

BEER AND THE HEART:

INSIGHTS ON THE EFFECTS ON ALCOHOLIC AND NON-ALCOHOLIC BEER



7TH EUROPEAN BEER AND HEALTH SYMPOSIUM – BRUSSELS -2014

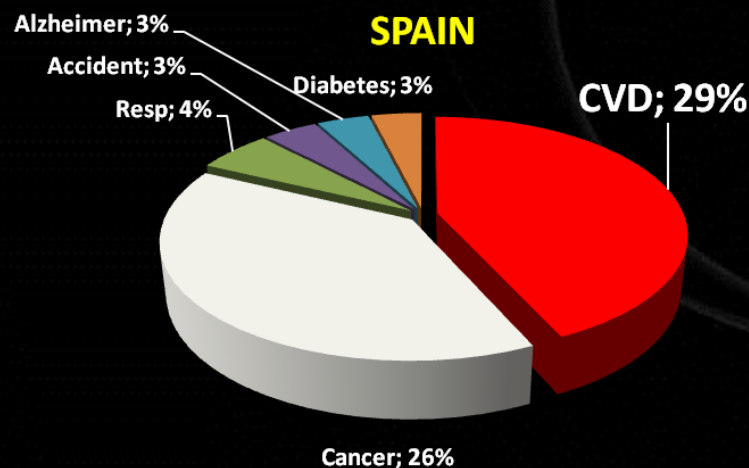
Mortality causes: impact of CVD



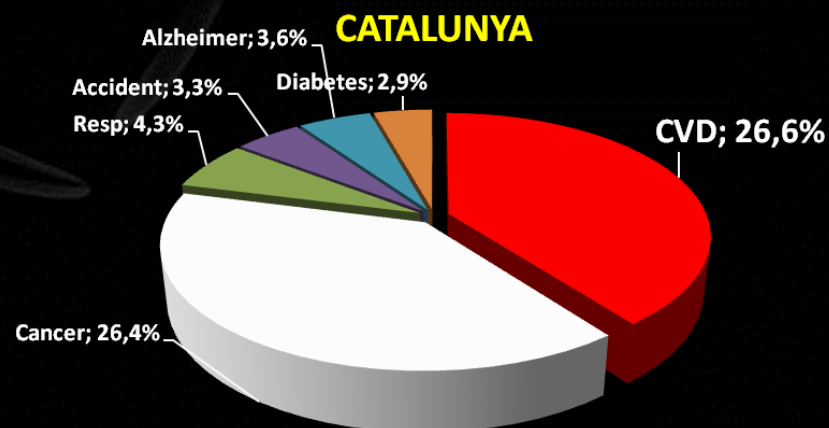
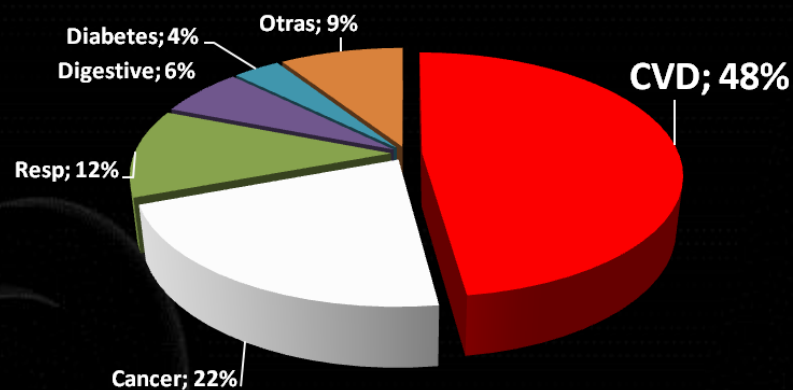
WORLD

OMS 2010

CVDs LEADING CAUSE OF DEATH
(30.5% total)



EUROPE



Recomended doses



Alcohol effect on GLOBAL DEATH

- 30g/day men: 2-3 beers, 2-3 glasses of wine
- 20g/day women: 1-2 beers, 1-2 glass of wine



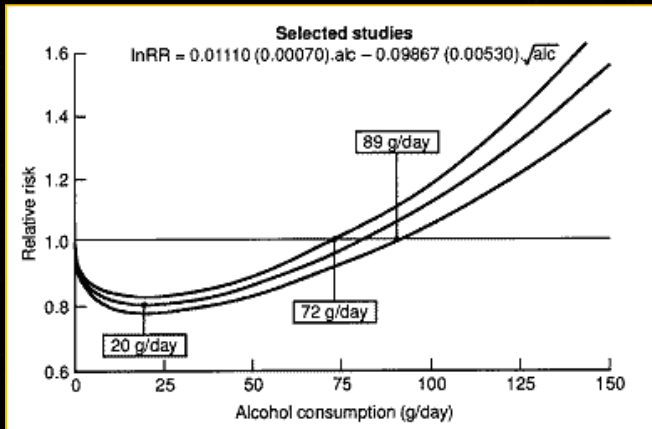
- Two drinks per day men
- One drink per day women

One drink =

12 oz. ($\approx$ 350 ml) of BEER

4 oz. ($\approx$ 120ml) of WINE

1.5 oz. ($\approx$ 45 ml) of SPIRITS



Corrao et al 2000

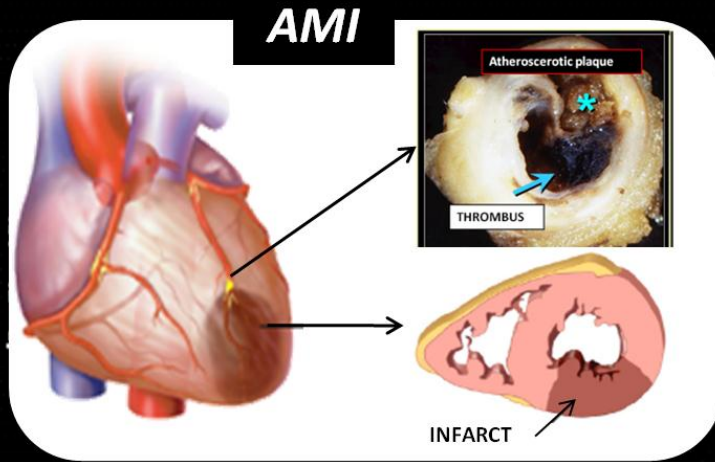
Alcohol intake in young and pregnant = 0

Moderate fermented beverages intake.....

✓ **Atheroprotective effects**
(lower incidence of CVD)

Cardioprotective effects?





**Certain pathological conditions
(HYPERCHOLESTEROLEMIA)**

G. Vilahur, L. Casani, L. Badimon. *Atherosclerosis* 2012

CARDIAC REMODELING

Repair process of the necrotic
area promoting myocardial
scarring

G. Vilahur, O. Juan-Babot, L. Badimon. *J Mol Cell Cardiol* 2011

**Aggravate and/or intensify cardiac
structural remodeling adversely affecting
cardiac function**



**Beer intake affords cardiac protection
and improves scar formation post-
AMI in the setting of dyslipidemia???**

Study protocol



10 days

Hypercholesterolemic diet
20% saturated fat
2% cholesterol
1% colic acid

Energy: 5252 Kcal
Distribution: 47 % protein
30 % carbohydrates
23 % fat

HC CONTROL

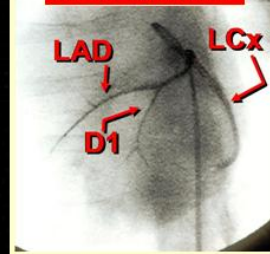
12.5g alcohol/day
(LOW DOSE)

25g alcohol/day
(MODERATE DOSE)

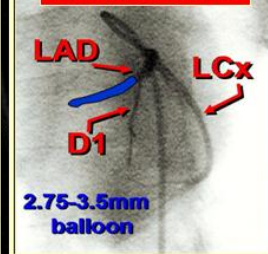
0g alcohol/day
(ALCOHOL-FREE)

AMI

sham-operation



90 min occlusion



Beer intake affords cardiac protection during ischemia???

21 days hypercholesterolemic diet

0g alcohol/day
(ALCOHOL-FREE)

25g alcohol/day
(MODERATE DOSE)

12.5g alcohol/day
(LOW DOSE)

HC CONTROL

Systemic effects???

SACRIFICE

Beer intake affords cardiac protection in the remodeling phase???

SYSTEMS BIOLOGY APPROACH

FUNCTIONAL STUDIES
CARDIAC FUNCTION
CORONARY FUNCTION

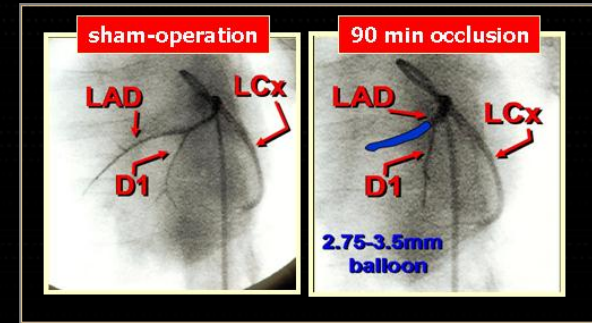
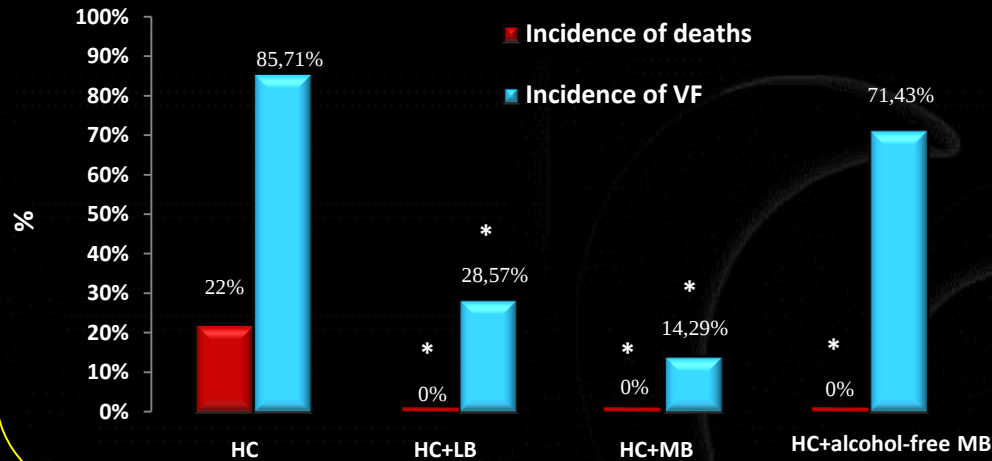
HISTOLOGICAL STUDIES
INFARCT SIZE
FIBROSIS / SCAR
CARDIAC LIPIDS

MOLECULAR STUDIES
RISK activation
eNOS activity
APOPTOSIS

TRANSCRIPTOMICS (ARRAYS)

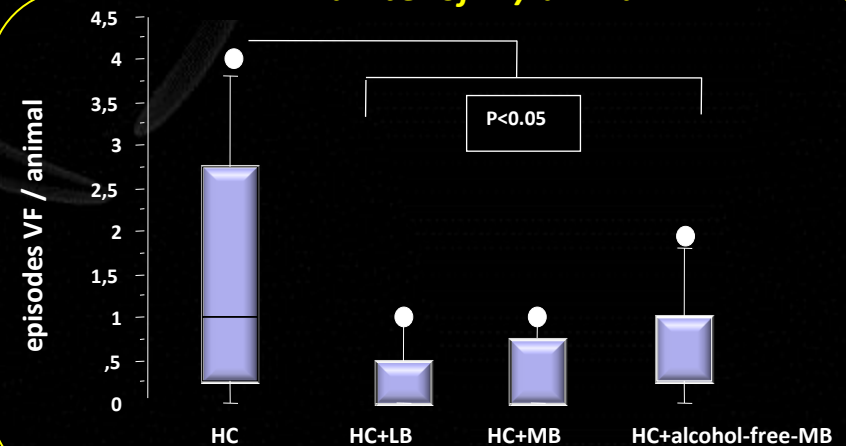
Cardiac protection during ISCHEMIA??

Incidence of ventricular fibrillations and mortality during STEMI-AMI

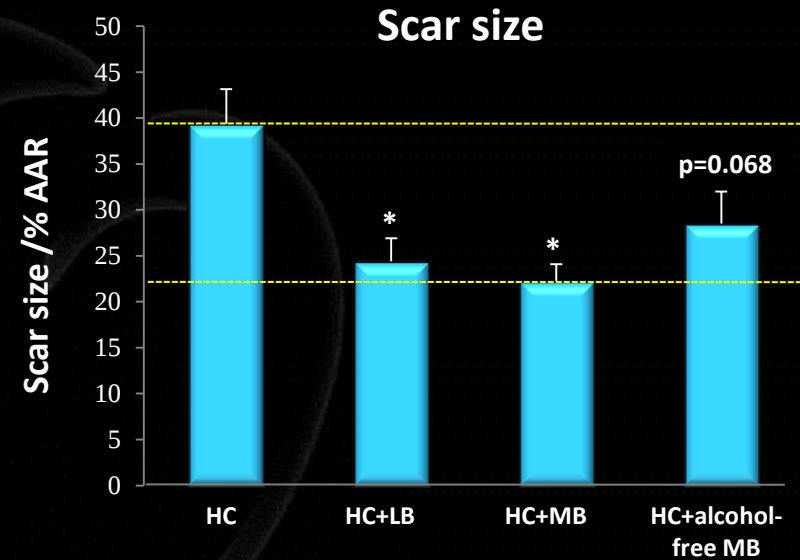
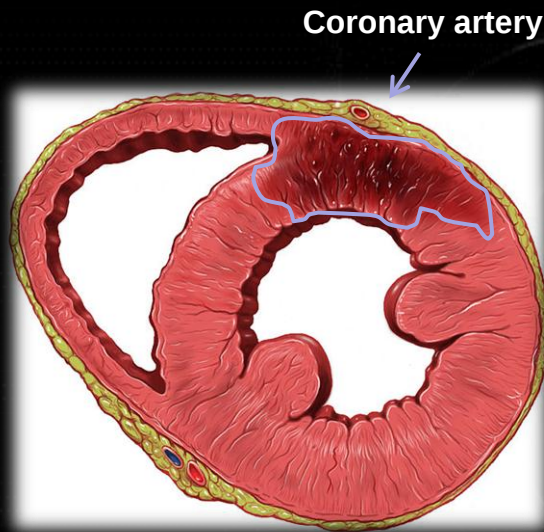


: AMELIORATES MYOCARDIAL ADAPTATION IN THE SETTING OF ACUTE MI

Number of VF/ animal



Cardiac protection post-AMI: scar size



Scar size and left ventricle remodeling

HC



229 ± 11 g

HC+LB



227 ± 10 g

HC+MB

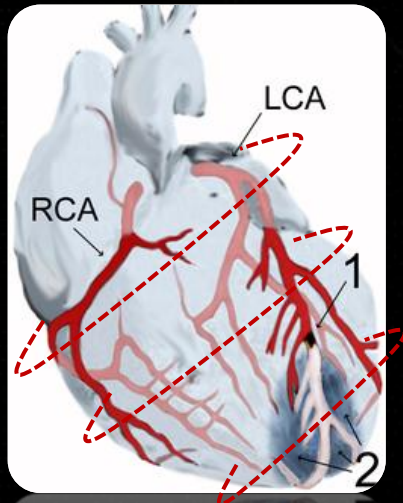


233 ± 9 g

HC+alcohol-free MB



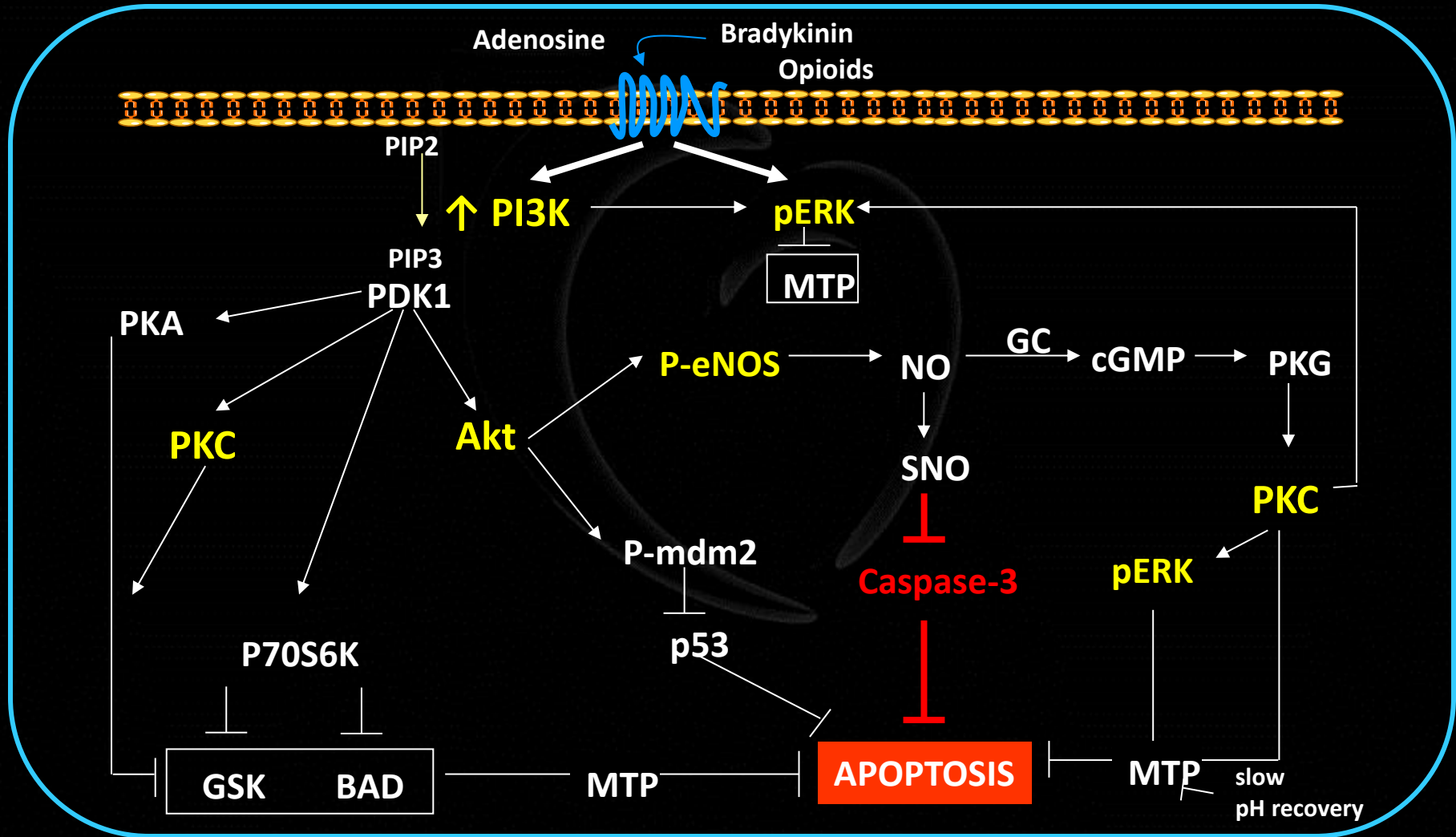
222 ± 7 g



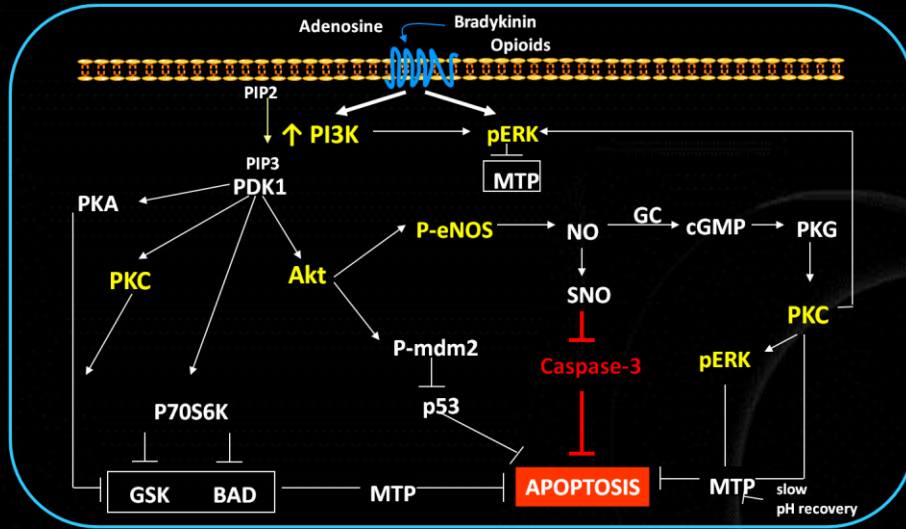
**:REDUCES SCAR SIZE WITHOUT
MODIFYING LV ARCHITECTURE**

Cardiac protection post-AMI: molecular mechanisms

Cardioprotective signaling pathways (RISK)

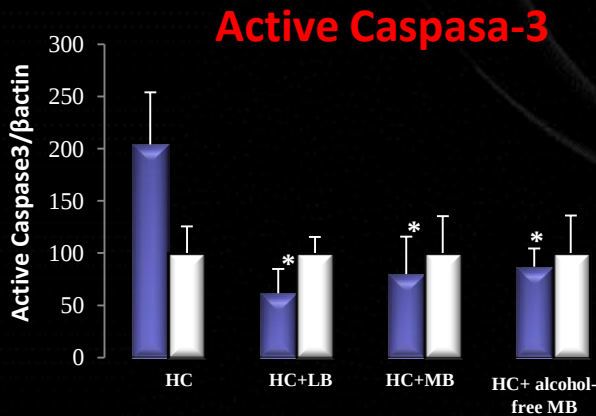


Apoptosis execution

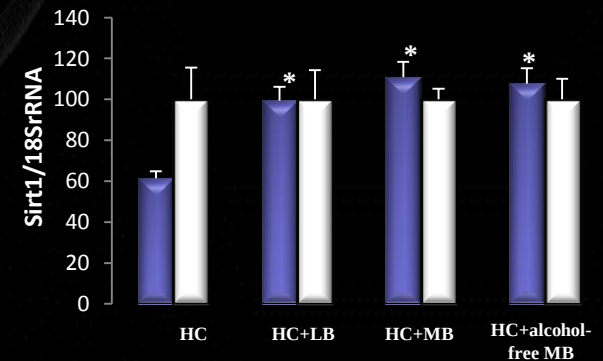


:ACTIVATES CARDIOPROTECTIVE KINASES AND REDUCES APOPTOSIS EXECUTION

Ischemic
Non-Ischemic



Sirtuin-1 (antioxidant)



↓ **Apoptosis cell death**

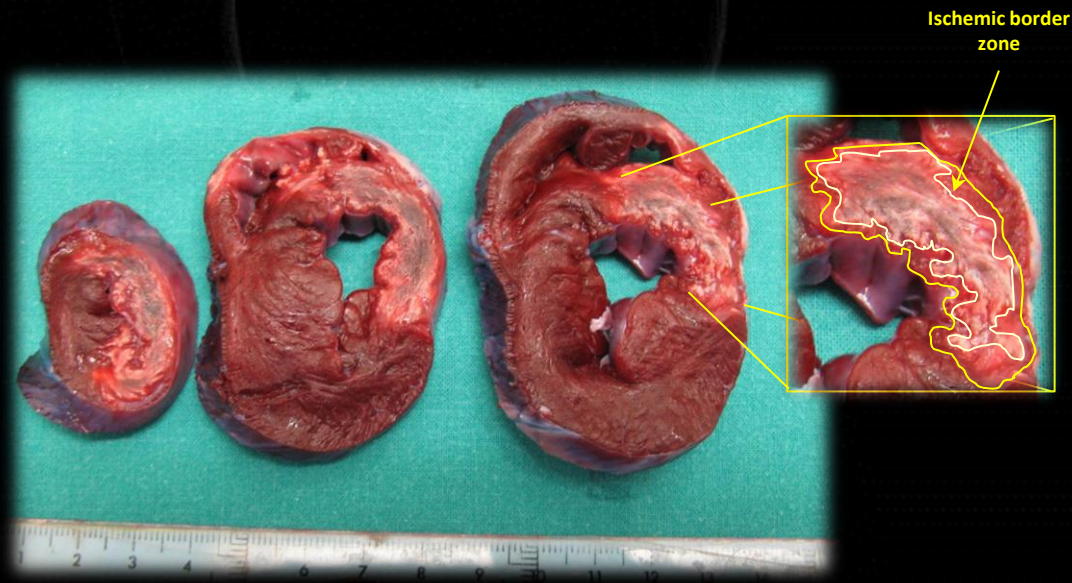


↓ **INFARCT SIZE**

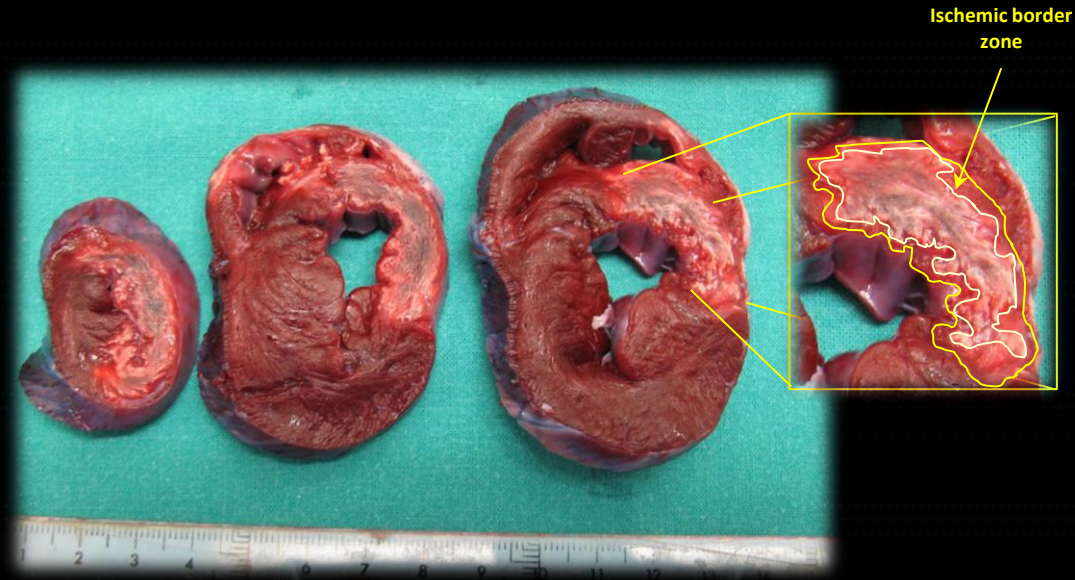
WHICH ARE THE GENES INVOLVED IN THE REGULATION OF THE OBSERVED FUNCTIONAL BENEFITS IN THE HEART ?



TRANSCRIPTOMICS



Porcine Genome Array - Microarray expression analysis

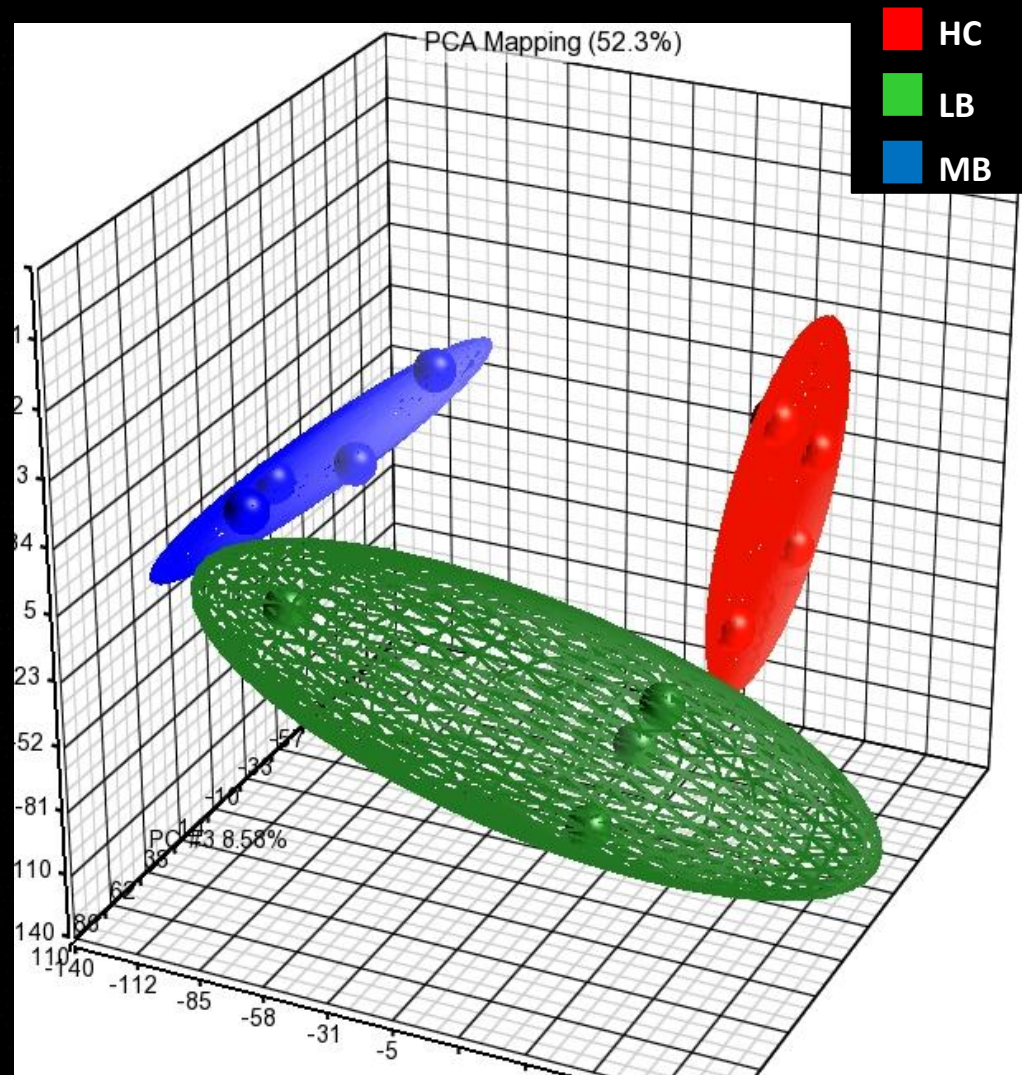


≈ 35.000 genes

Differential expressed Genes: **Software Partek Genomics Suite**

Networks and functional analysis: **Software Ingenuity Pathways Analysis**

PCA analysis – gene cluster



Associated Network Functions

Associated Network Functions

Cell Death, Cell Morphology, Cellular Compromise

Cellular Movement, Immune Cell Trafficking, Cellular Development

Cell Cycle, Cellular Development, Cellular Growth and Proliferation

Small Molecule Biochemistry, Developmental Disorder, Cellular Growth and Proliferation

Cell Cycle, Gene Expression, DNA Replication, Recombination, and Repair

Score

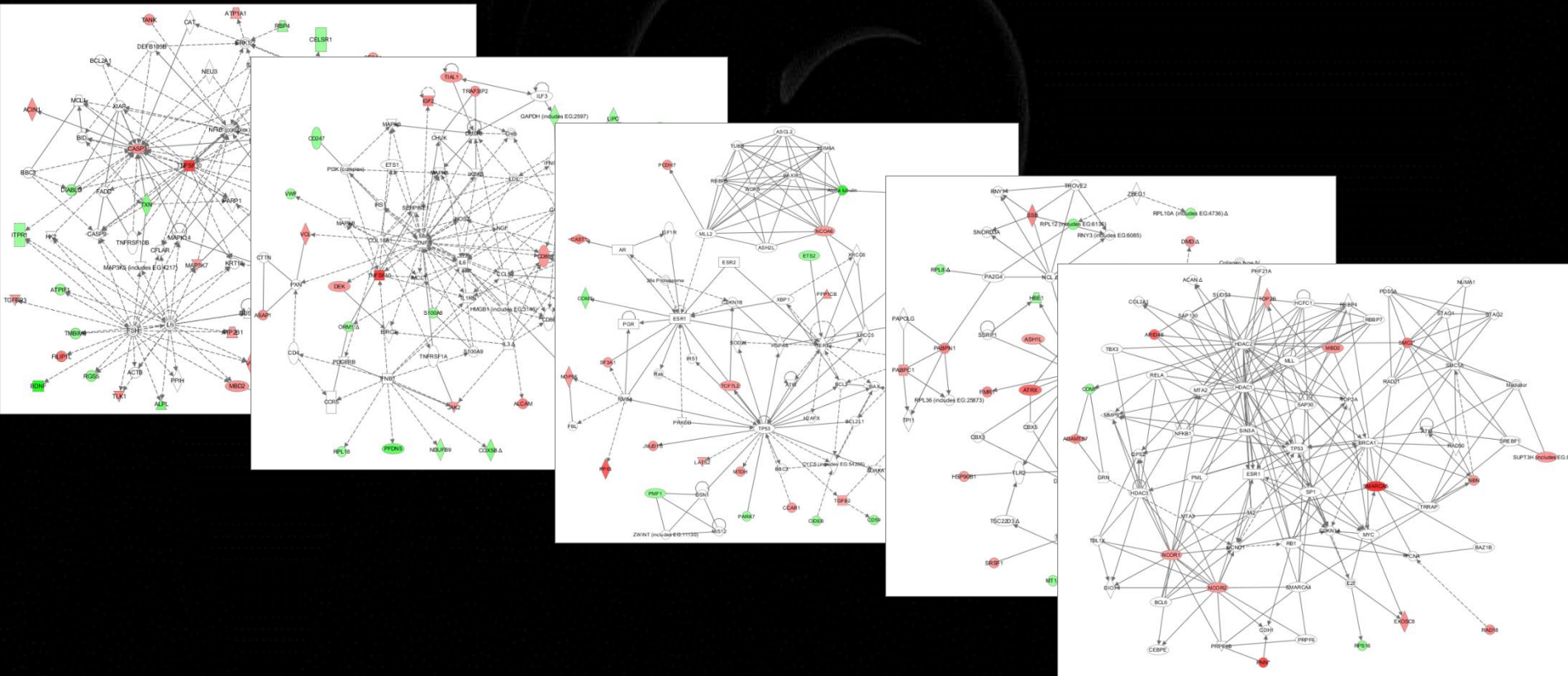
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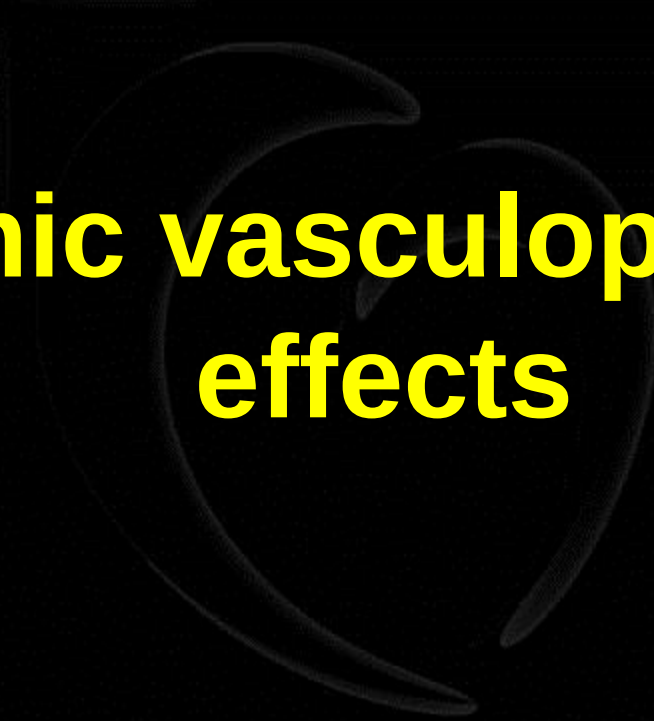
22

21

21

9





Systemic vasculoprotective effects



Does beer intake improves hypercholesterolemia-related endothelial dysfunction?



10 days

Hypercholesterolemic diet

20% saturated fat

2% cholesterol

1% colic acid

Energy: 5252 Kcal

Distribution: 47 % protein

30 % carbohydrates

23 % fat

+



12.5g alcohol/day
(LOW DOSE)



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(MODERATE DOSE)



0g alcohol/day
(ALCOHOL-FREE)

HC CONTROL

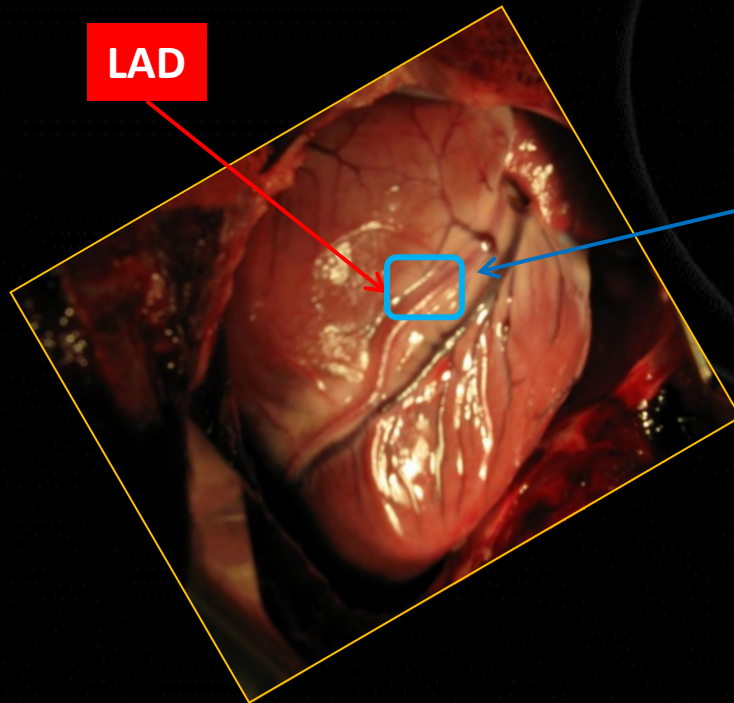
- CORONARY ENDOTHELIAL FUNCTION
- CORONARY

OXIDATIVE DNA-DAMAGE
Akt/eNOS ACTIVATION

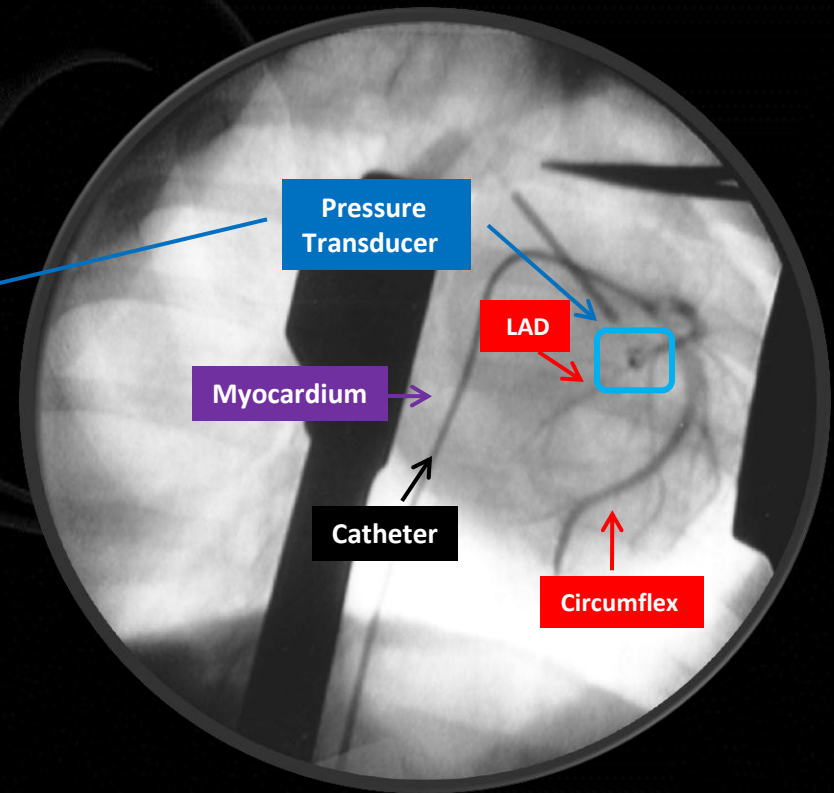
CORONARY FUNCTION - REACTIVITY

Changes in coronary regional blood flow upon pharmacological induction

Open-chest approach



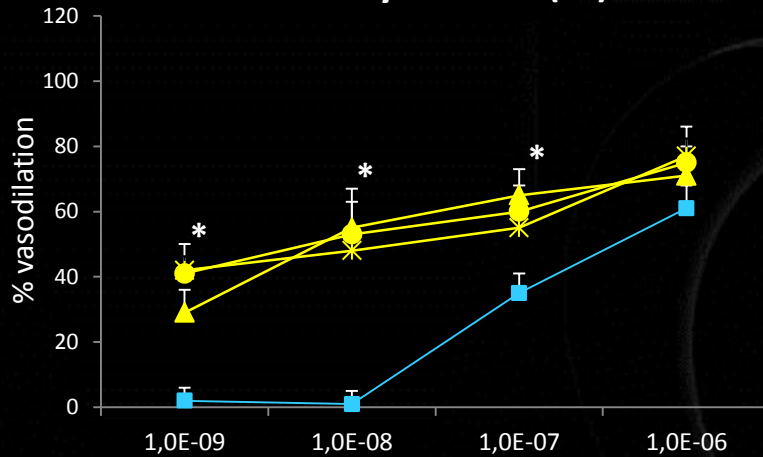
Fluoroscopy guidance (Rx)



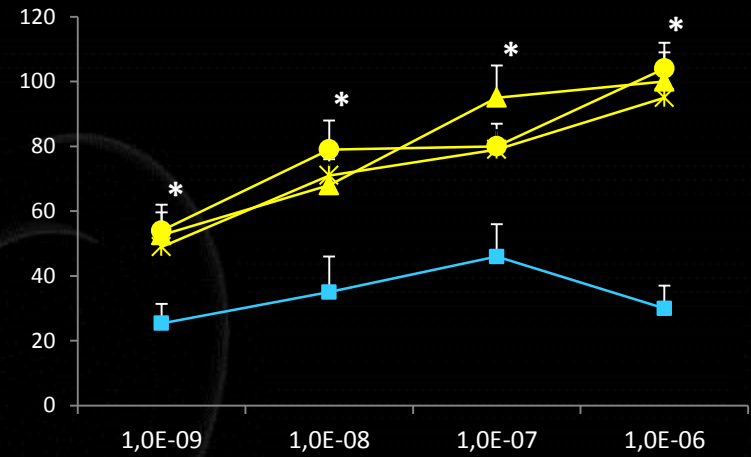
Changes in coronary regional blood flow upon pharmacological induction

—■— WD —▲— WD+LB —●— WD+MB —✱— WD+OH-free beer

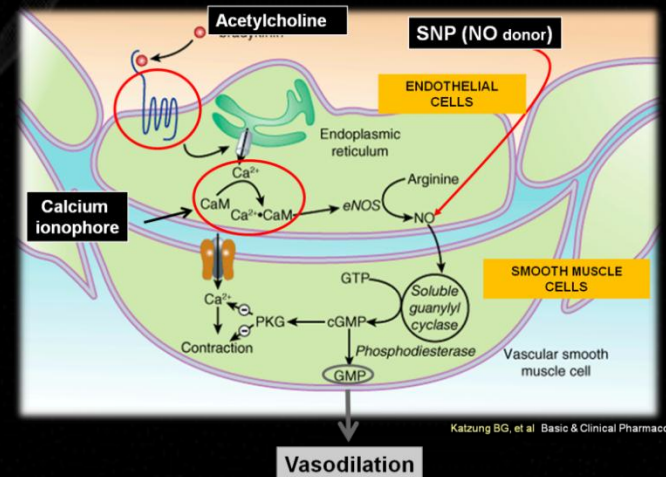
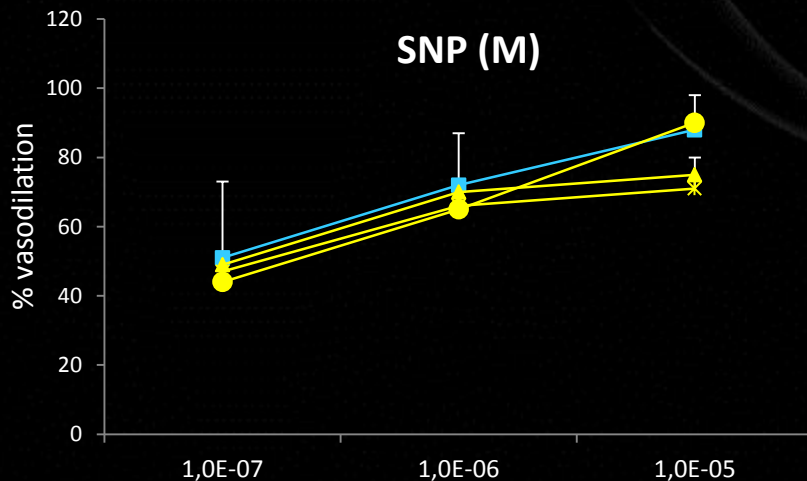
Acetylcholine (M)



Calcium Ionophore (M)

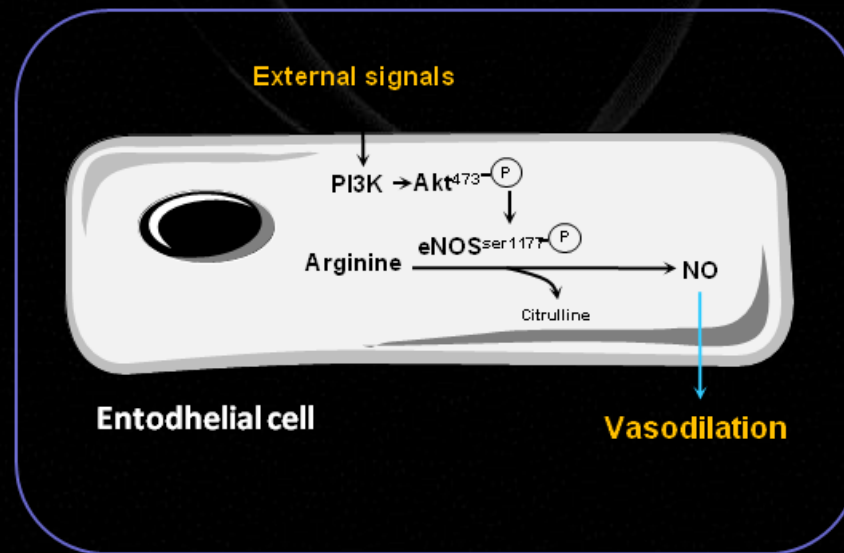
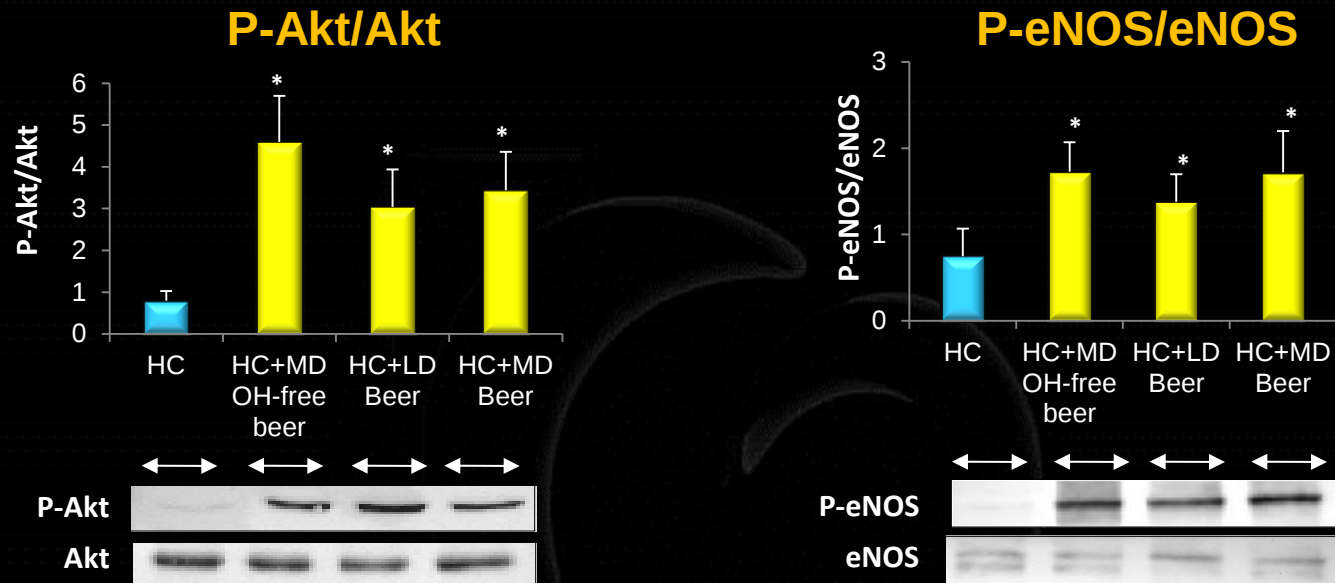


SNP (M)

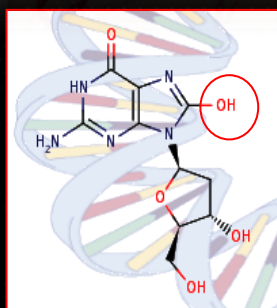
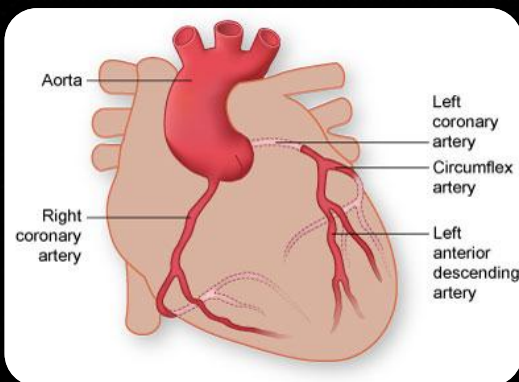


Katzung BG, et al Basic & Clinical Pharmacology

CORONARY ARTERY: Akt/eNOS signaling



CORONARY ARTERY: DNA-oxidative damage (8-OHdG staining)



8-OHdG





TAKE HOME MESSAGES

- **Light-to-moderate regular beer intake (with and without alcohol) during 31 days exerts cardioprotection overcoming the detrimental effects associated with dyslipidemia in the ischemic myocardium**
- **Antioxidant properties of beer rather than alcohol in itself may protect against hyperlipemia-induced coronary endothelial dysfunction by favorably counteracting vascular oxidative damage and activating the Akt/eNOS pathway.**

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