# Potential Clinical application of BPC157


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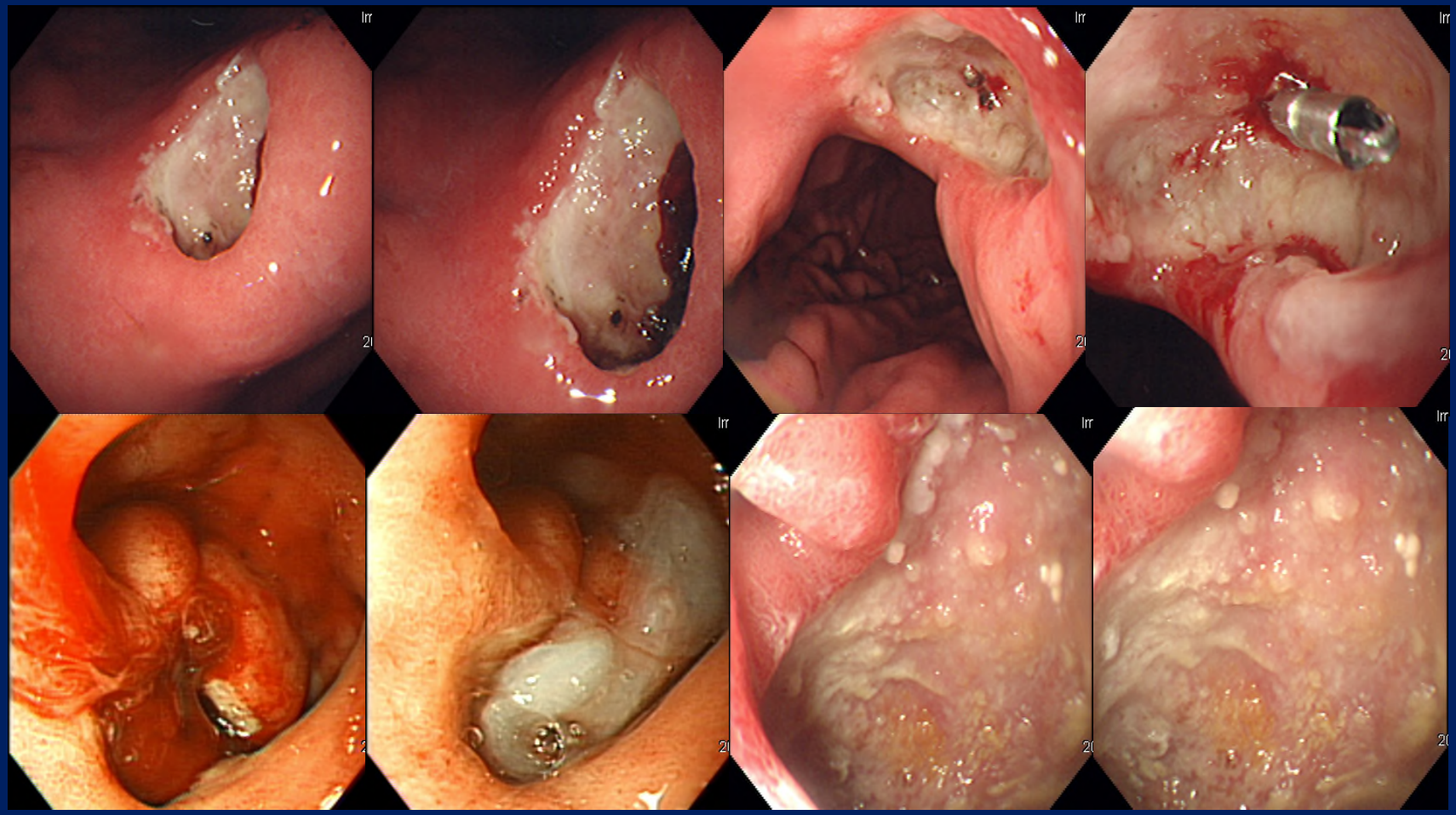
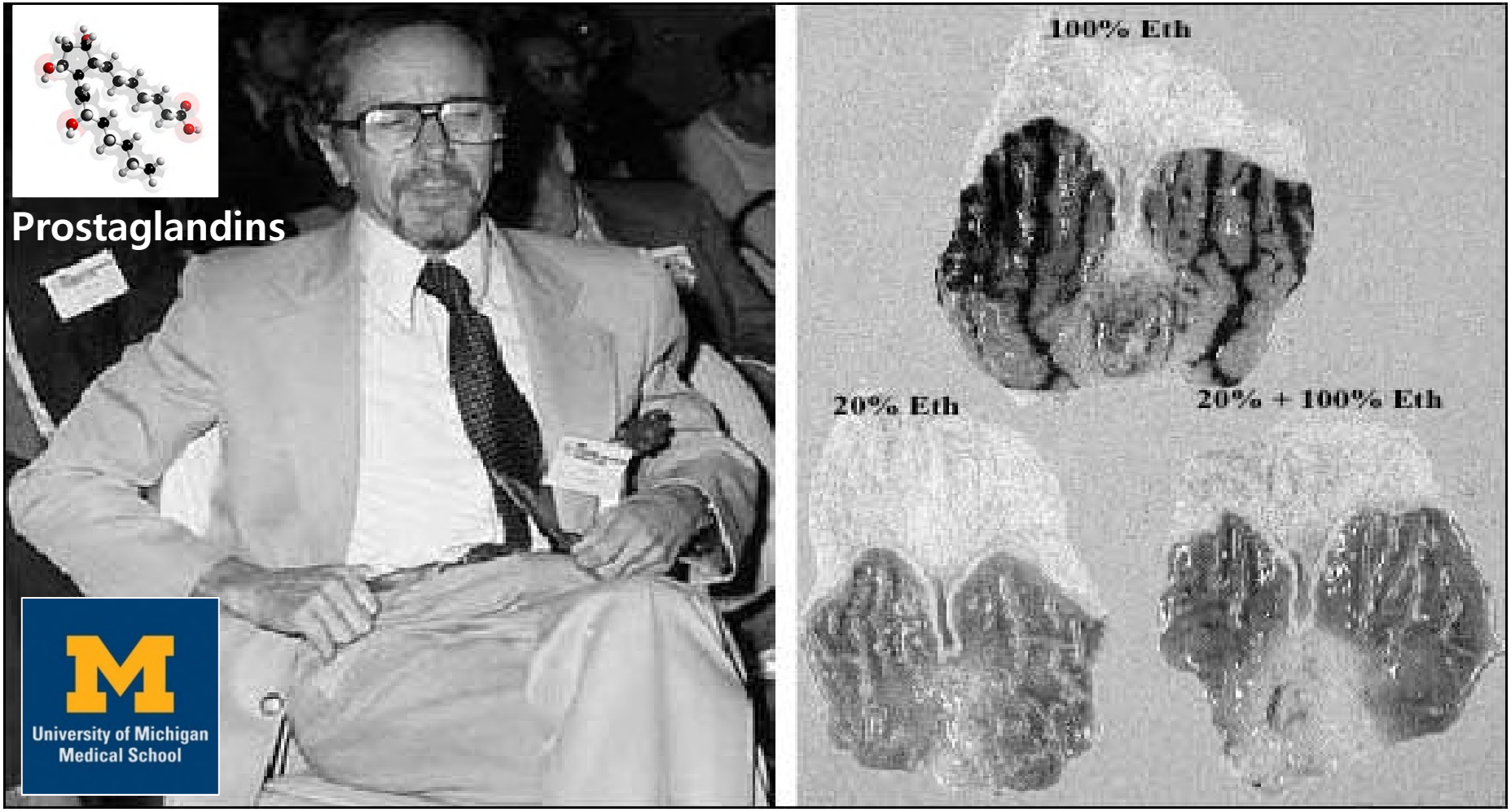
# In some patients, in spite of strict gastric acid control

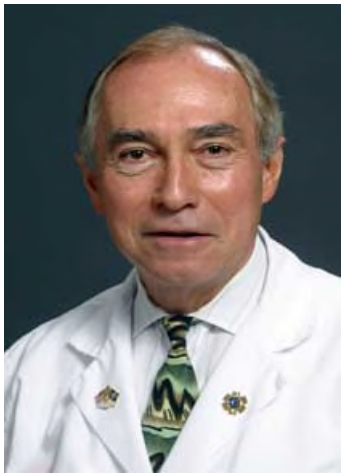
High relapse of PUD
Malignant transformation
Sustained symptoms



# *Cytoprotection/ Adaptive Cytoprotection* (prostaglandins)

*Andrea Robert (Univ. of Michigan, 1979)*



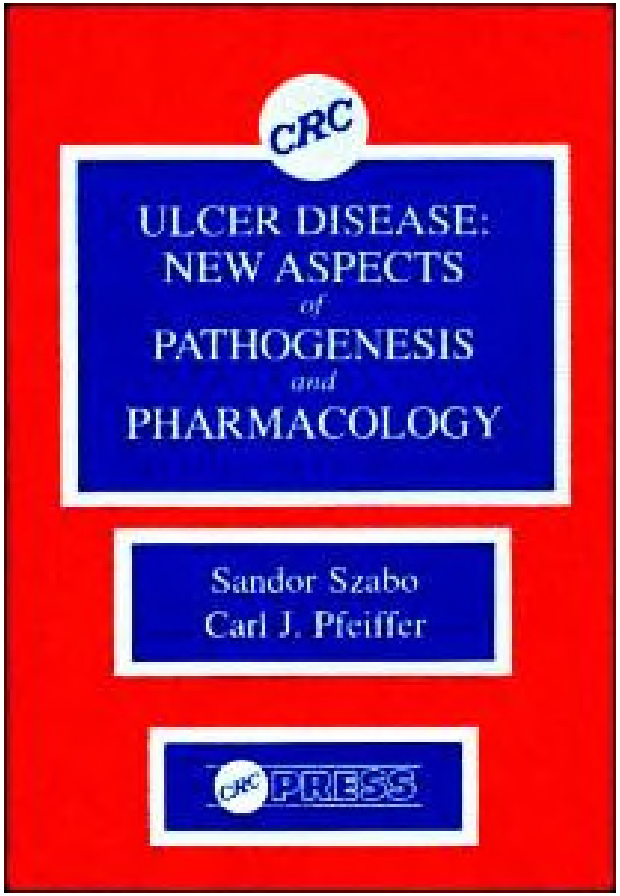


# Prof. Sandor Szabo

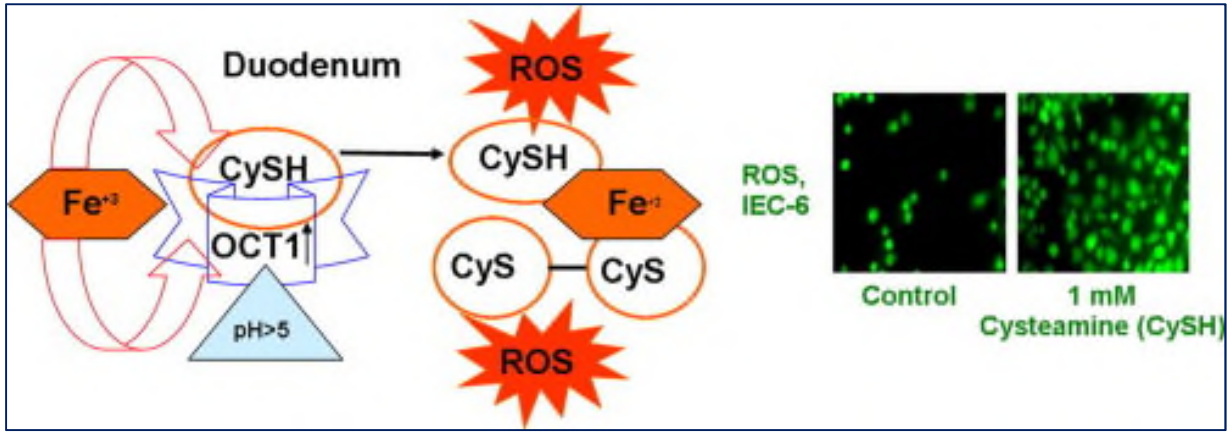
(UC Irvine) *Cytoprotection in early 1990*

***Sulfhydryl & endothelin***

President, GI Club/ICUR
IUPHAR GI Section




**Oxidative stress and Antioxidant system**



# *Enhancing gastric defenses,*

## Rebamipide (Mucosta)


## Sucralfate (Ulcermin)

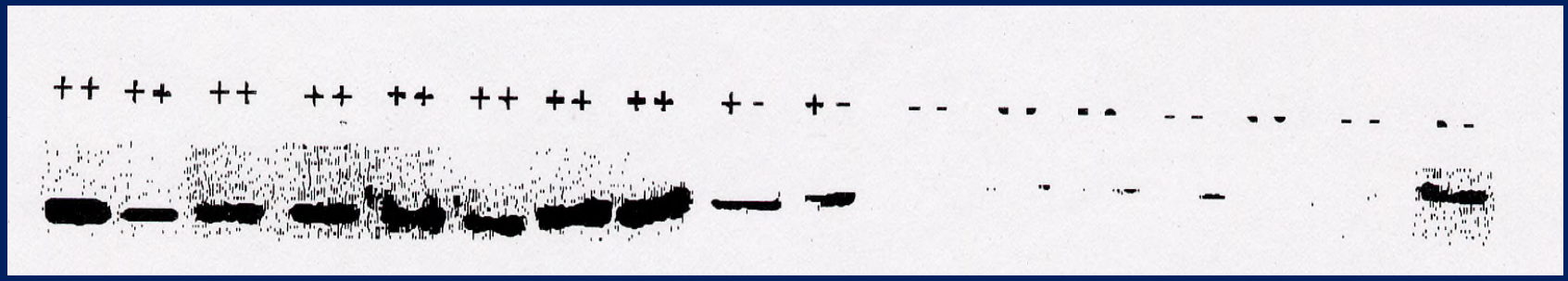

## Ecabet sodium (Gastrex)


## Teprenon (Selbex)


## Irsogladine maleate (Gaslon-N)


## Gliptide

# HSP 70 expression

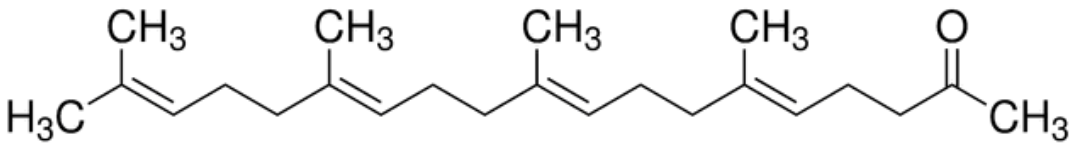



Well healed wounds  Poorly healed wounds

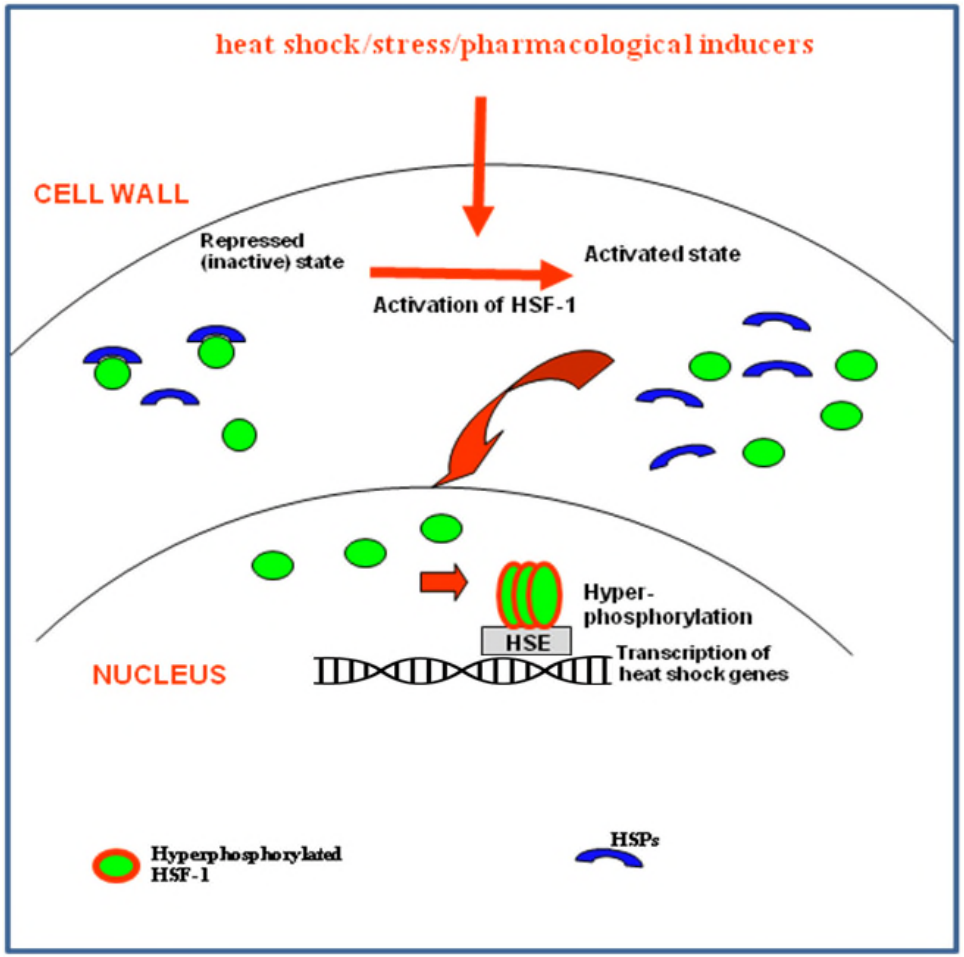
Differential expression of heat shock protein 70
in well healing and chronic human wound tissue

*Oberringer M et al, BBRC 214:1009, 1995*

# Geranylgeranylaceton (GGA, Teprenone, Selbex)

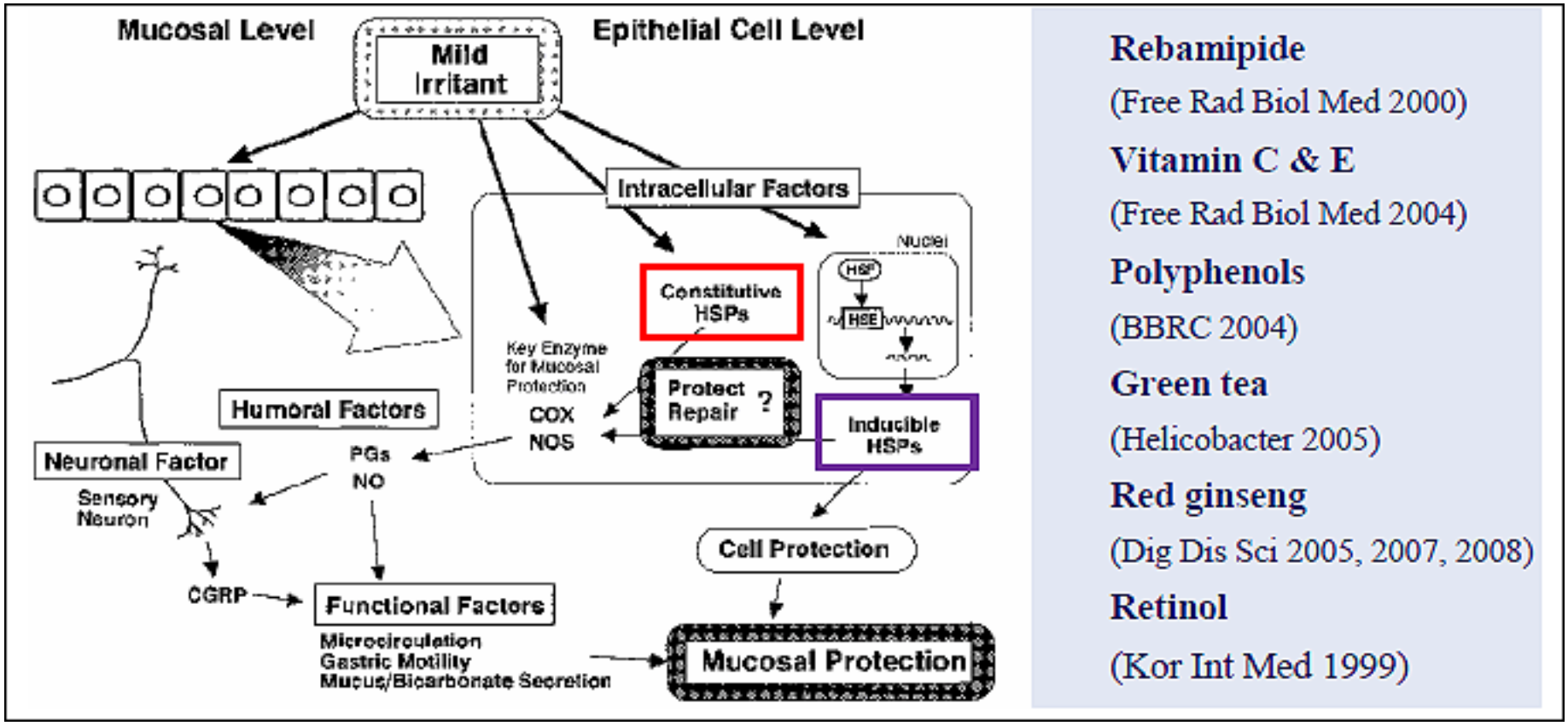

**Gastroprotective**
**HSP70 inducer**



# Molecular Chaperone for GI protection

Hahm KB *et al*, HSP70, HSP60, HSP27

## HSPs inducer for gastric protection

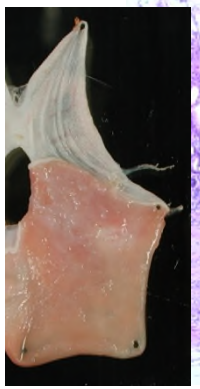


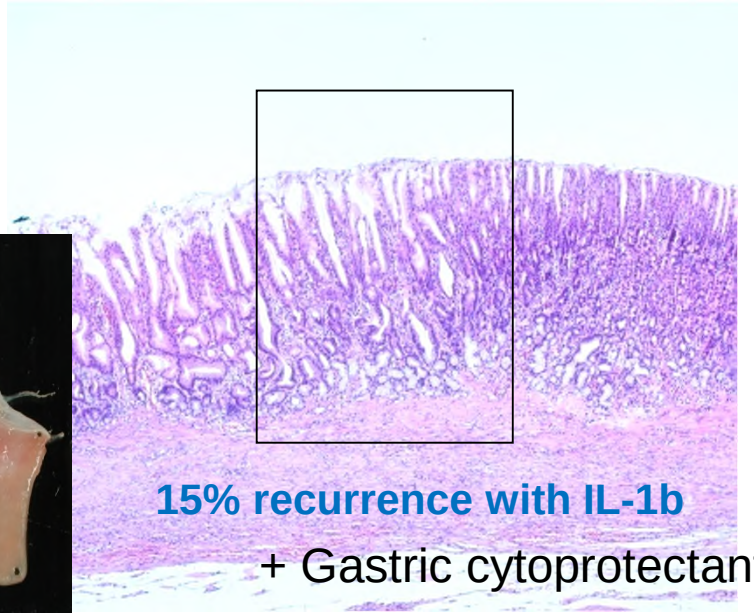

**Rebamipide**
(Free Rad Biol Med 2000)
**Vitamin C & E**
(Free Rad Biol Med 2004)
**Polyphenols**
(BBRC 2004)
**Green tea**
(Helicobacter 2005)
**Red ginseng**
(Dig Dis Sci 2005, 2007, 2008)
**Retinol**
(Kor Int Med 1999)

# Quality of ulcer healing

**Ulcers**

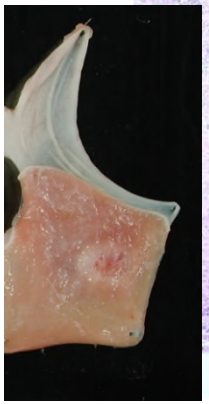
8 weeks

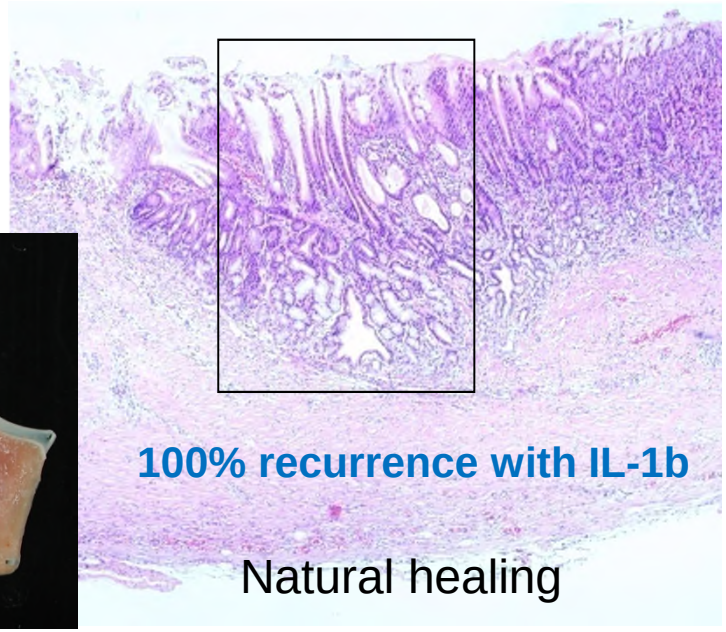




**15% recurrence with IL-1b**

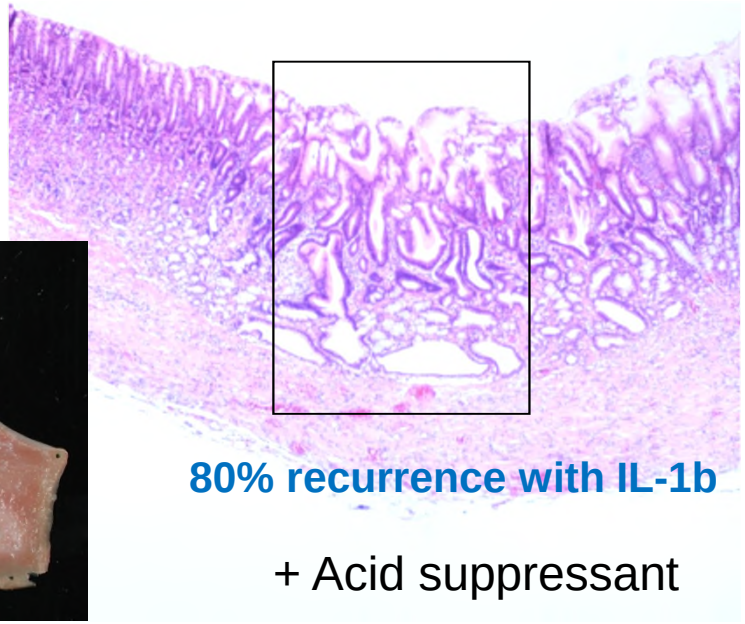
+ Gastric cytoprotectant





**100% recurrence with IL-1b**

Natural healing

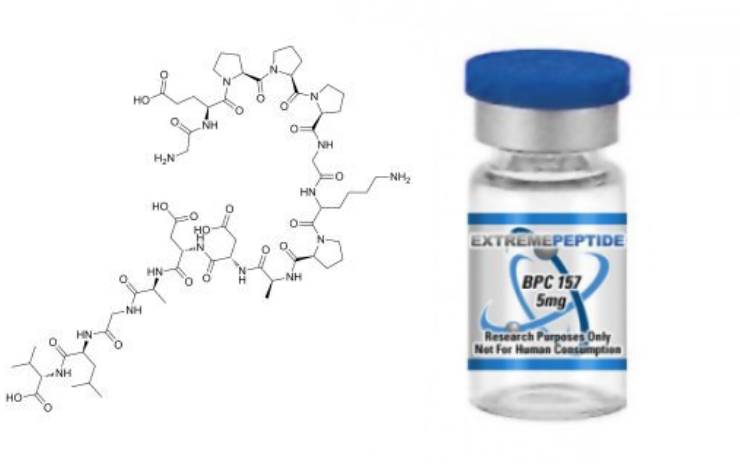


**80% recurrence with IL-1b**

+ Acid suppressant

Hahm KB et al, J Gastroenterol

# BPC157 as Potent GI Cytoprotectant




## What is BPC157?

**Body protection compound (BPC) 157** = Pentadecapeptide – comprised of a chain of 15 amino acids.
It can be isolated from gastric juices. It possesses a molecular mass of 1419.53552, and its molecular formula is $C_{62}H_{98}N_{16}O_{22}$.

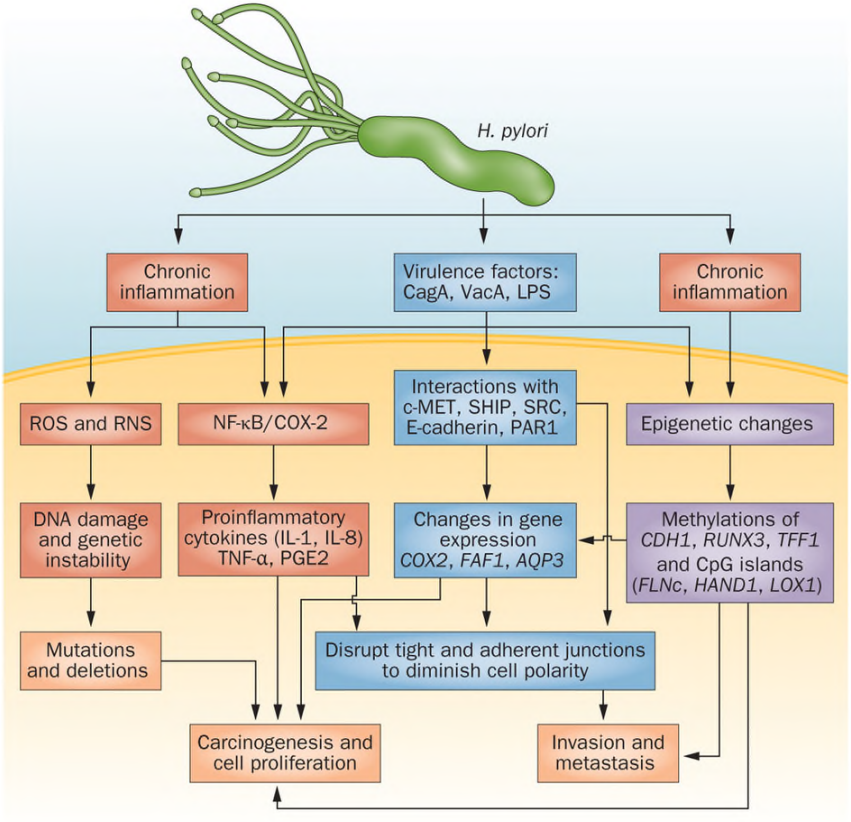
## Properties of BPC157

It has been determined that BPC 157 exhibits the capacity to regulated and control the manner in which the digestive tract can operated.

-Anti-ulcer
-Anti-inflammation
-Wound healing
-Angiogenic potential
-Free radical scavenger

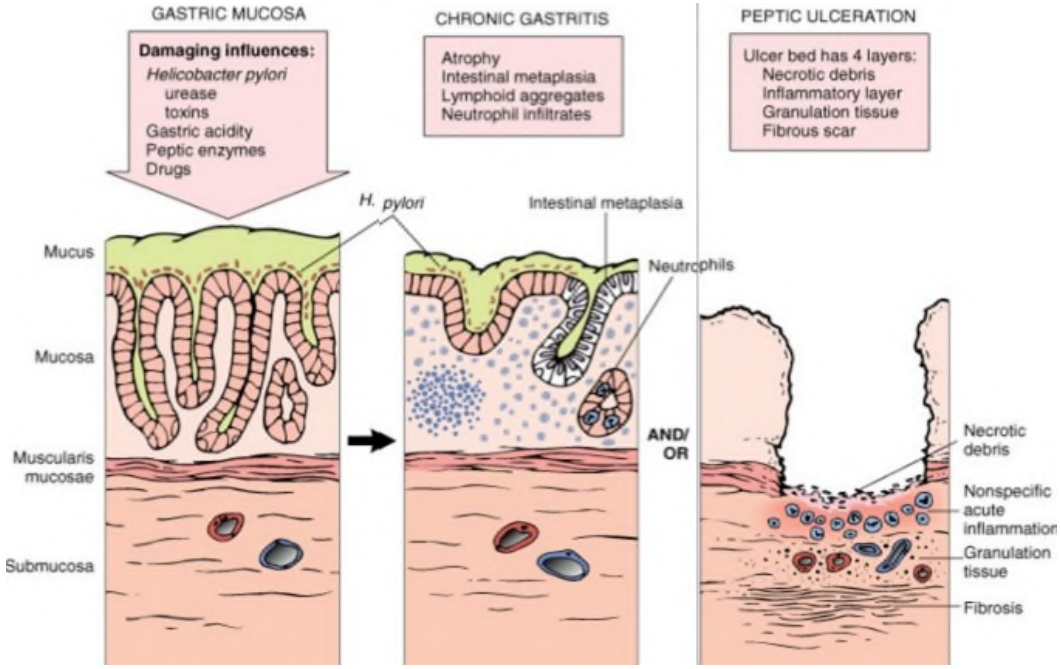
# BPC 157 as ‘”potent mucoprotectants”

## (collaboration with Prof. Predrag Sikiric)

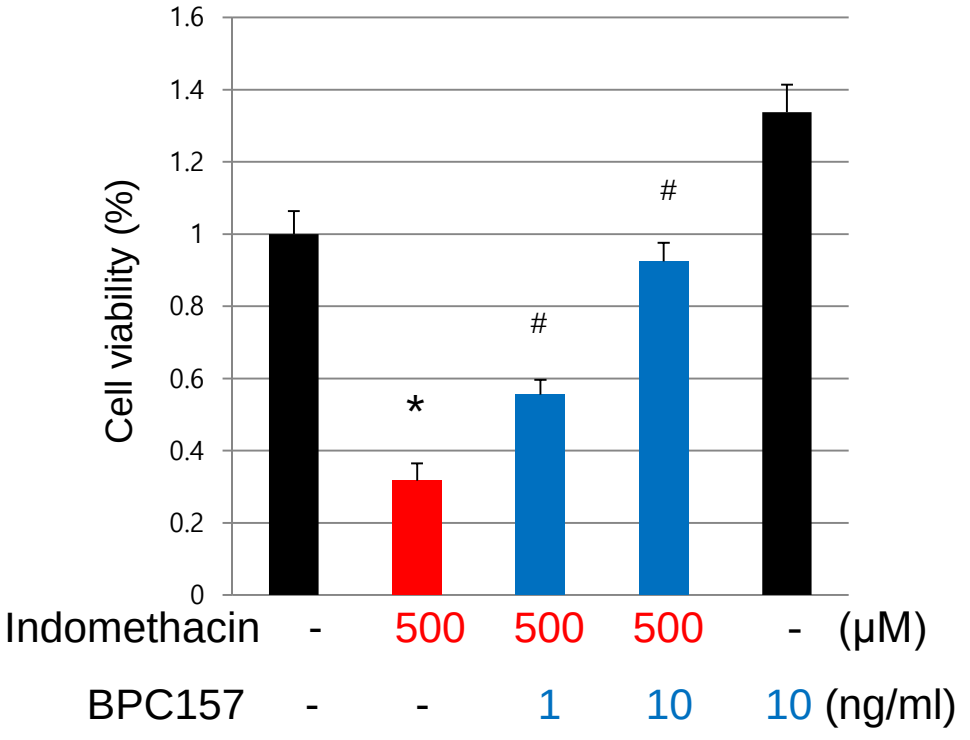


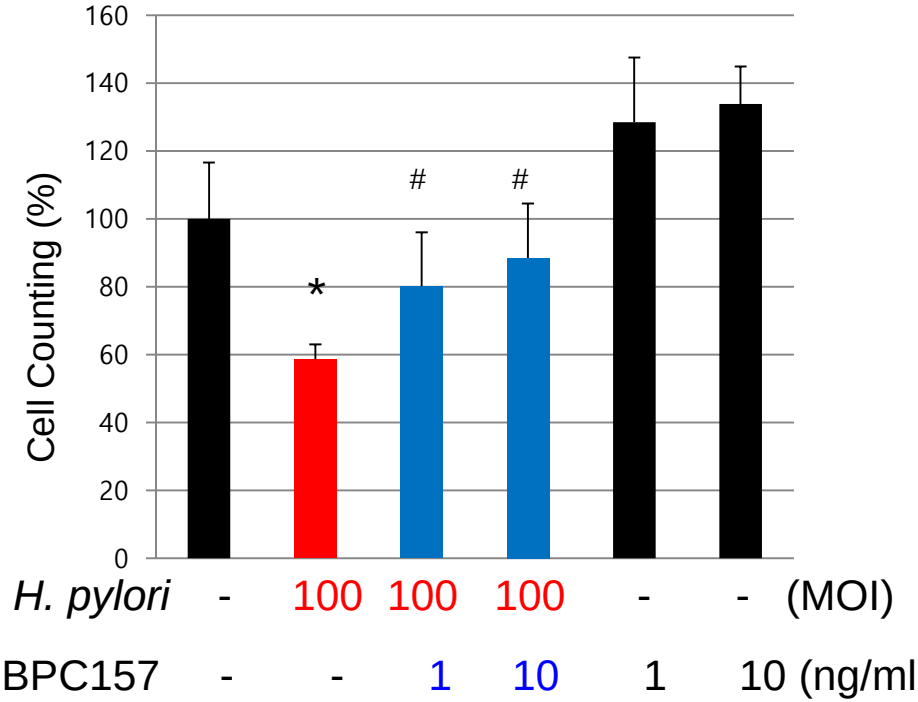

H. Pylori –associated gastritis

NSAID –induced gastrointestinal damages

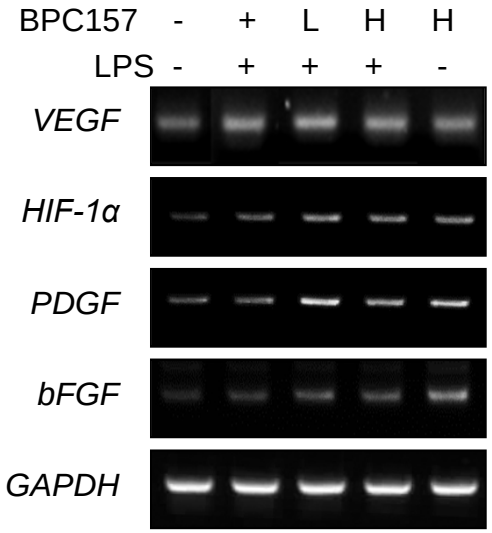


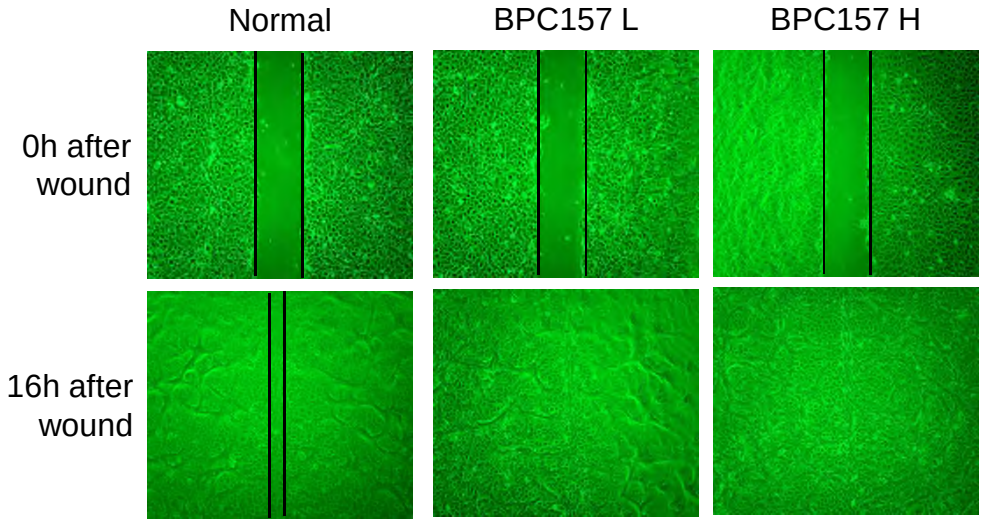
# Cytoprotection by BPC157 against indomethacin or *H.*pylori in gastric epithelial cells, RGM1 cells



# **BPC 157 accentuated wound healing**
## angiogenic growth factors in RGM1 cells

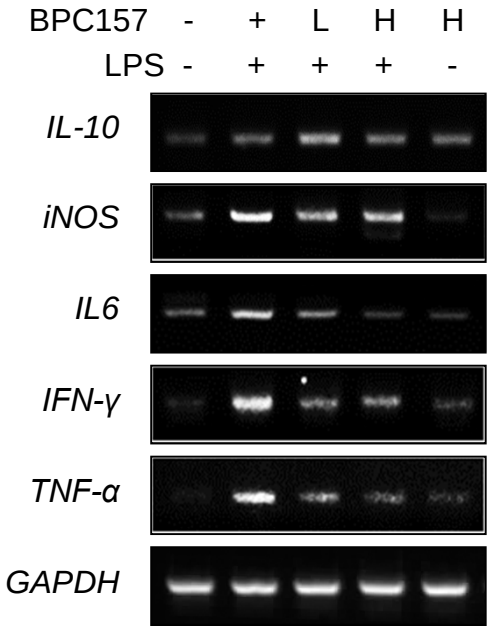


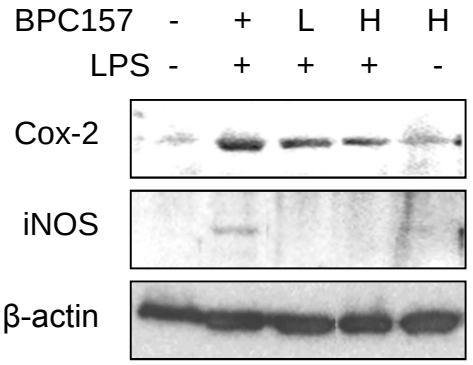




LPS: 1 ug /ml
BPC157 : low dose _ 1 ng / ml
BPC 157 :high dose _ 10 ng / ml

# BPC 157 afforded anti-inflammation

## Mitigated inflammatory mediators in RGM1 cells

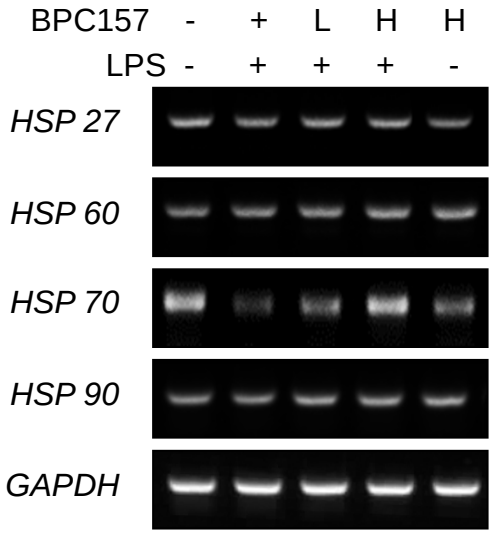


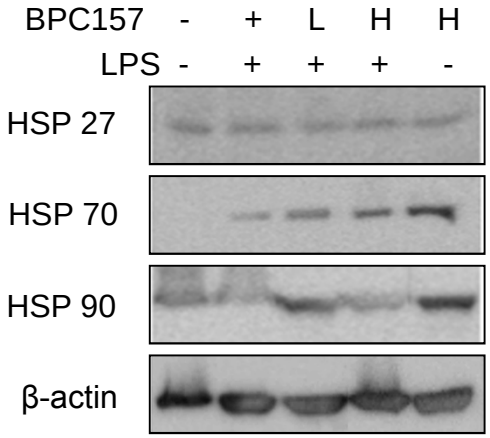




LPS: 1 ug /ml
BPC157 : low dose _ 1 ng / ml
BPC 157 :high dose _ 10 ng / ml

# BPC 157 increased chaperones for cytoprotection

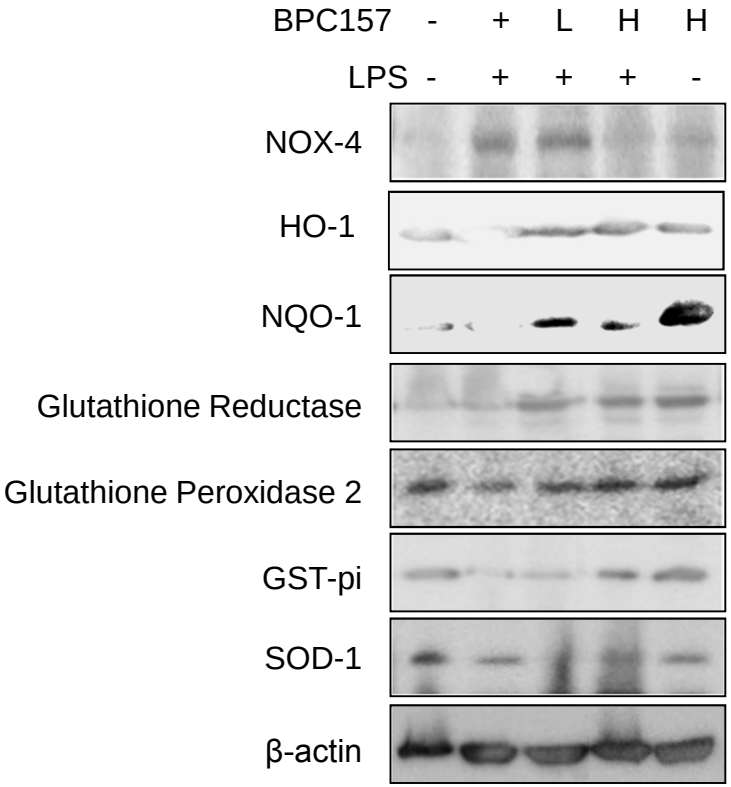
## Increased HSPs in RGM1 cells

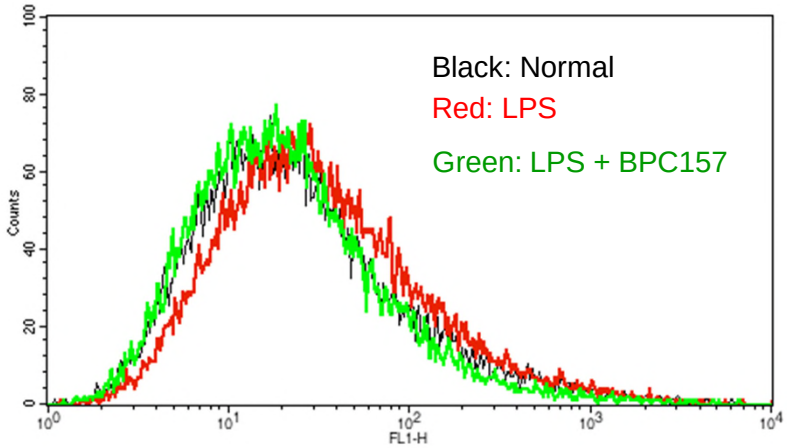



LPS: 1 ug /ml
BPC157 : low dose _ 1 ng / ml
BPC 157 :high dose _ 10 ng / ml

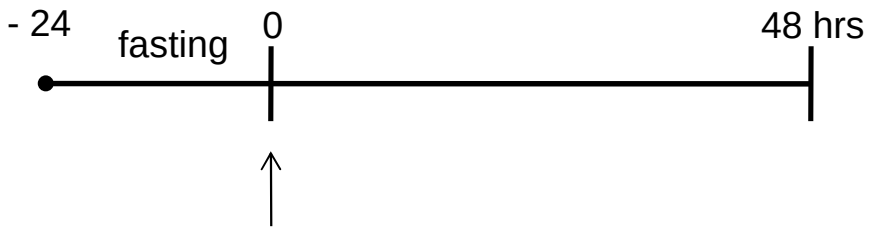
# Antioxidative action of BPC 157



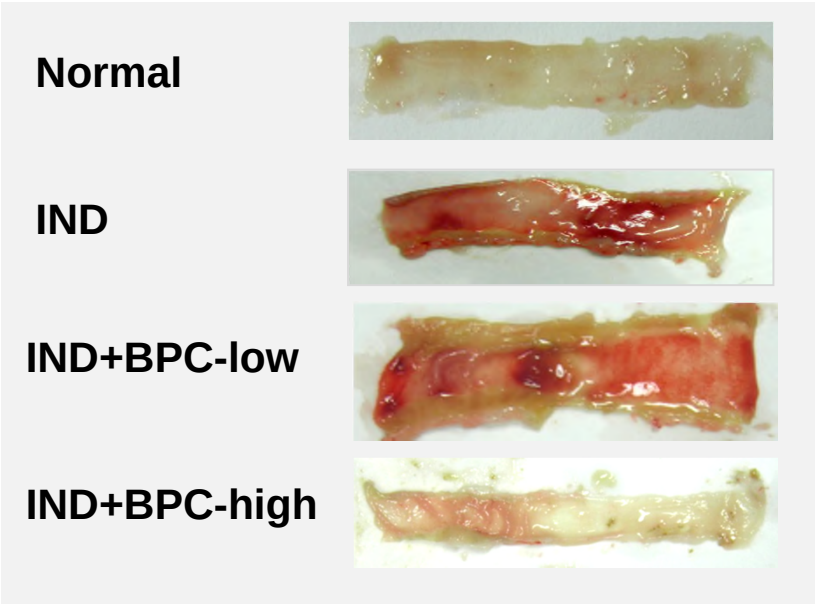

LPS: 1 ug /ml
BPC157 : low dose _ 1 ng / ml
BPC 157 :high dose _ 10 ng / ml

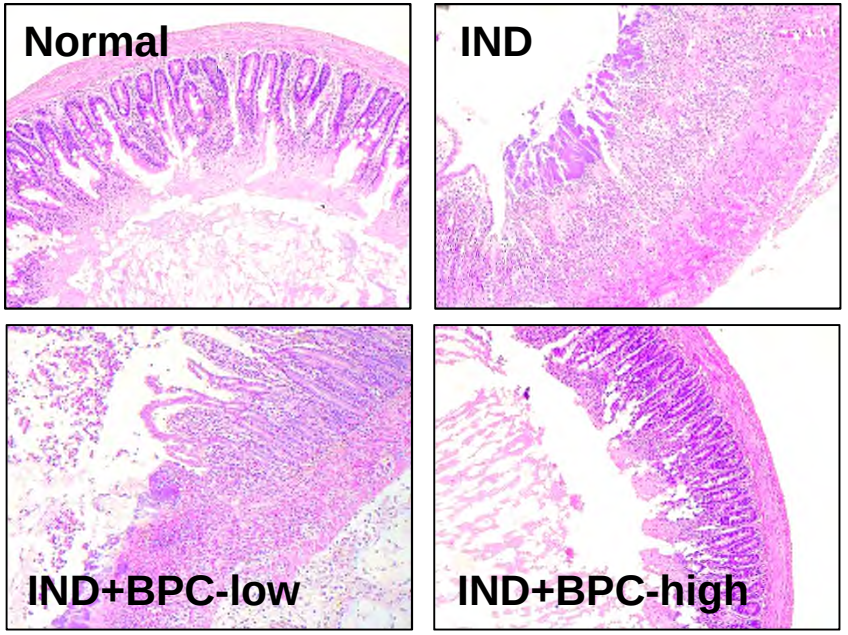
## Scheme of animal model



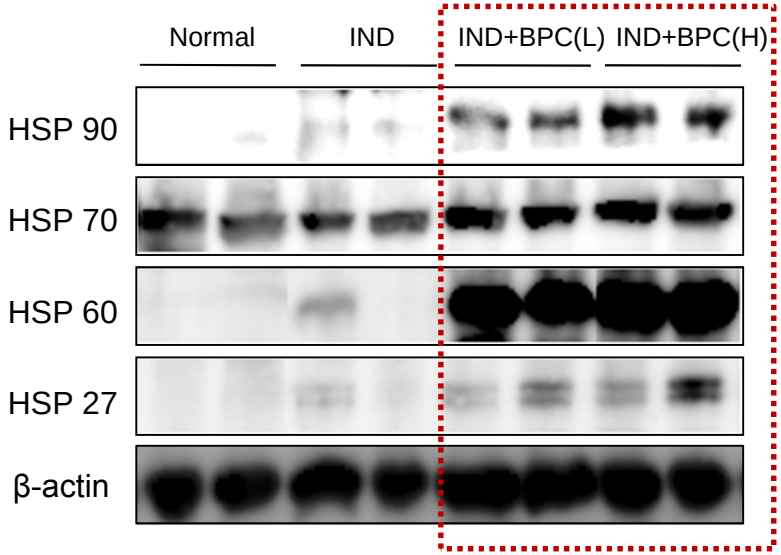

Indomethacin injection (oral gavage 30 mg/kg)
BPC 157 (*i.p.* administration)
: low dose _ 10 ng/kg
: high dose _ 10 ug/kg

## Gross lesions after indomethacin-induced small intestinal damages



# BPC 157 increased HSPs in small intestinal damage animal model



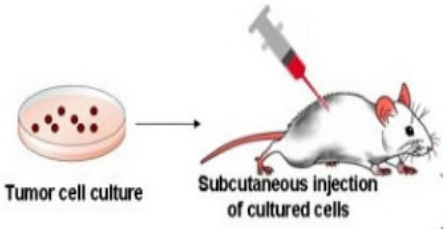
# Summary (1)

## BPC157 can be potential cytoprotectant

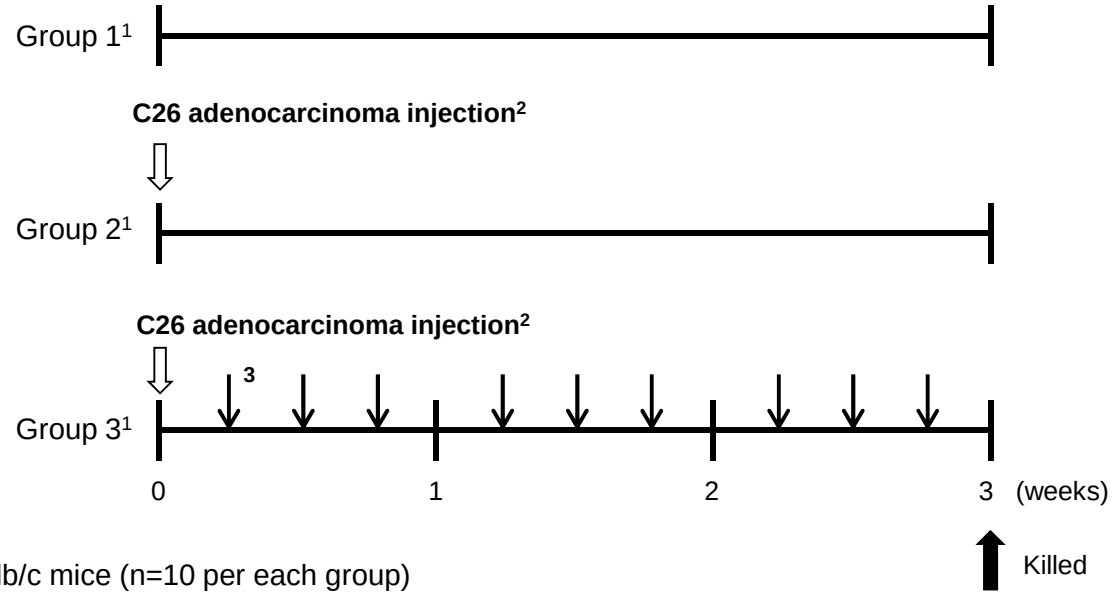
- ✓ **BPC157** inhibits indomethacin & H. pylori-induced cell death.
- ✓ **BPC157** accelerates angiogenesis.
- ✓ **BPC157** inhibits inflammatory mediators.
- ✓ **BPC157** increases cytoprotective mechanisms such as HSPs induction.
- ✓ **BPC157** induces antioxidant enzymes and decreases ROS generation.
- ✓ **BPC157** decrease IND-induced small intestinal damage and induces HSPs

# *Therapeutic effects of BPC157 in Cancer Cachexia model*

# Scheme of animal experiment



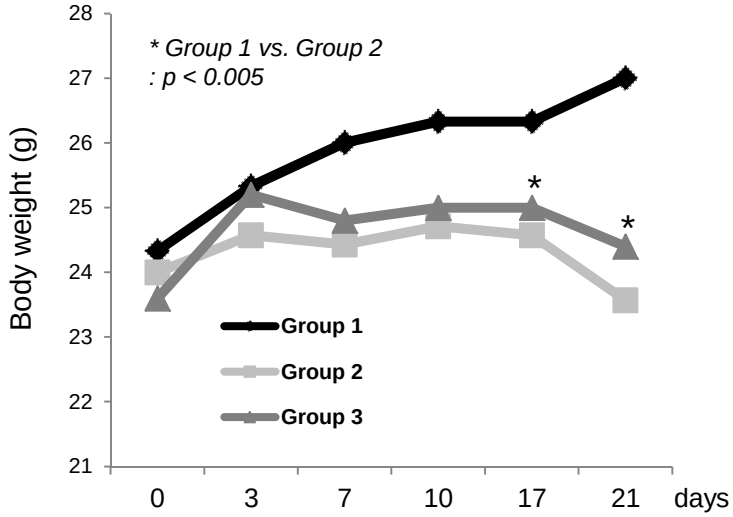

**C-26: colon adenocarcinoma cells**

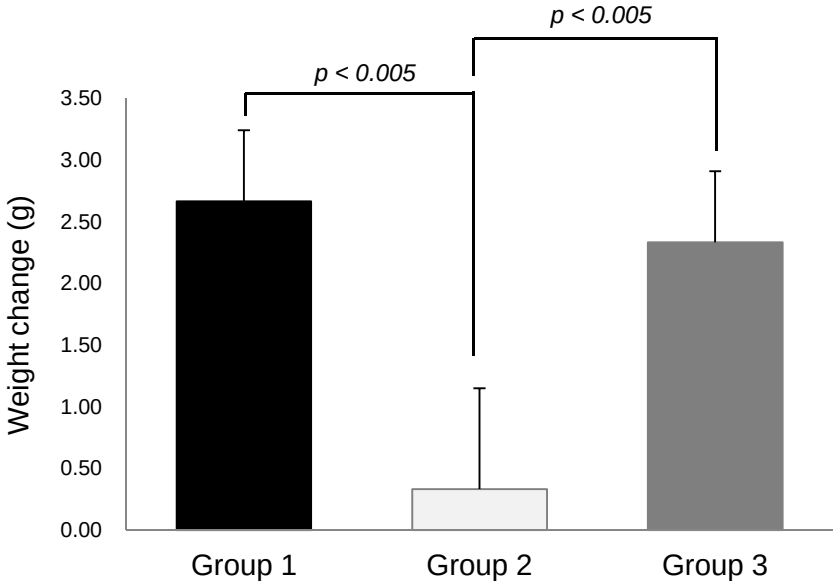



1. Balb/c mice (n=10 per each group)
2. C26 adenocarcinoma cells ($1x10^7$ cells) xenografted on flank
3. BPC157 10 ug/ kg administered via *i.p* thrice per week

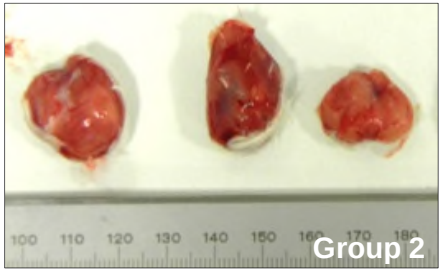
# Result 1; Body and tumor weight

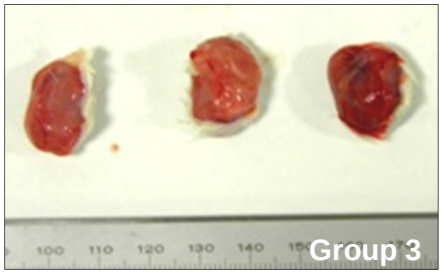
(A)

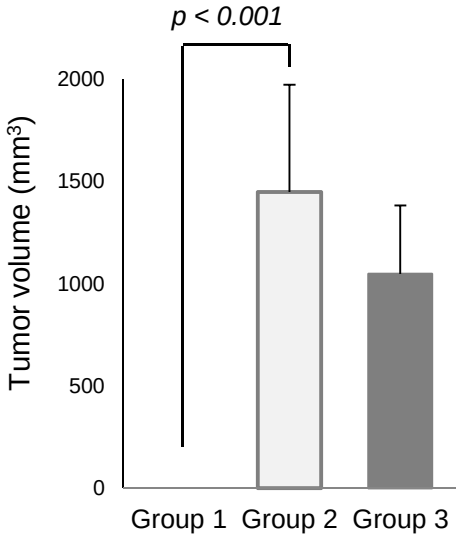


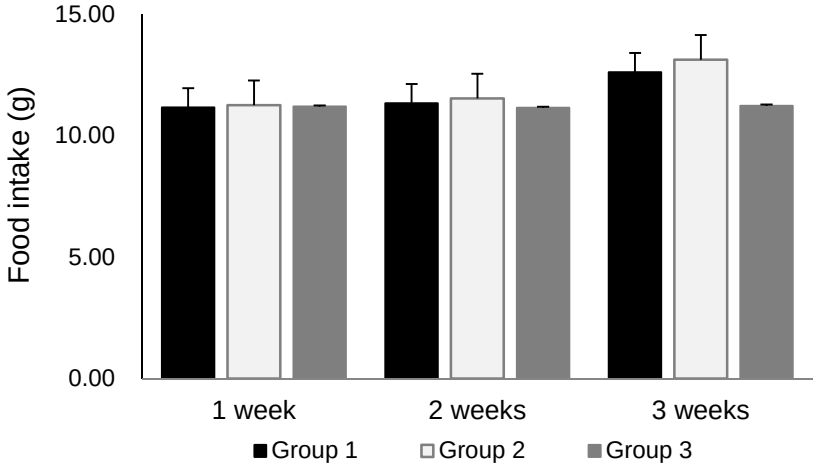

(B)



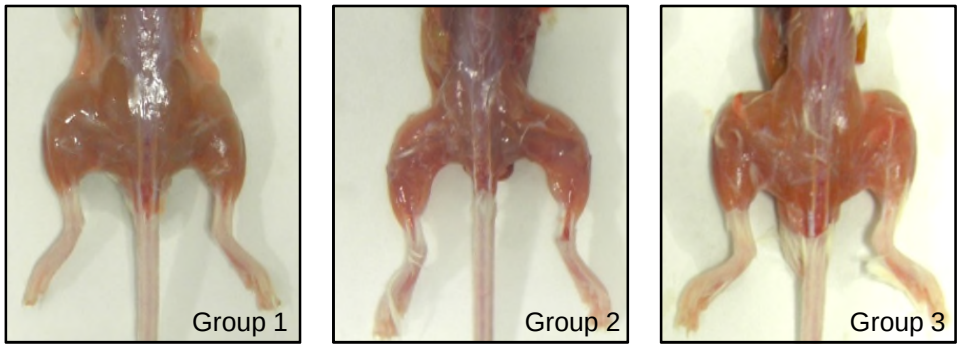



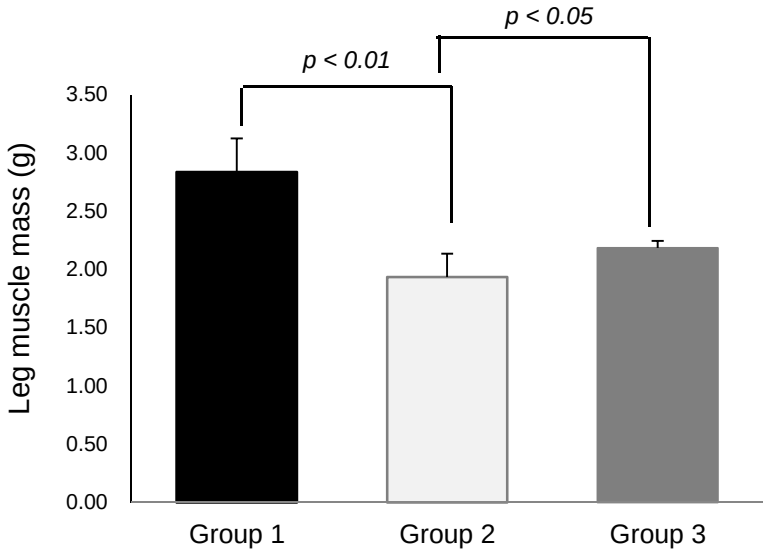

(C)



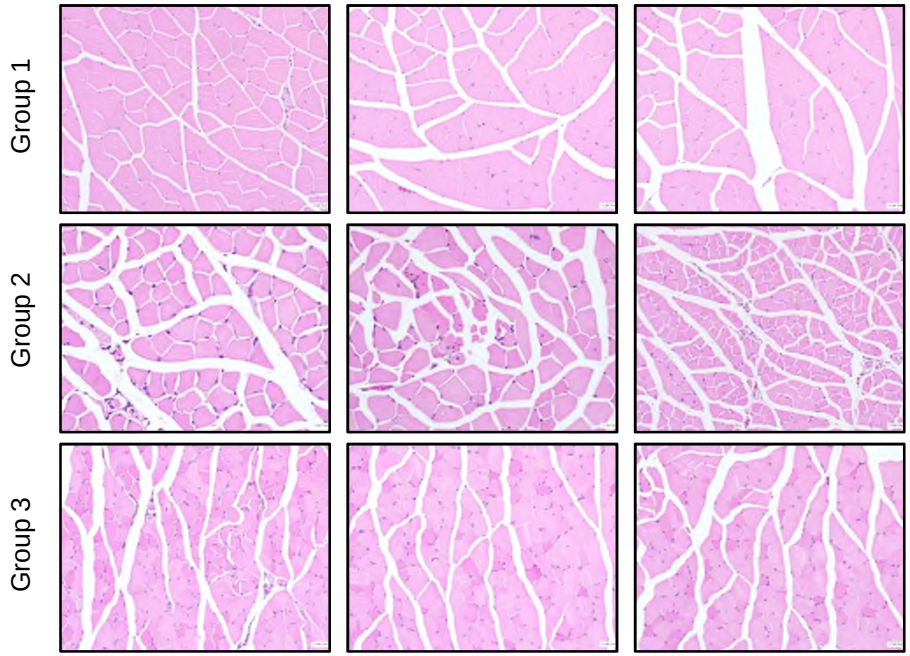
# Result 2; gross and pathology

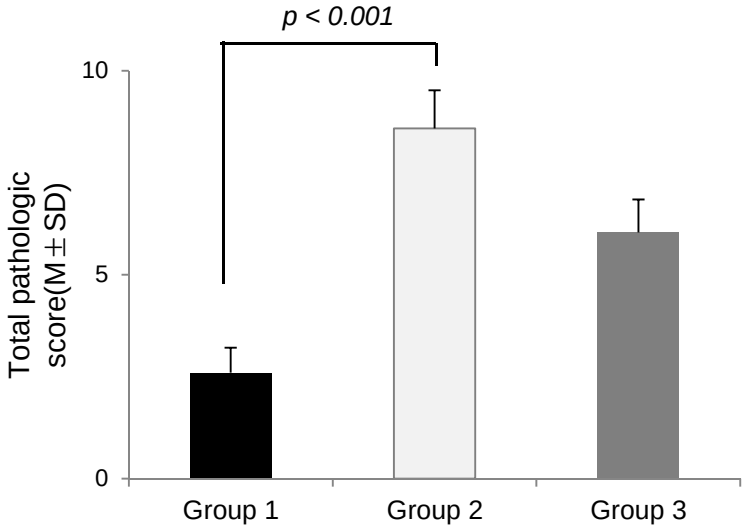
(A)



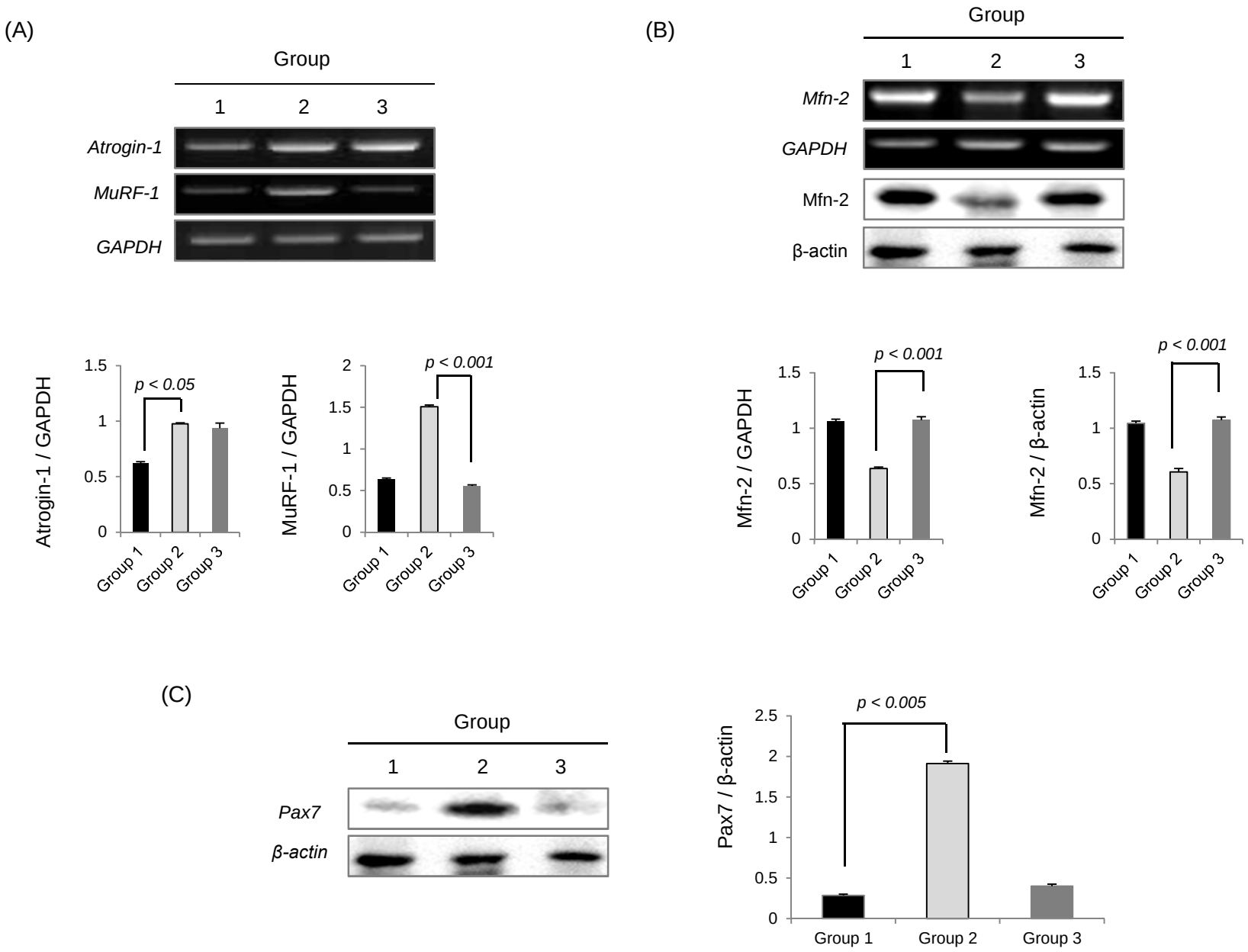




(B)



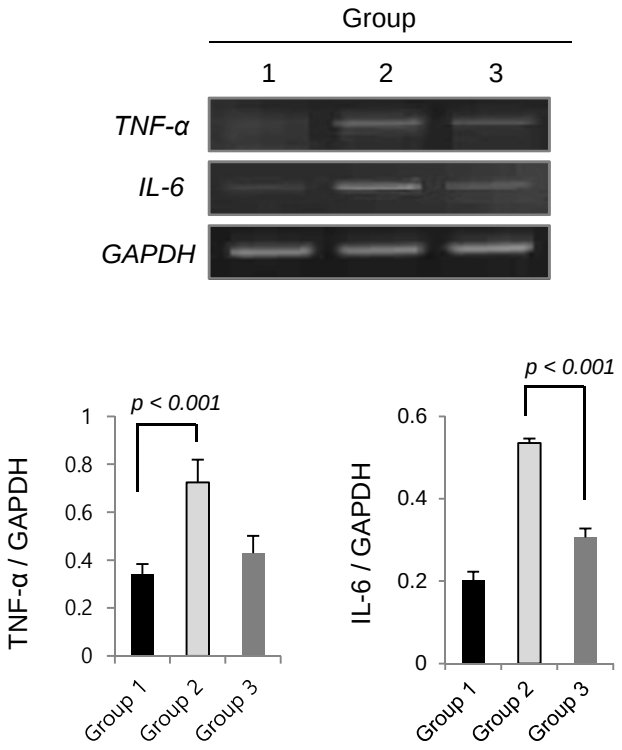



# Result 3: Muscle atrophy & Mitochondrial biogenesis



# Result 4: inflammation & Muscle synthesis

(A)

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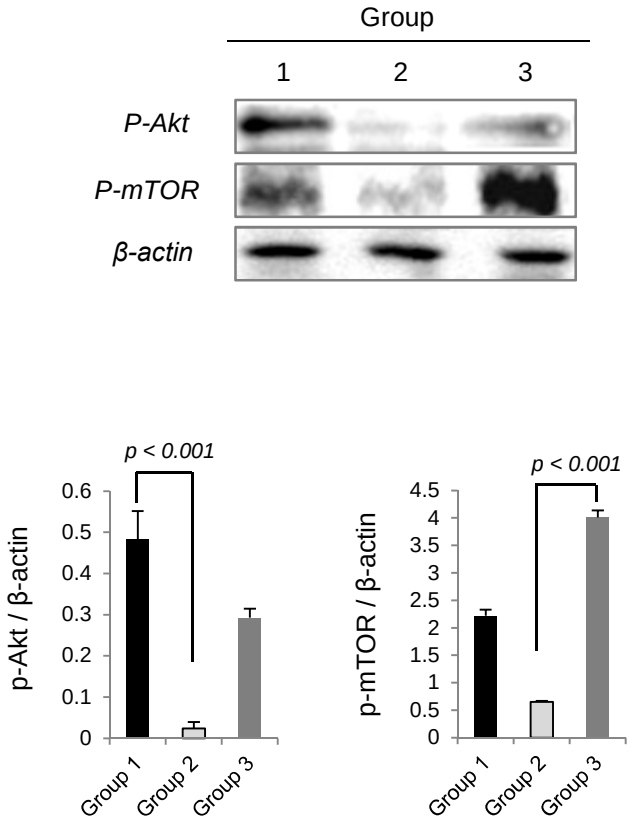
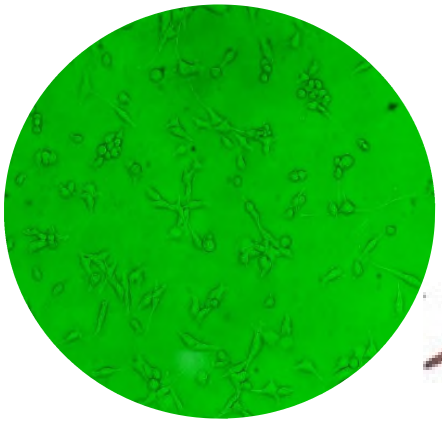


# Summary (2)



Cancer cachexia

- *Inflammatory cytokines ↑*
- *Muscle atrophy ↑*
- *Muscle synthesis; AKT,mTOR ↓*
- *Muscle biogenesis ↓*
- *Skeletal muscle mass ↓*

+ BPC157 Treatment

- *Inflammatory cytokines ↓*
- *Muscle atrophy ↓*
- *Muscle synthesis; AKT,mTOR ↑*
- *Muscle biogenesis ↑*
- *Skeletal muscle mass ↑*