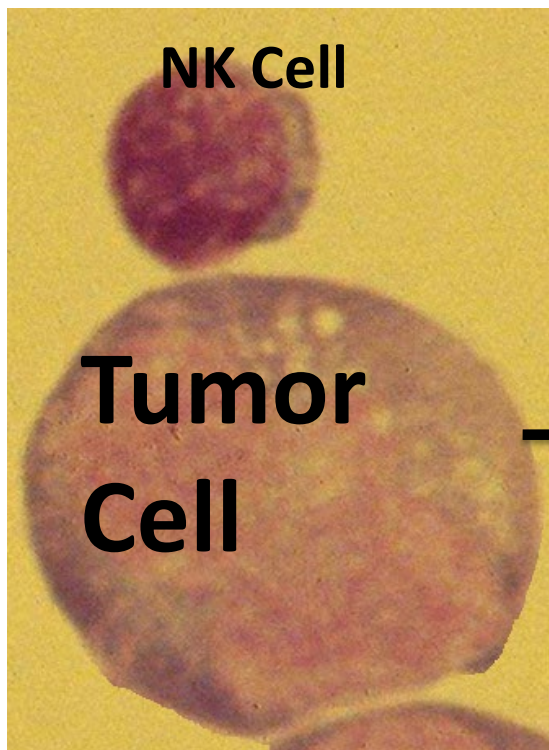
MRN-100 Enhances NK Cell Activity of 10 Cancer Patients



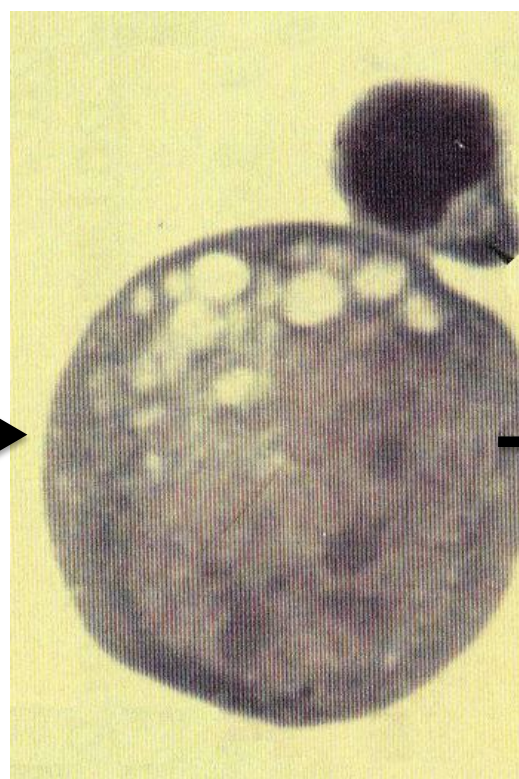
- MNC from 10 subjects with different malignancies
- NK cytotoxicity was measured by ^{51}Cr -release assay
- 4th International Symposium on Predictive Oncology and Therapy, Nice, France Oct 24-27, 1998.

Dissecting the pathway of NK cell killing the cancer cell

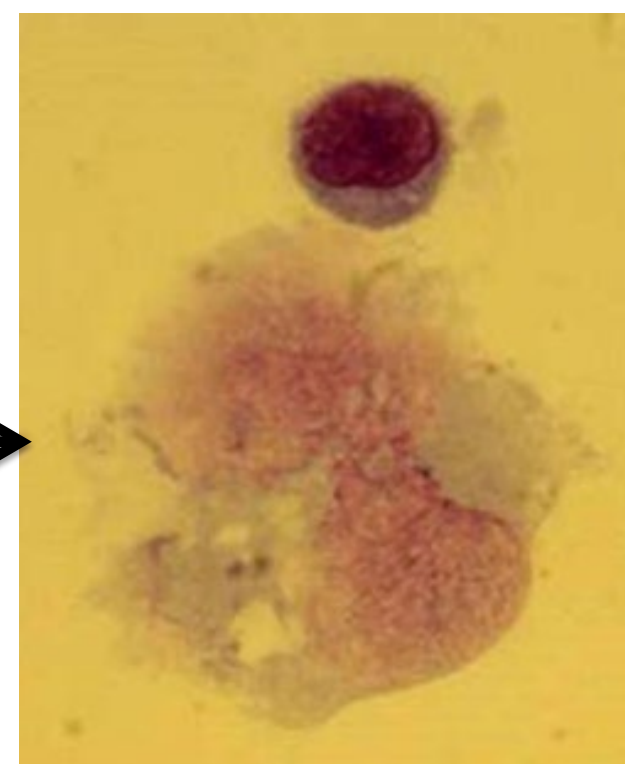
1. NK cell binds to cancer cell



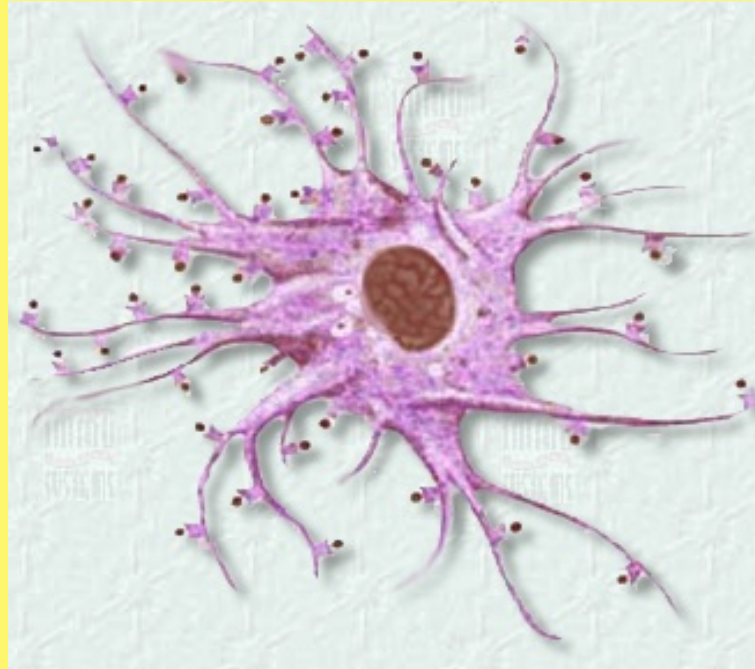
2. NK cell induces holes in cancer cell



3. Cancer cell is dead



MRN-100 activates Dendritic Cells (DC)



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](#).

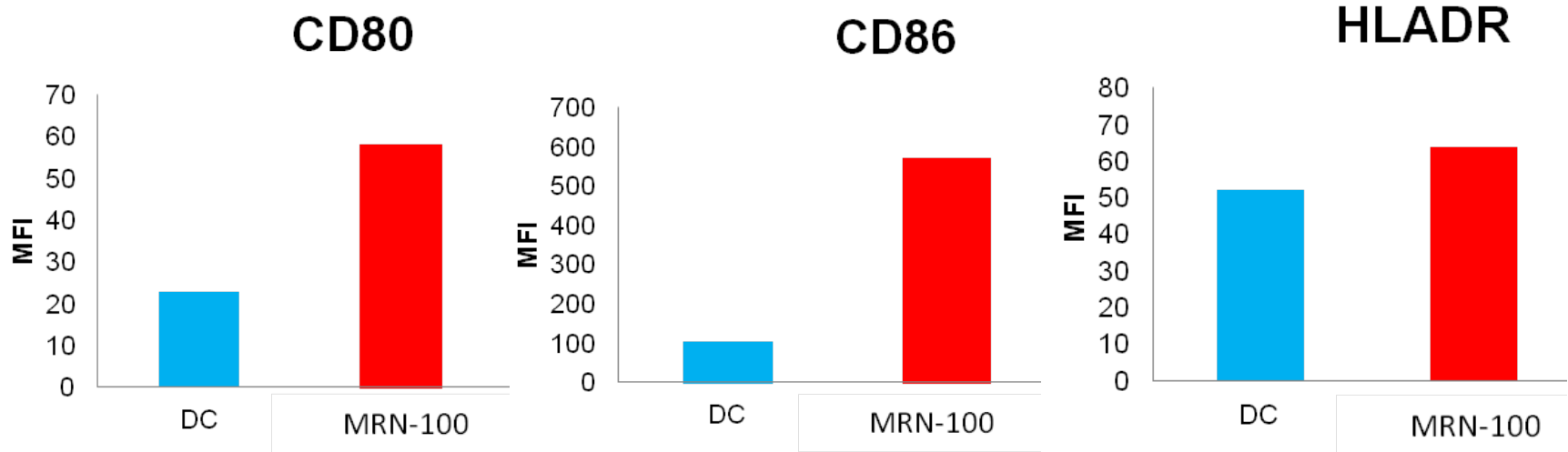
They act as messengers between the innate and adaptive immunity.

MRN-100

**as a DC Activator
via**

**Increased Expression of Co-
Stimulatory Molecules**

MRN-activated Dendritic Cells Up-regulate Co-stimulatory Markers and HLADR

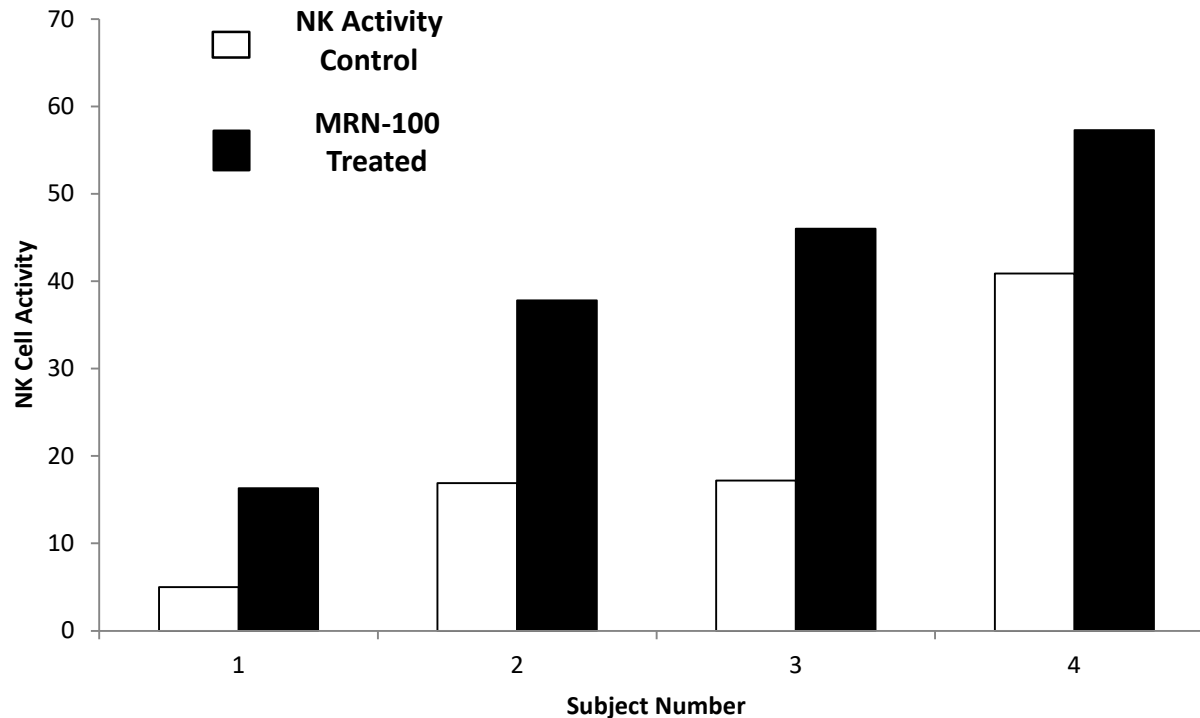




4.

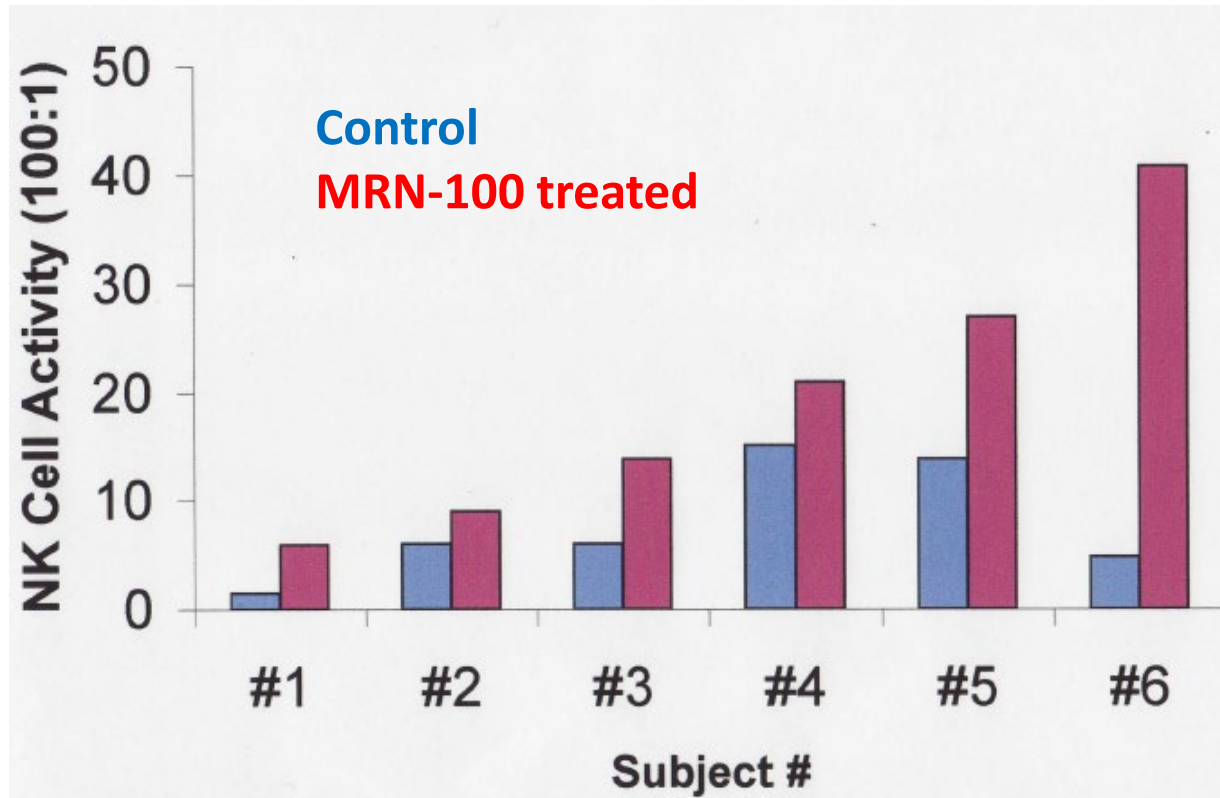
**MRN-100 increases
susceptibility of
cancer cells to NK
cells**

MRN-100 increases human head & neck carcinoma Calu-27 sensitivity to human NK cell cytotoxicity in vitro*



- MNC from 4 healthy subjects
- NK cytotoxicity was measured by ^{51}Cr -release assay at E:T ratio 100:1
- 4th 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 Squamous Cell Carcinoma of the Skin (SCC) sensitivity to human NK cell cytotoxicity



MNC from 6 Healthy subjects/patients with different types of malignancies

NK cytotoxicity was measured by ^{51}Cr -release assay at E:T ratio 100:1

*Data presented at the 4th International Symposium on Predictive Oncology and Therapy. Nice, France, October 24-27, 1998.

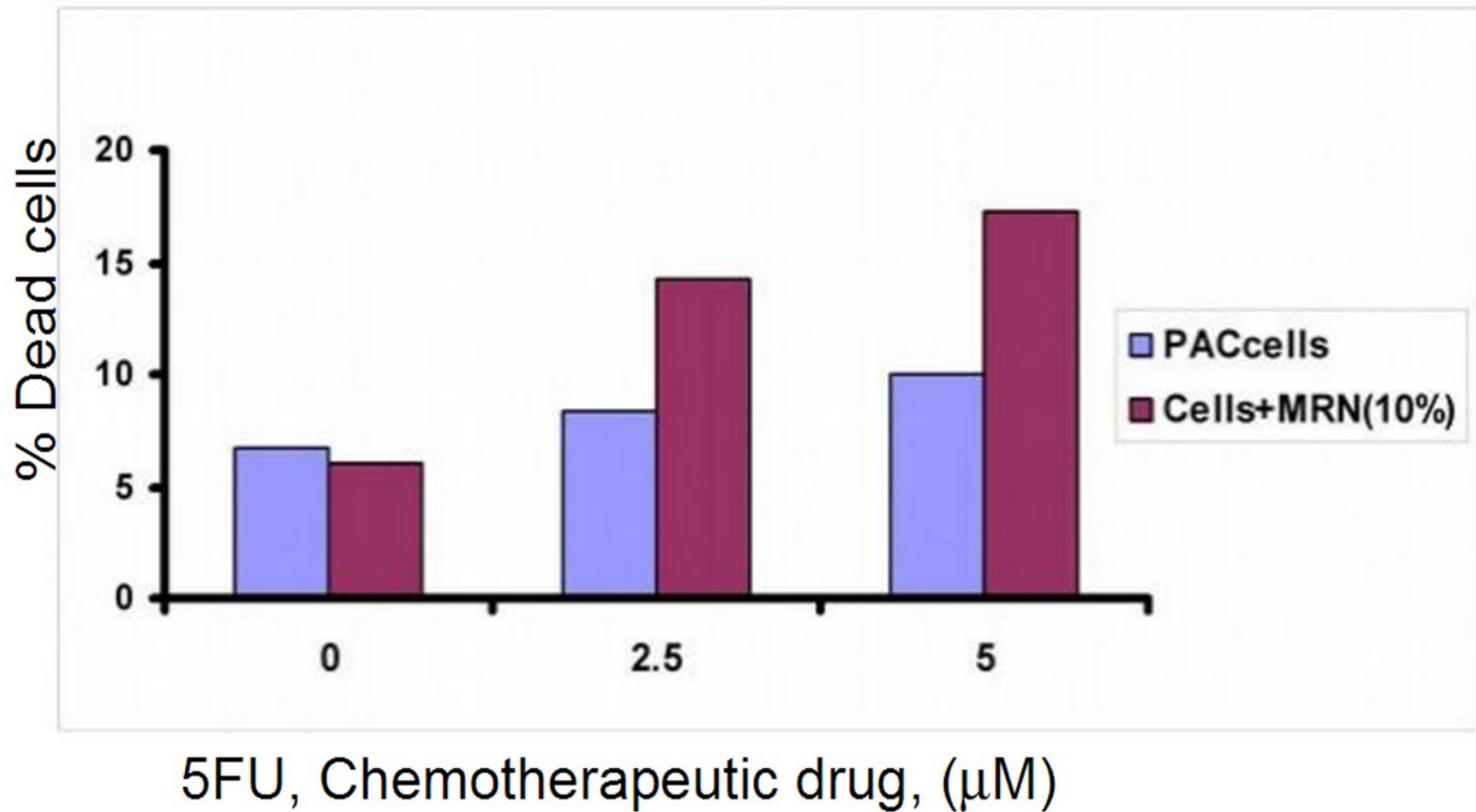


5.

**MRN-100 increases
susceptibility of
Pancreatic cancer cells to
Chemotherapy.**

MRN-100 increases susceptibility of cancer cells to Chemotherapy.

Pancreatic cancer





Conclusion

**1- Bedil Ai may be a useful agent for:
improving eye vision and astigmatism**

2- MRN-100 Exerts Anti-Cancer Activity

Mechanisms of protection against cancer:

A) Apoptosis

B) Antioxidant Potential

C) Immunomodulatory Effect

D) Increases susceptibility of cancer cells to NK cells

E) Increases susceptibility of Pancreatic cancer cells to chemotherapy(5FU)

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. 4th 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. 4th 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 19th 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 γ -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 γ -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に関する論文および学会発表

- 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).
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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

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MEMBER OF COMMITTEES
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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
2nd District State Representative

Japanese Society of Complimentary and Alternative Medicine.

Japanese Immunology Society



感謝状

Mandook Choneum, Ph. D. 殿

あなたに 私立 東洋医学免疫研究会
の研究に際し 始終一貫誠意を以つ
て事にあたり多大な成果をおげ当会
の業種に参与して下さりまして、
本日はここに当会を代表し 深く感謝
の意を表します。

平成七年十一月十六日


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.
3RD SCIENTIFIC MEETING AND
2ND 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
3RD Scientific Meeting and 2ND 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.

CARMENCITA LO, M.D.
President

SUSAN LEE, M.D.
Chairman
Scientific Committee

NELSON LIM, M.D.
Secretary

TERESITA DY UY, M.D.
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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

29

32

36

gypt

Legend:
International boundary
National capital
Railway
Road
Scale: 1:100,000,000

