Cholesterol and Skeletal Muscle Health

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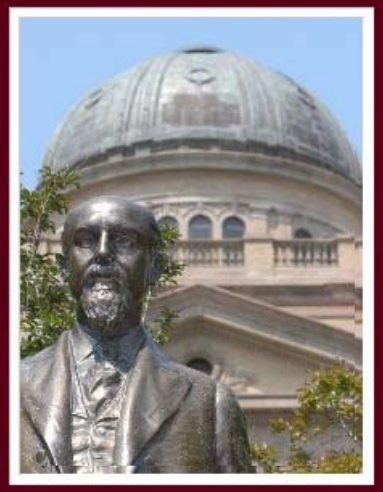
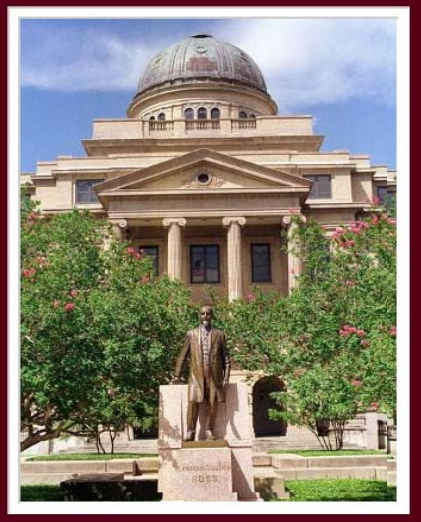




Main Objective

To explain why individuals respond differently to identical exercise interventions

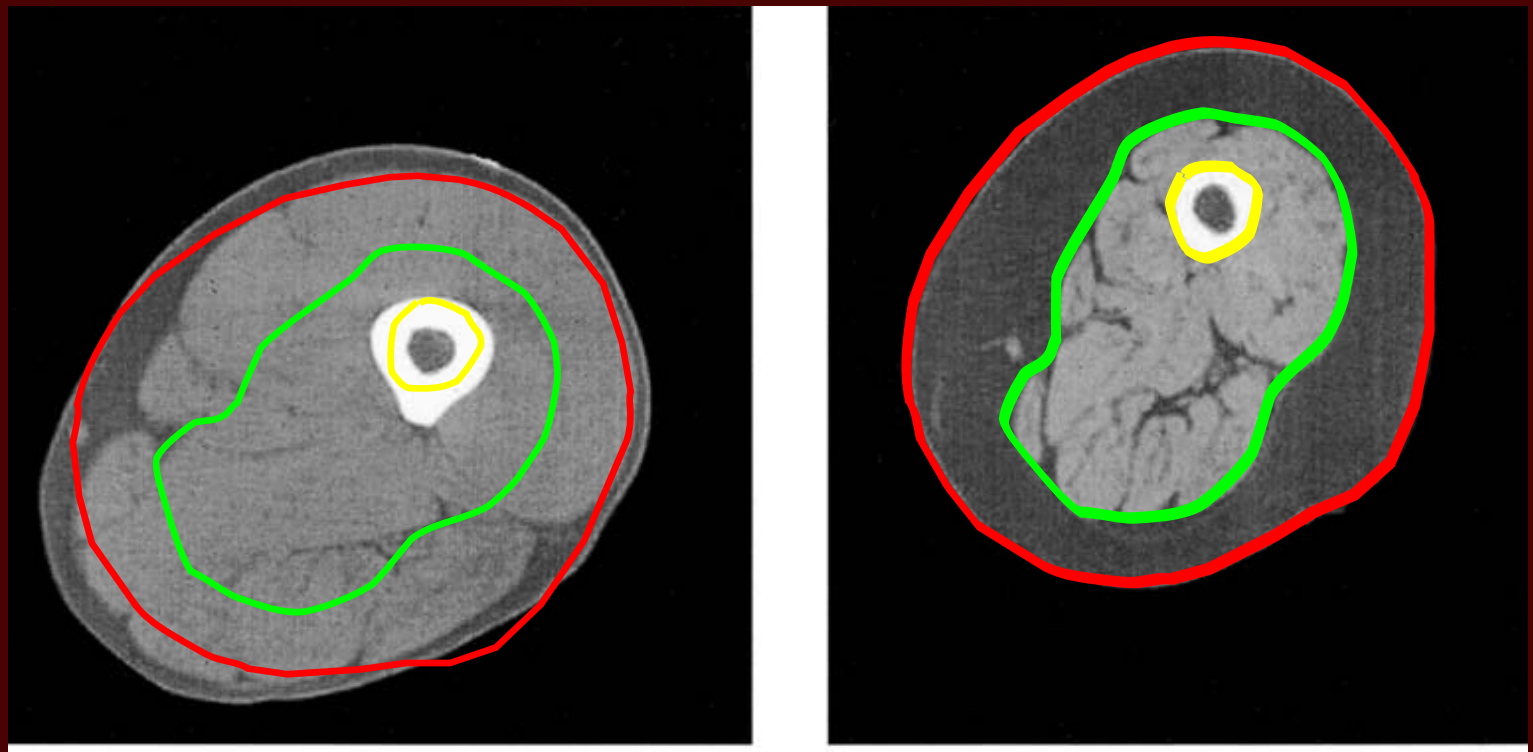
- Variable responses are explained by:
  - Genetics
  - Environment (nutrition)

Applications

- Sarcopenia: muscle loss with aging
- Muscle loss with space flight
- Cachexia: disease associated muscle loss (AIDS, cancer)
- Sport performance

Sarcopenia

Aging:
↑ fat
↓ Muscle
weight =



Roubenoff, 2003

MERET II: Subjects

- This study includes 60-69 year old men and women
- Inclusion criteria: healthy, mobile, and able to perform exercise and testing
- Exclusion criteria: CVD, blood pressure >160/100, atrial fibrillation, hernia, aortic aneurysm, cancer, kidney or lung disease

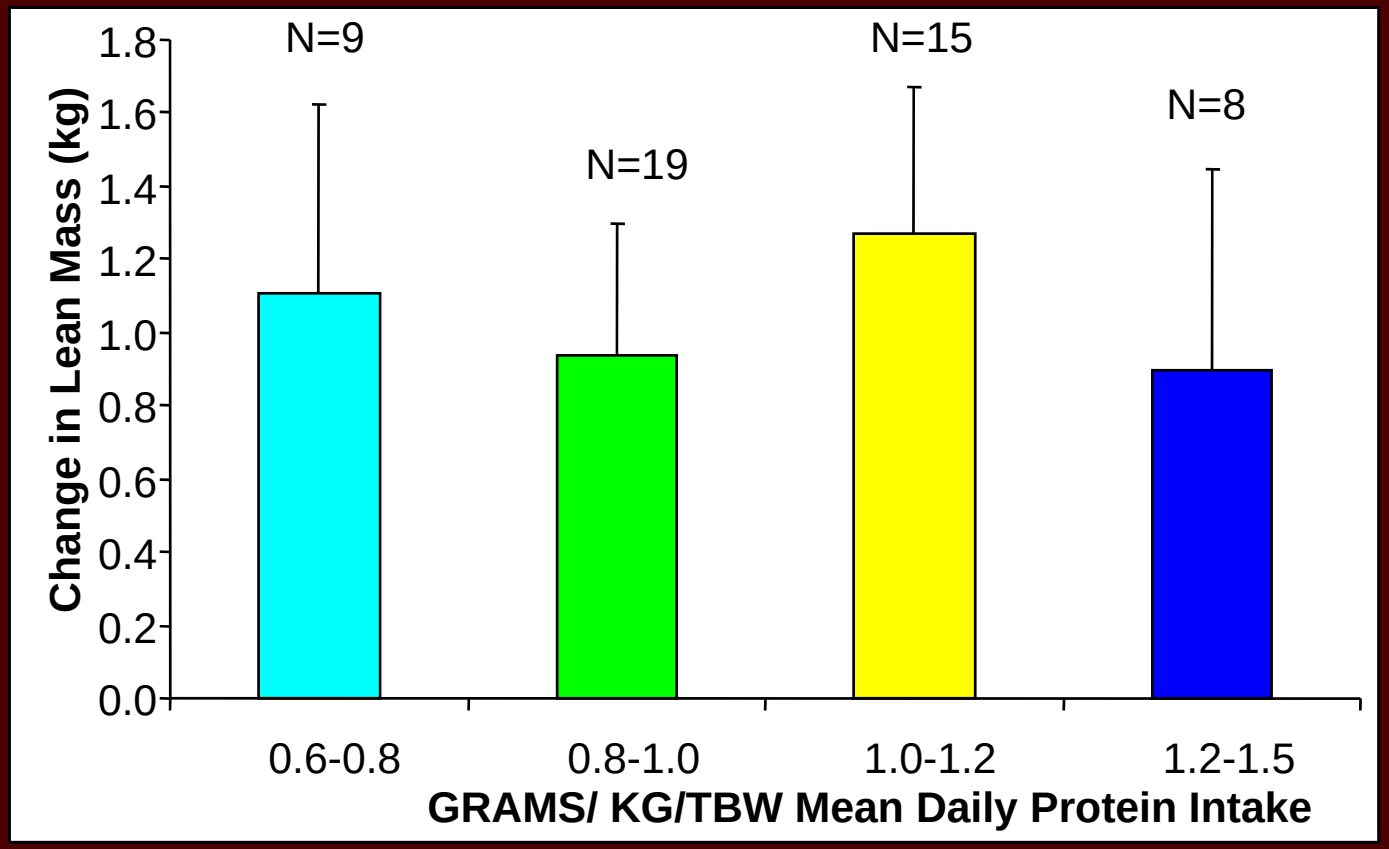
Orientation/Education

- 6 sessions/ 2 weeks
  - Nutrition seminar (20-25 min)
  - Introduction to weight lifting

Training

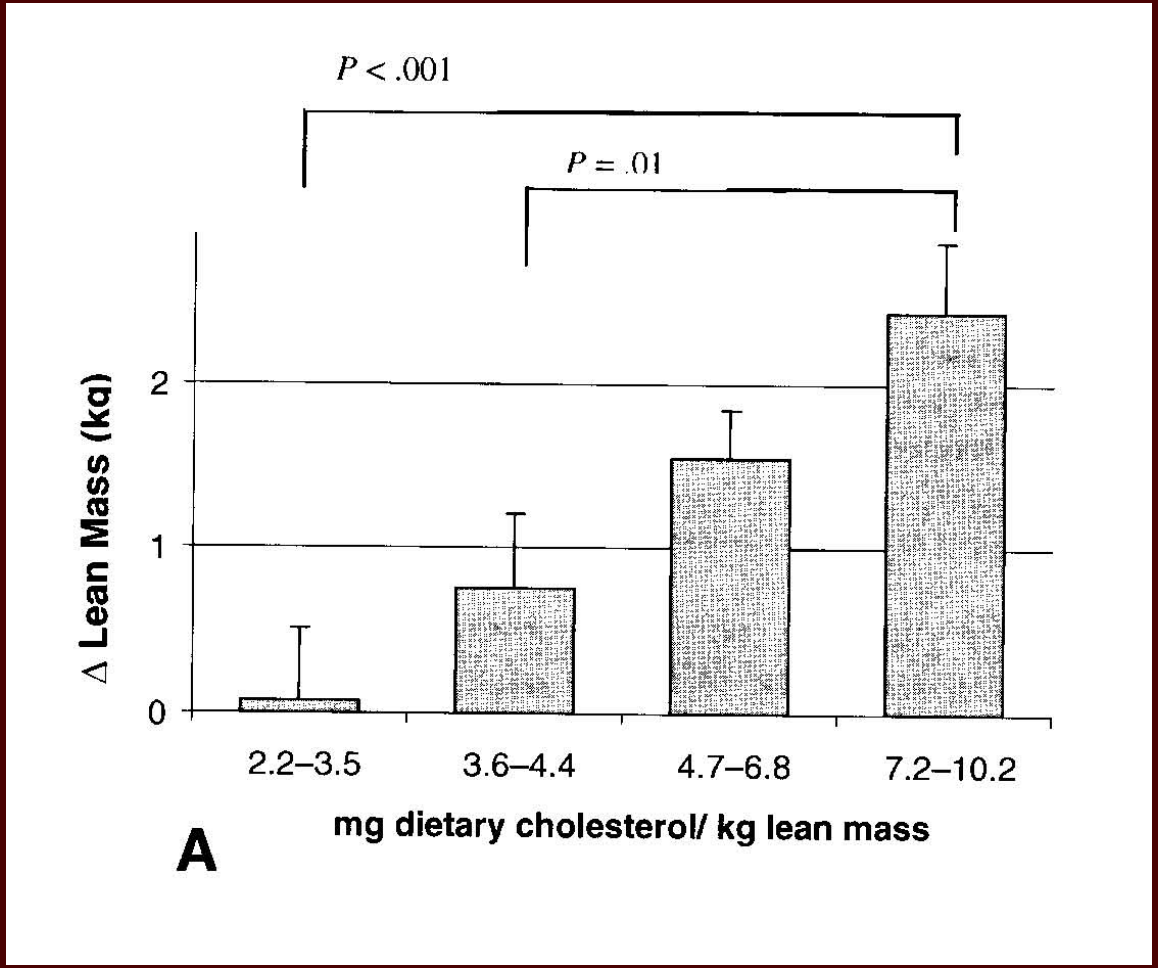
- 12 weeks, 3 times per week
- 8 exercises, 3 sets of 8-12 repetitions
- Resistance @70% of maximal strength
- Post Exercise protein supplement
- 24 hour food log (>36 total), Nutribase software
- Pre/Post blood, DEXA for body composition

Protein Intake and Muscle Gain



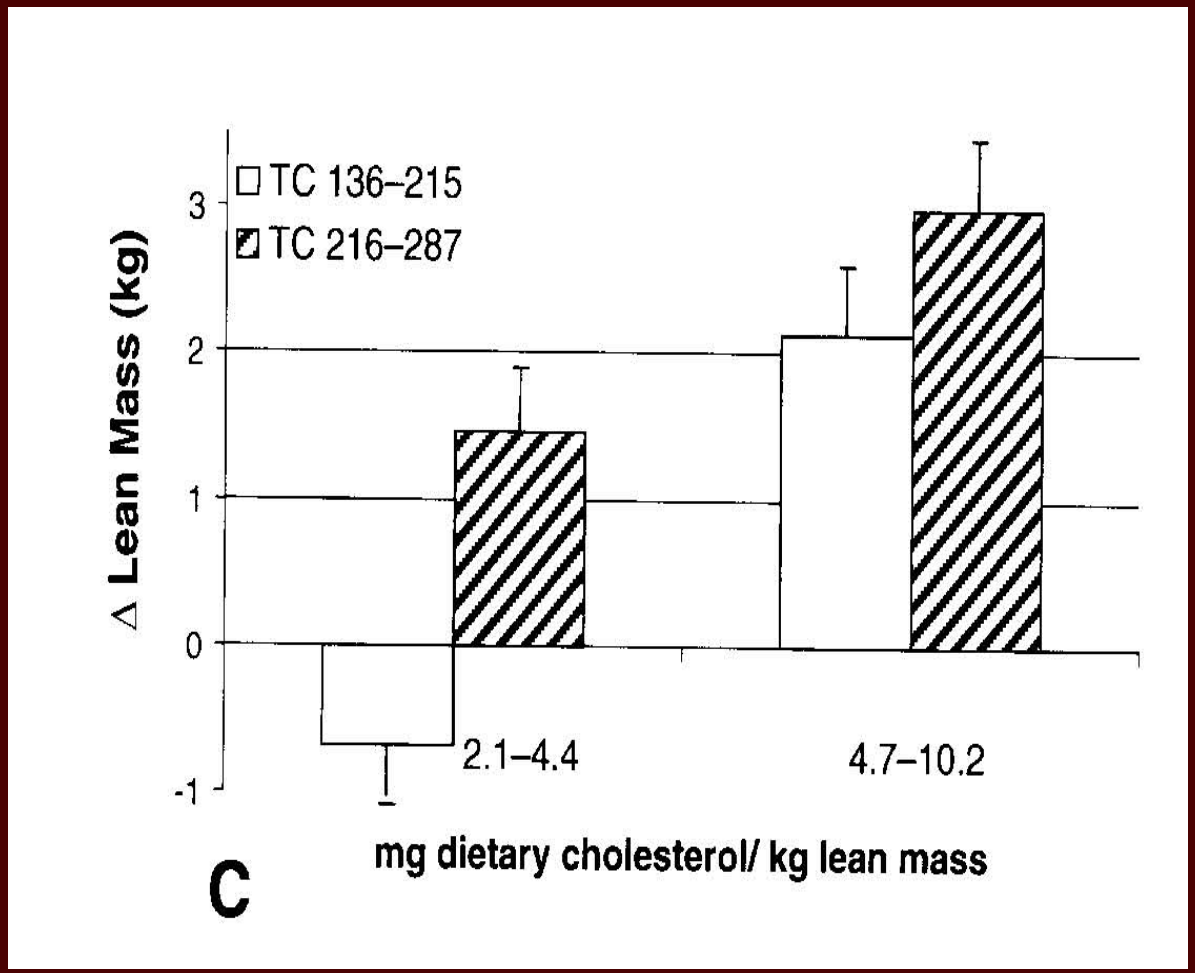
Andrews, IJSNEM, 2006

Dietary Cholesterol and Muscle Gain



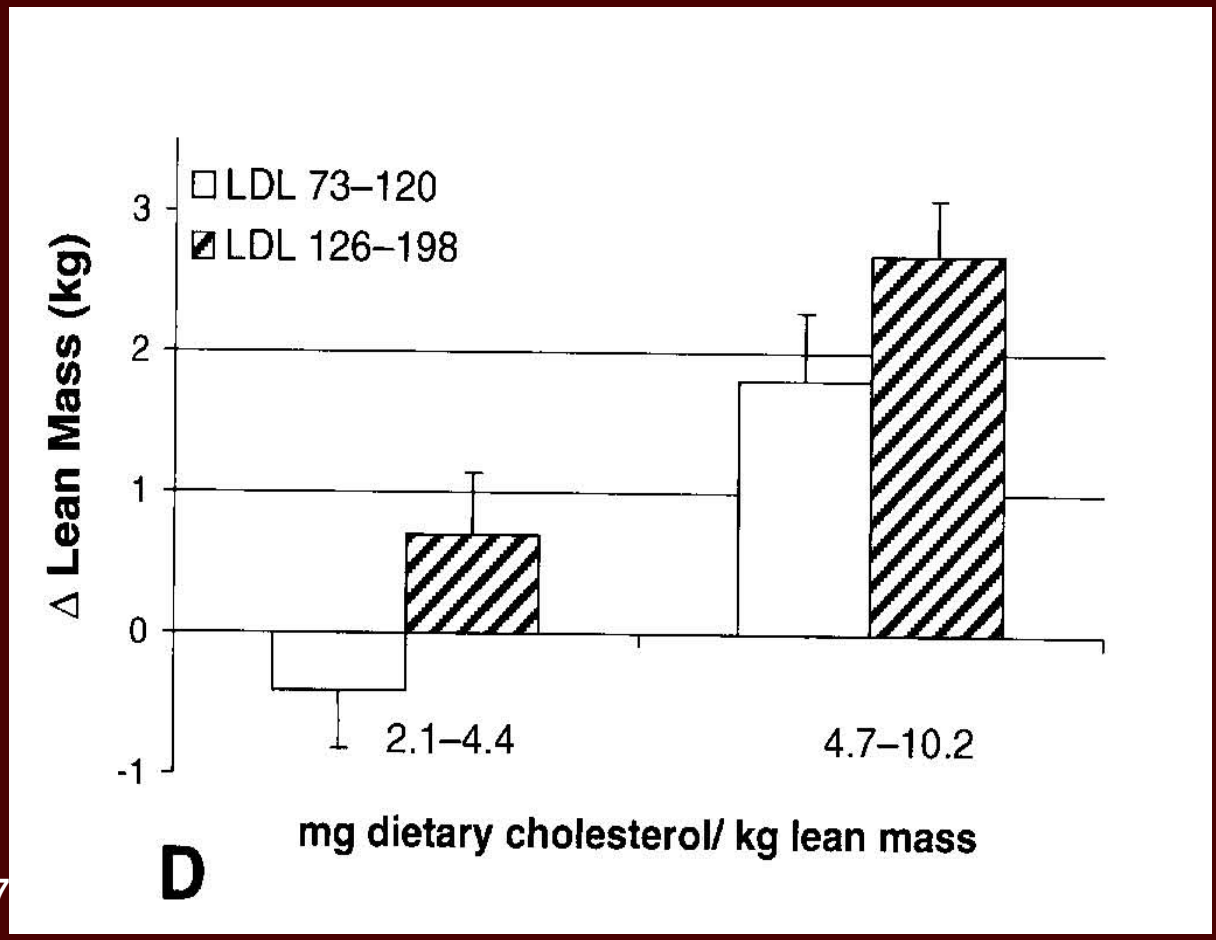
Riechman SE, J Gerontol, 2007

Blood Cholesterol and Muscle Gain



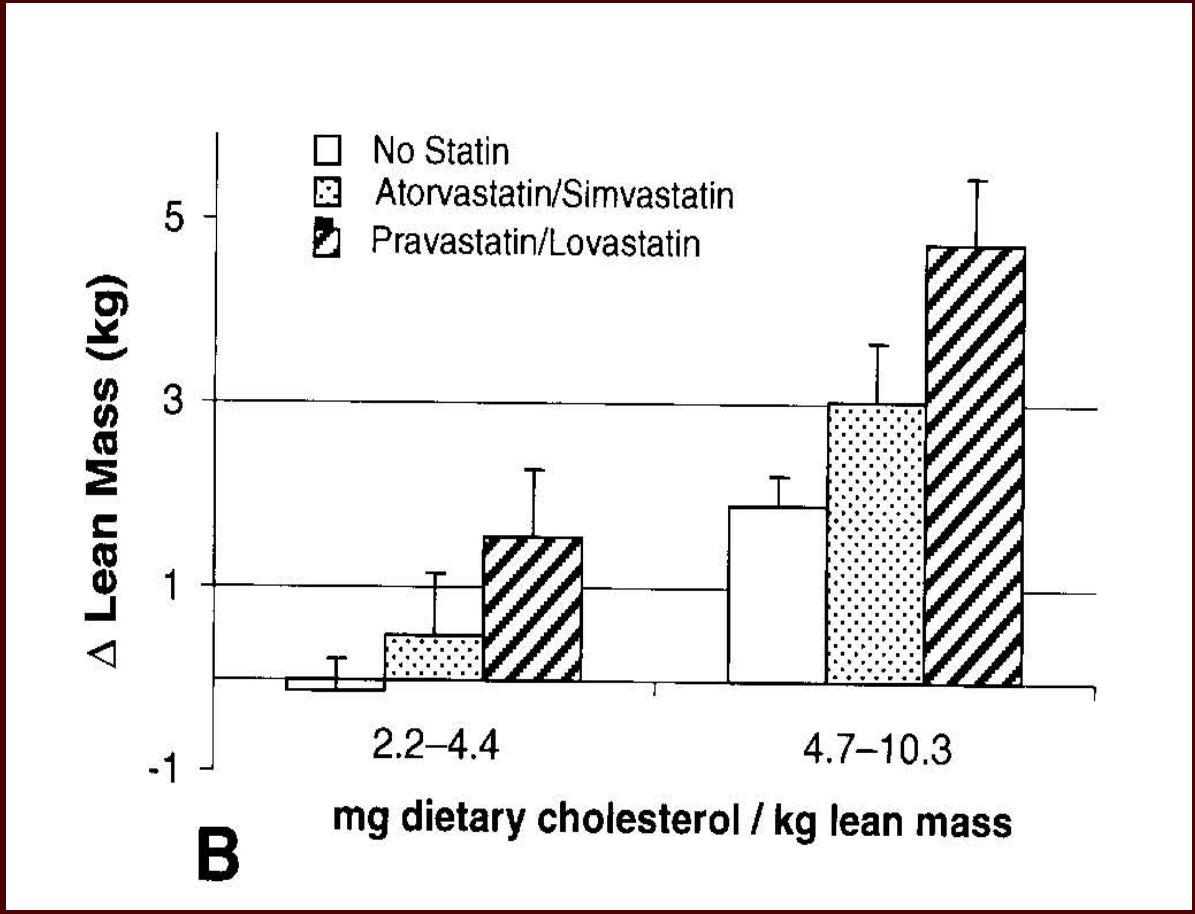
Riechman SE, J Gerontol, 2007

LDL and Muscle Gain



Riechman SE, J Gerontol, 2007

Statin and Muscle Gain



Riechman SE, J Gerontol, 2007

Regression

Change in lean mass: Dietary and blood cholesterol and statins

Cholesterol

Variable	Coefficient	p-value	r^2
Dietary (mg chol/kg)	0.5	<0.001	0.29
Blood (low/high)	0.7	0.007	0.10
Statins (no,Ato/Sim, Pra/Lov)	0.8	0.020	0.09
Constant	-3.0	0.001	

$r^2 = 0.48$

Riechman SE, J Gerontol, 2007

Alternate Explanation

- Dietary protein sources may have other micronutrients such as creatine that are highly correlated to dietary cholesterol and are responsible for the muscle effects.
- Current dietary databases do not include creatine though creatine is well established as enhancing muscle performance with exercise training.

Possible Mechanisms

- Building Block
- Inflammatory Response
- Steroids
- Lipid Rafts

Lipid Rafts

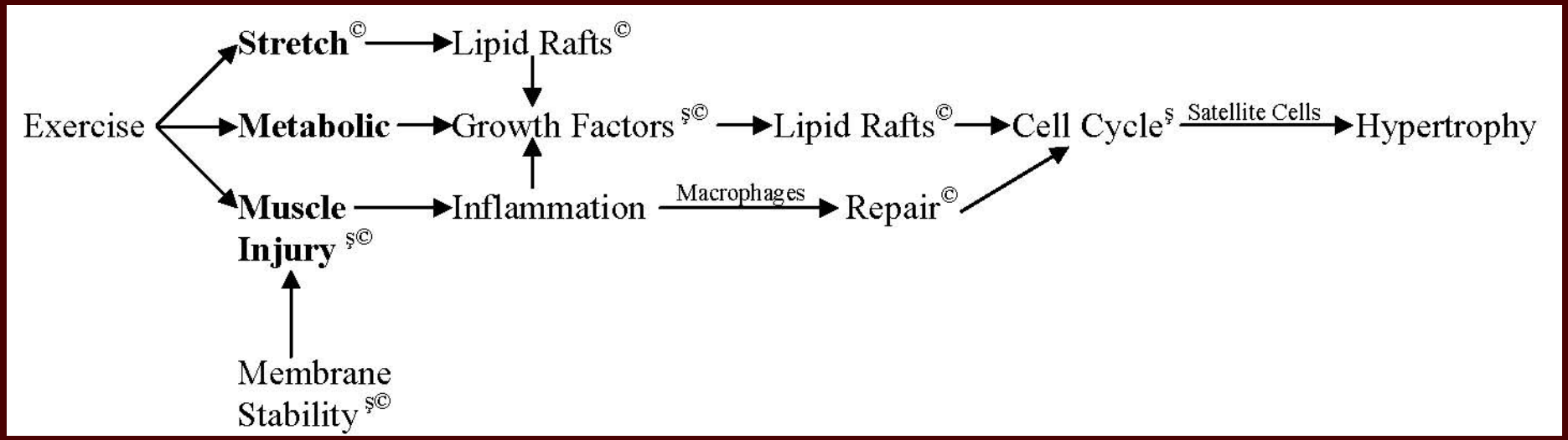
- **Cholesterol is essential to the formation of lipid rafts which function as platforms for the assembly of components of signaling pathways**

- **Cholesterol depletion can induce protein missorting and reduced signal transduction**

- **Lipid rafts have been implicated as essential for signaling through many pathways**

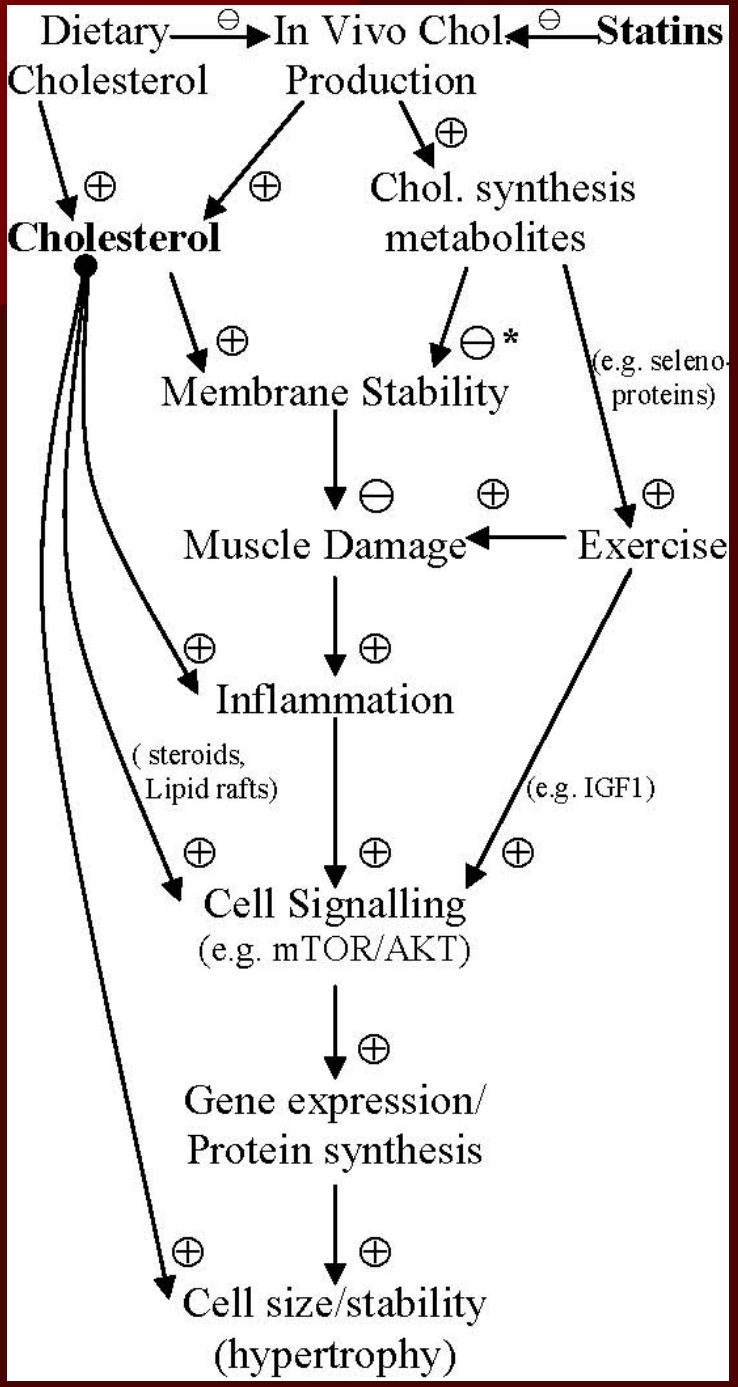
  (Src tyrosine kinases, Ras , NOS, PKCα, GPI-linked proteins, G-protein α subunits, **insulin** receptor, **IGF1** receptor, TNFα, NF-κβ, PI3K, PKC, EGFR, PDGFR, IL6, ERK2, AKT1 and **steroid hormone** receptor)

Exercise & Muscle Hypertrophy



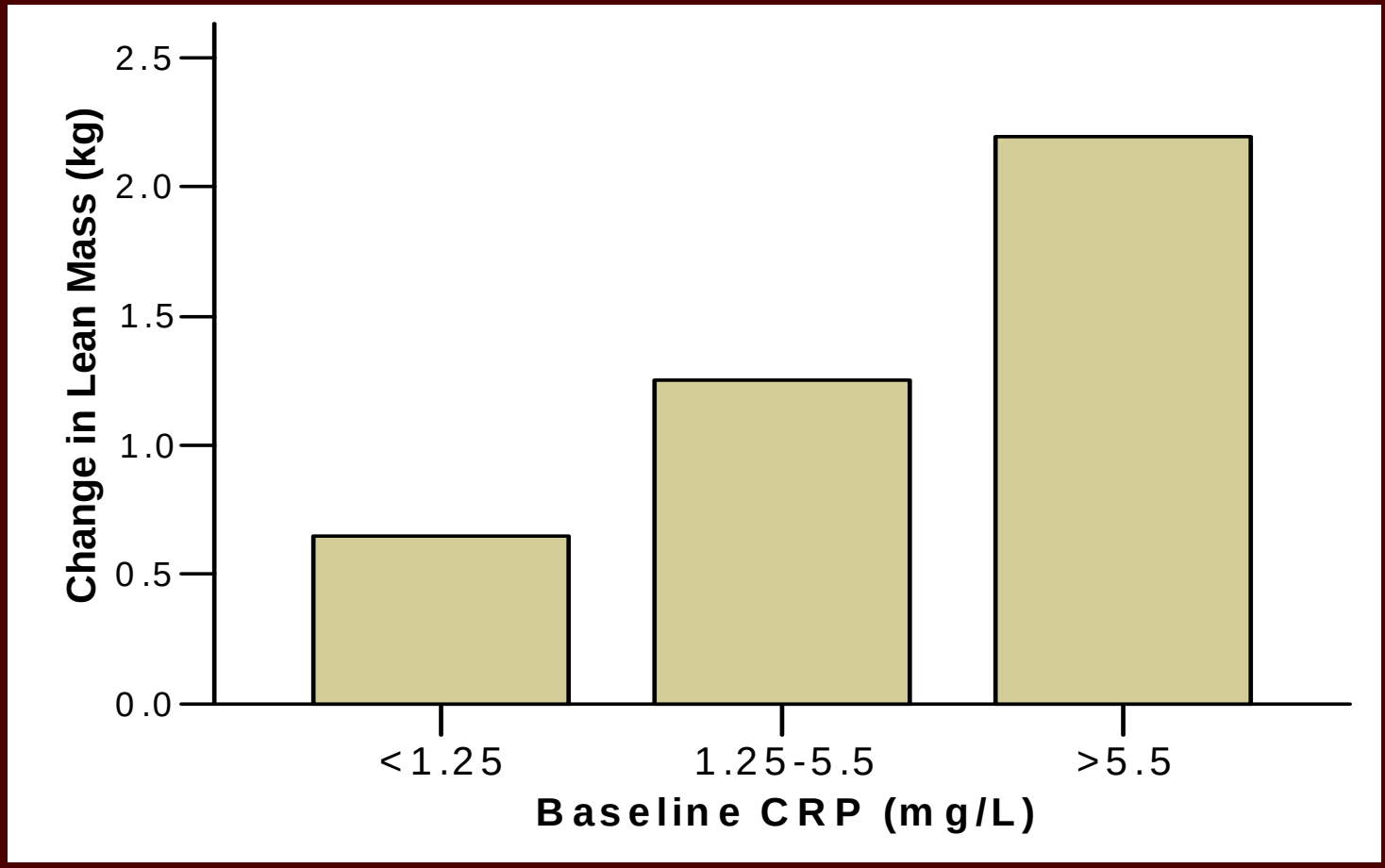
Riechman SE et al. World Rev Nutr 2009, 100: 71-79.

Cholesterol and Hypertrophy



Riechman SE et al. World Rev Nutr 2009, 100: 71-79.

Inflammation and Hypertrophy

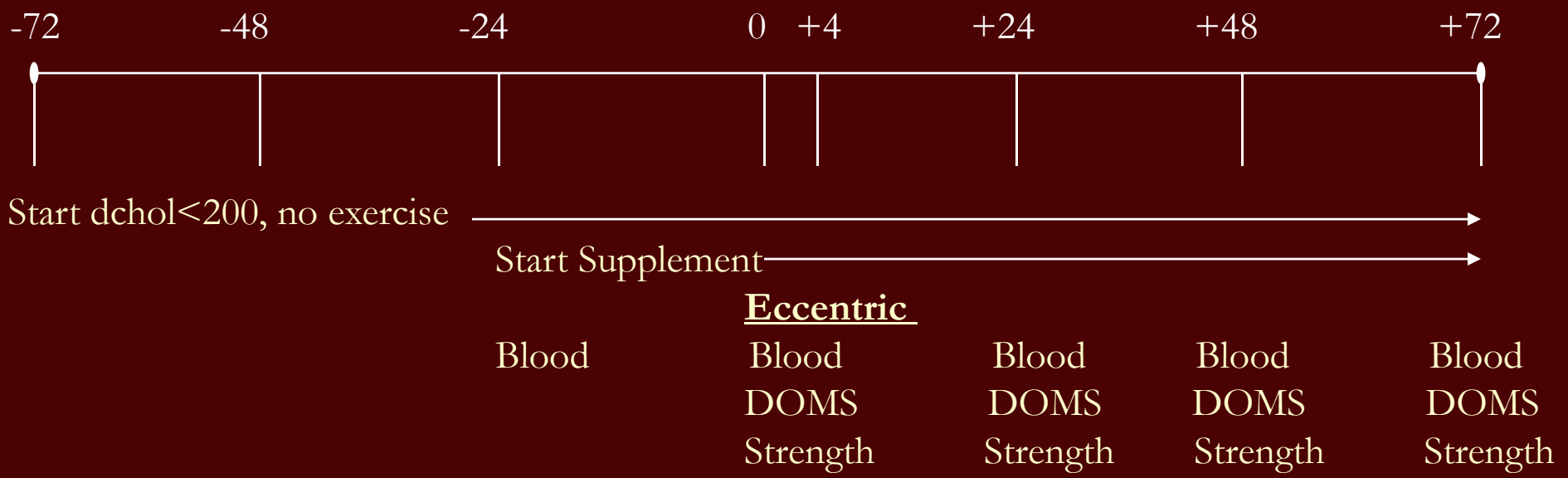


Riechman SE, J Gerontol, 2007

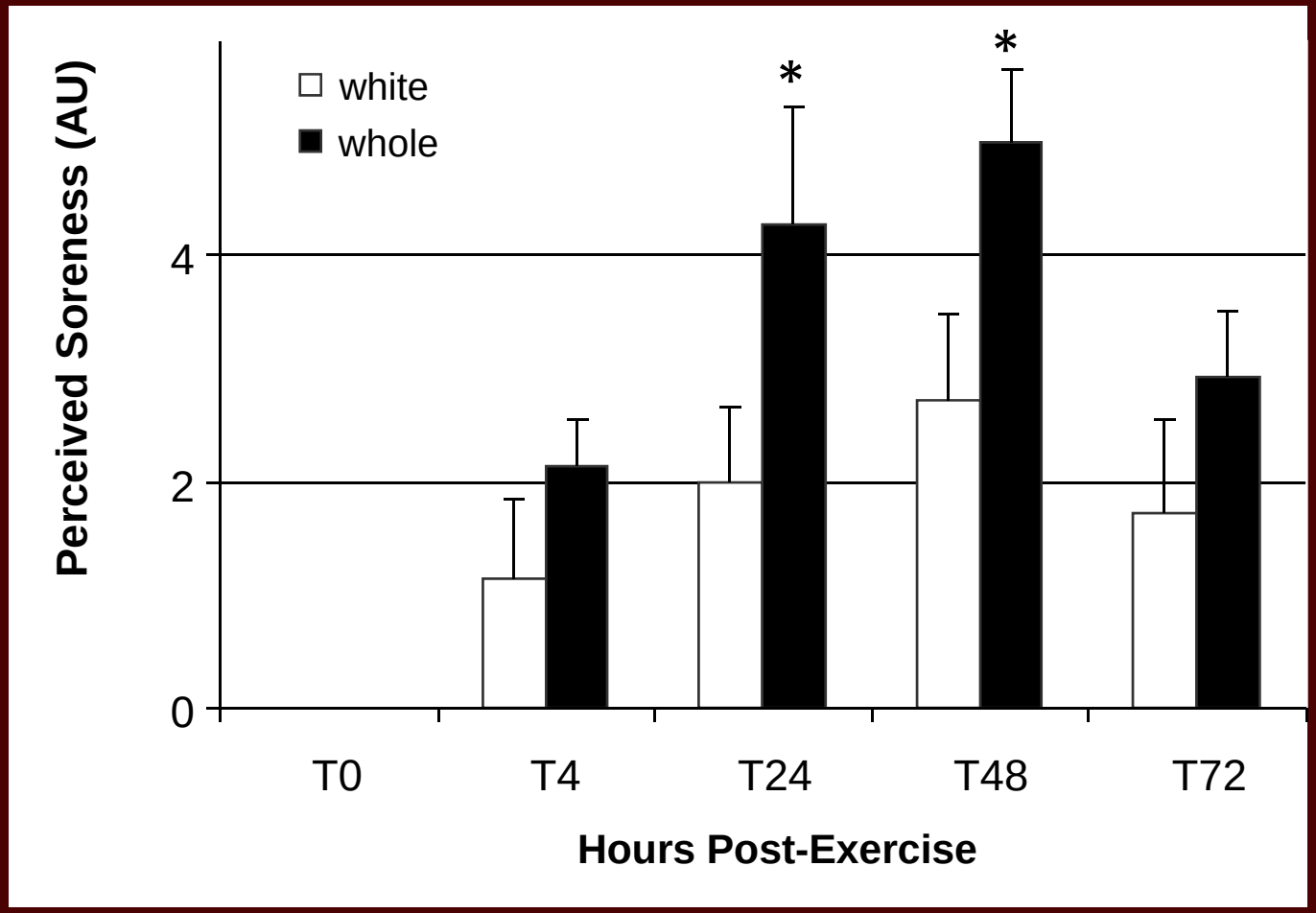
Dietary Cholesterol and Muscle Damage

- 8 recreationally active subjects underwent a rigorous 100 repetition training session of eccentric knee flexion and extension on a Biodex Isokinetic Dynamometer
- Subjects performed two trials, one under restricted dietary cholesterol (<200 mg) and one with supplemental dietary cholesterol (600 mg, ~800 total)
- Hypothesis: Supplemental cholesterol will reduce markers of muscle damage suggesting faster recovery

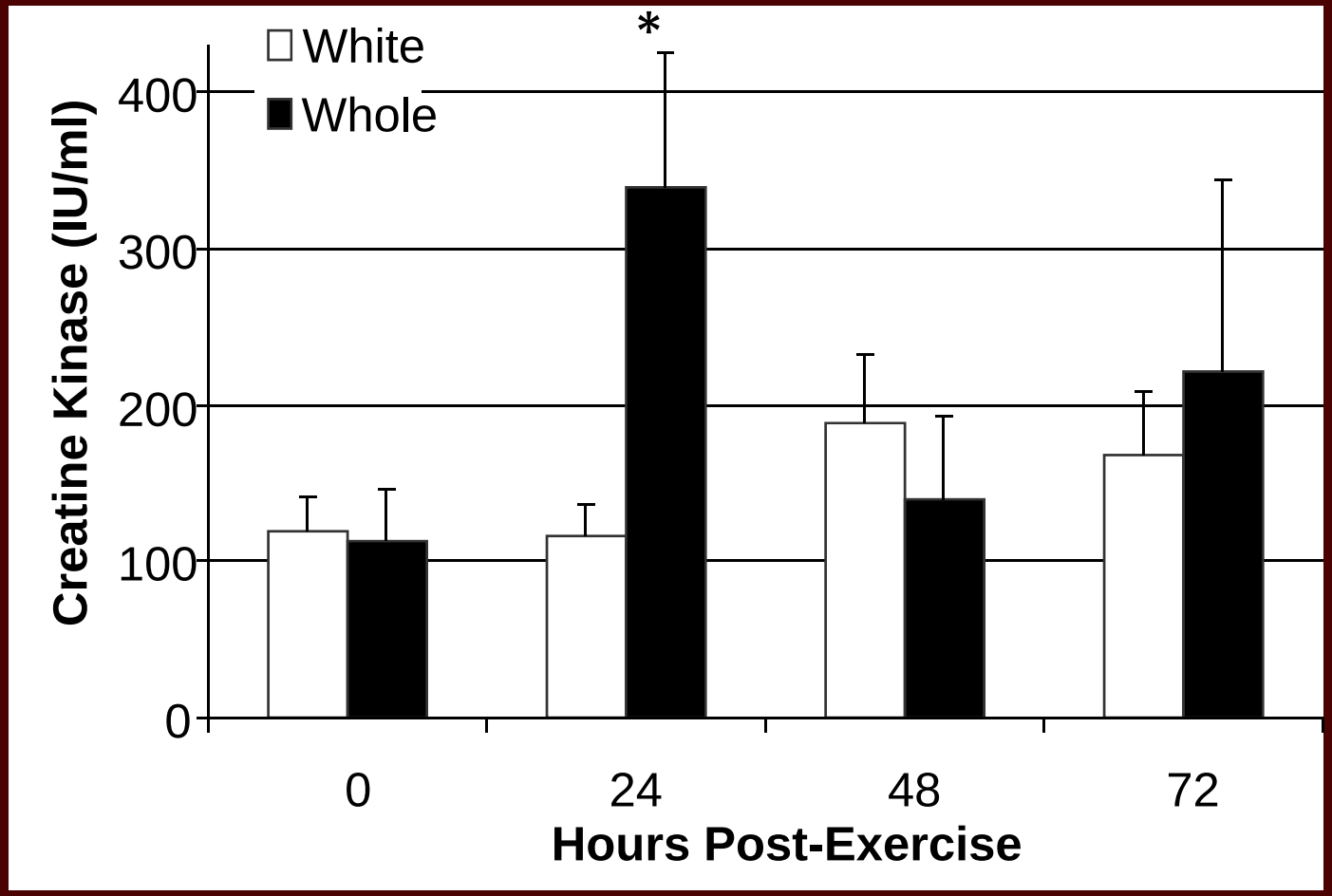
Muscle Damage Study Design



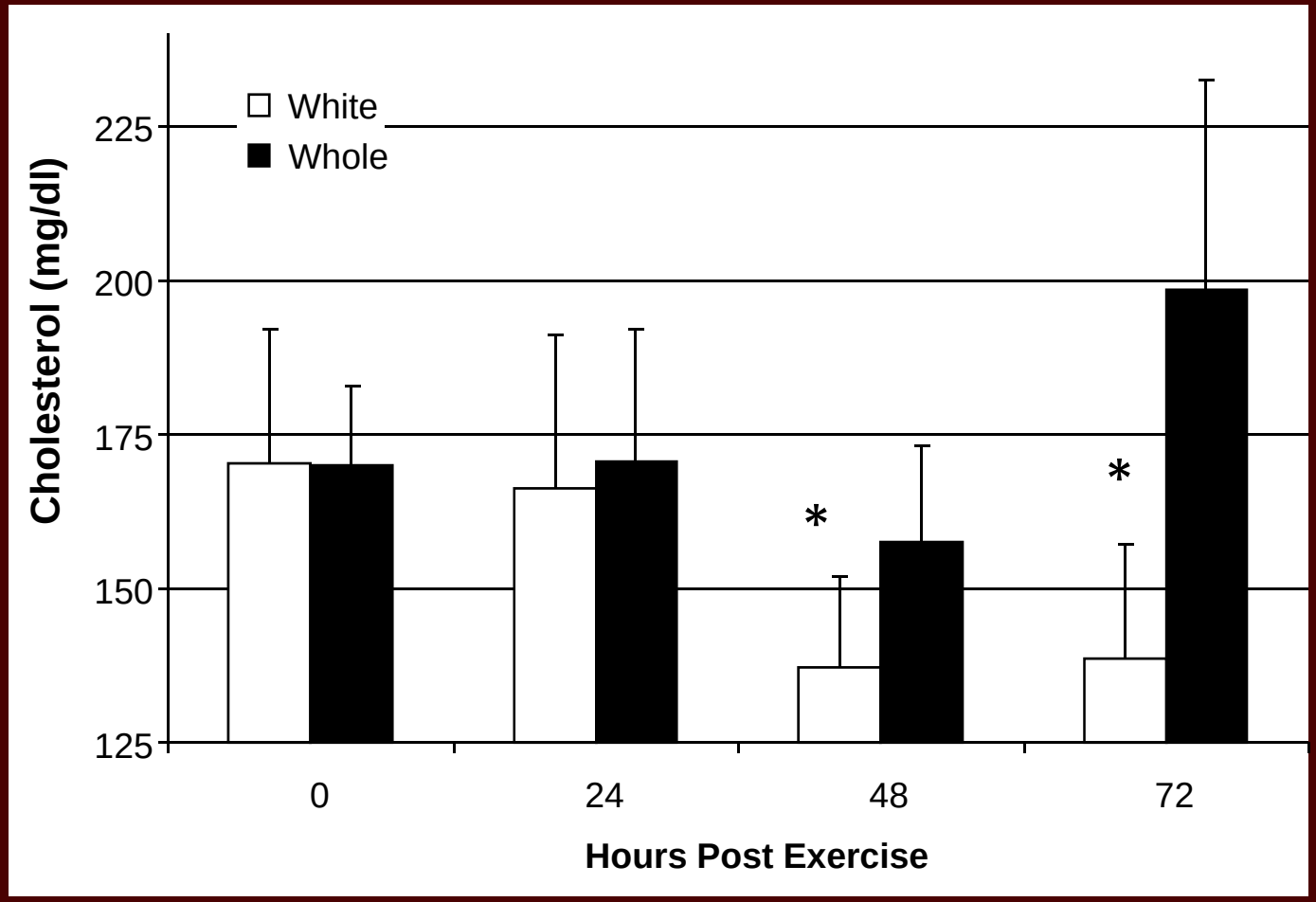
Soreness


white
whole
*
*
Perceived Soreness (AU)
0
2
4
T0
T4
T24
T48
T72
Hours Post-Exercise

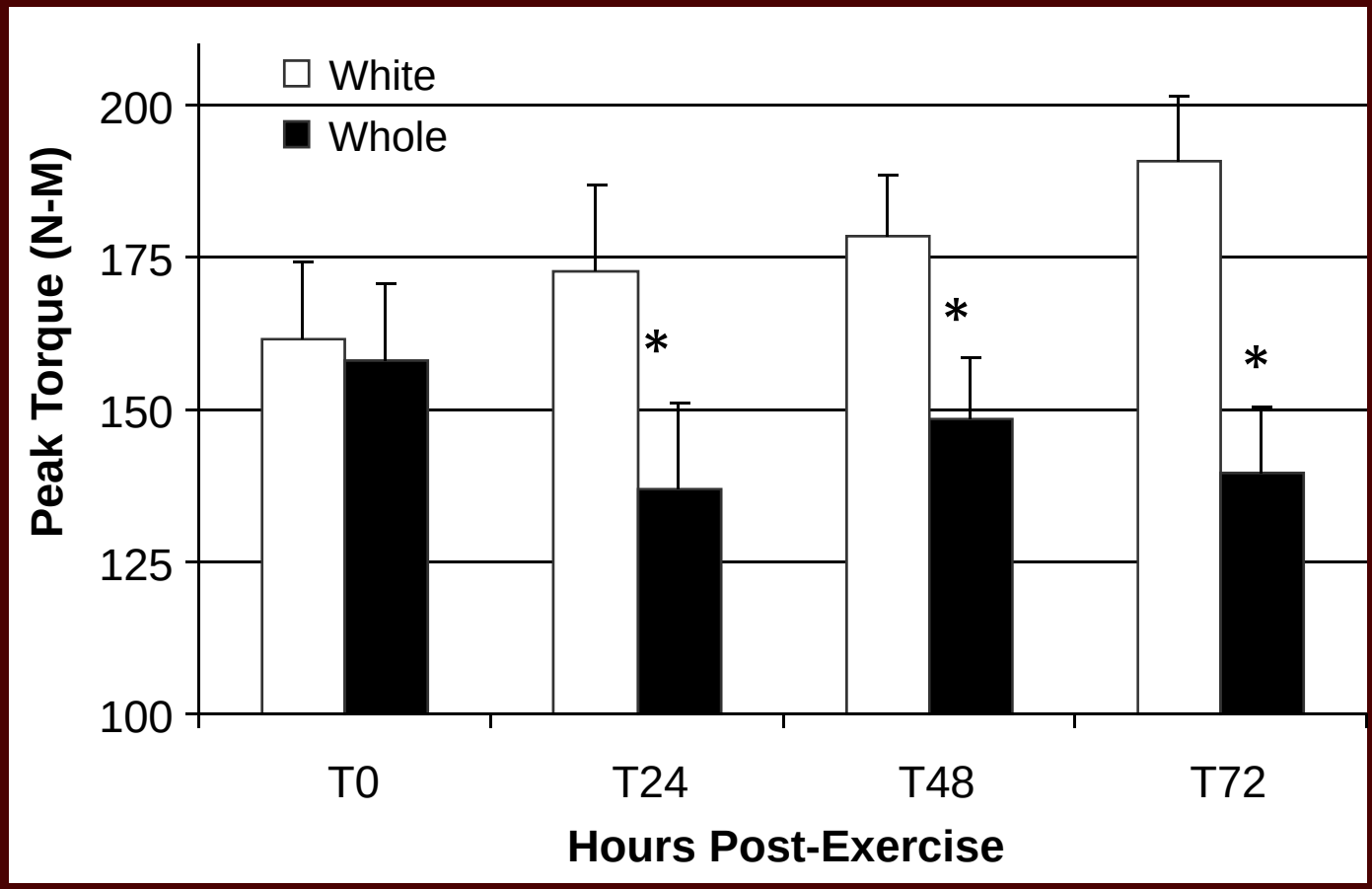
Blood Creatine Kinase



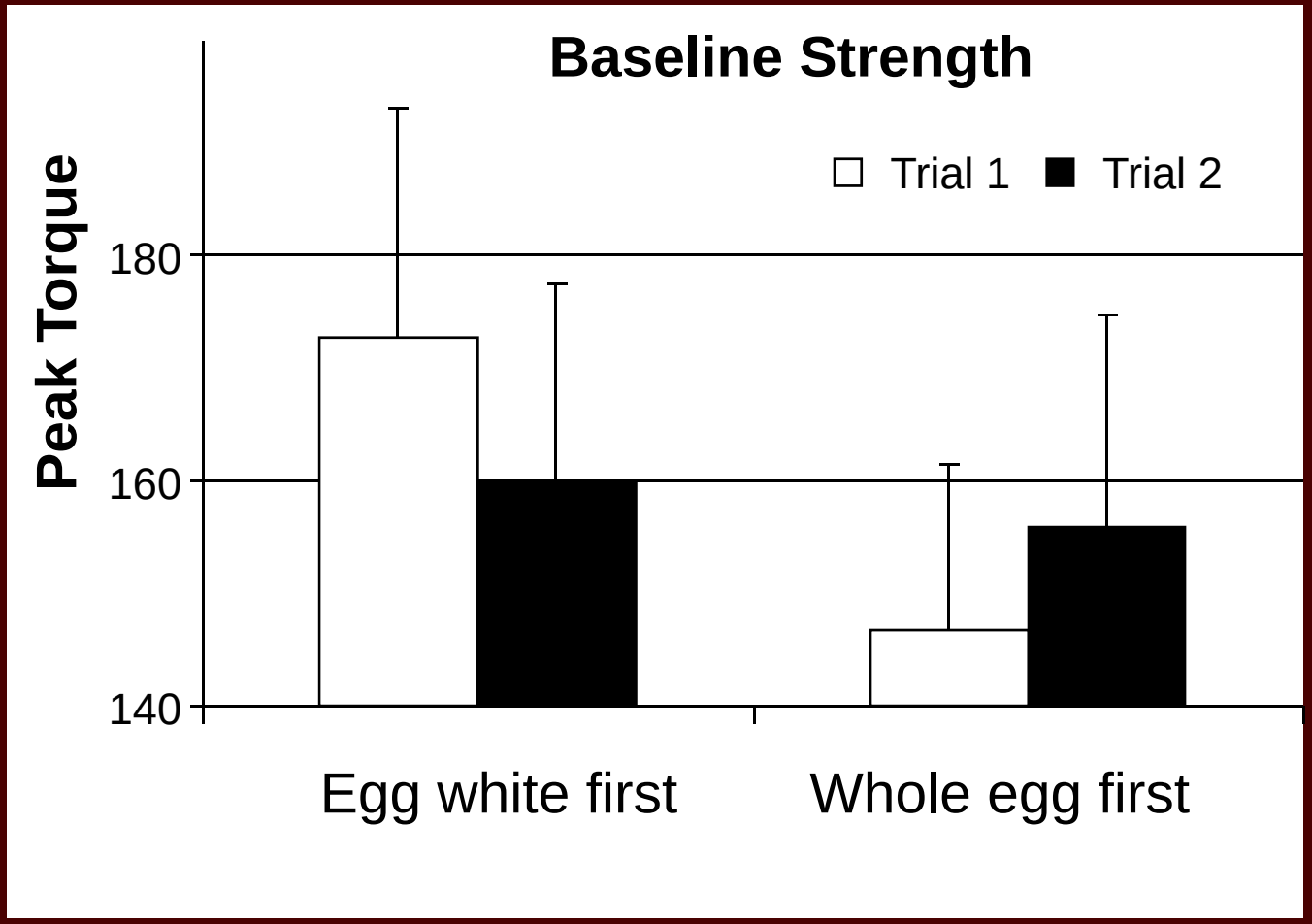
Blood Cholesterol



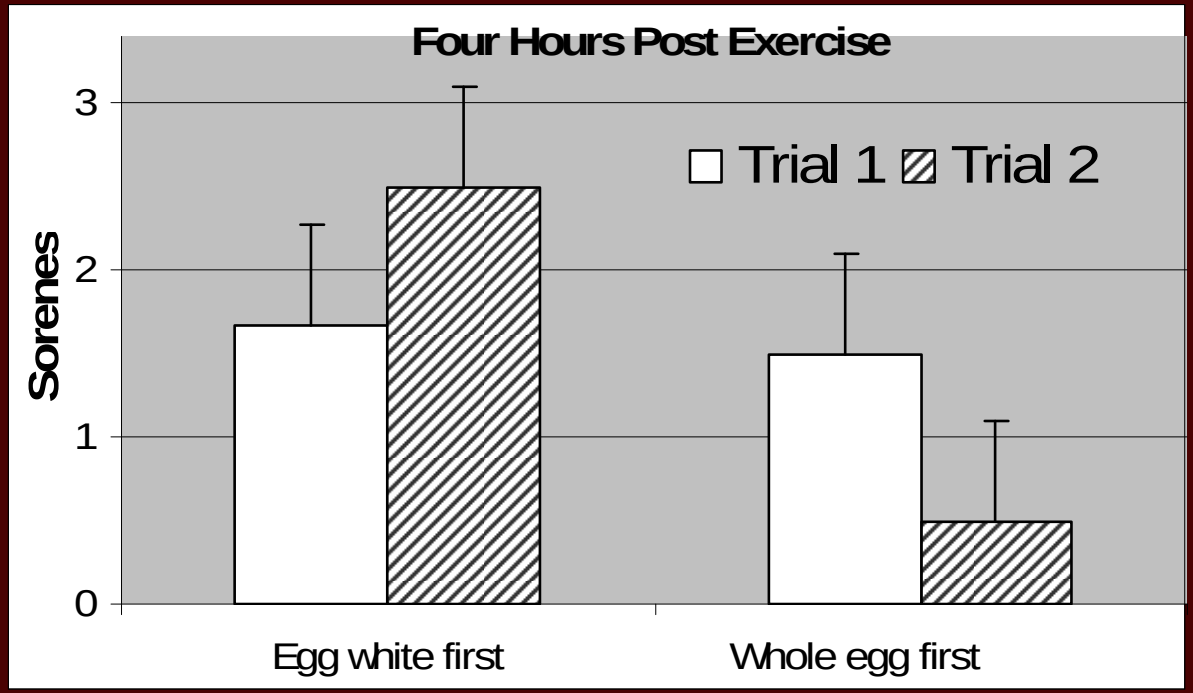
Strength Loss



Repeated Trial Strength



Repeated Trial Soreness



Tentative Conclusion : Dietary Cholesterol exacerbates the short-term negative impact of an eccentric exercise bout but improves long term recovery

Resistance Training and Dietary Cholesterol

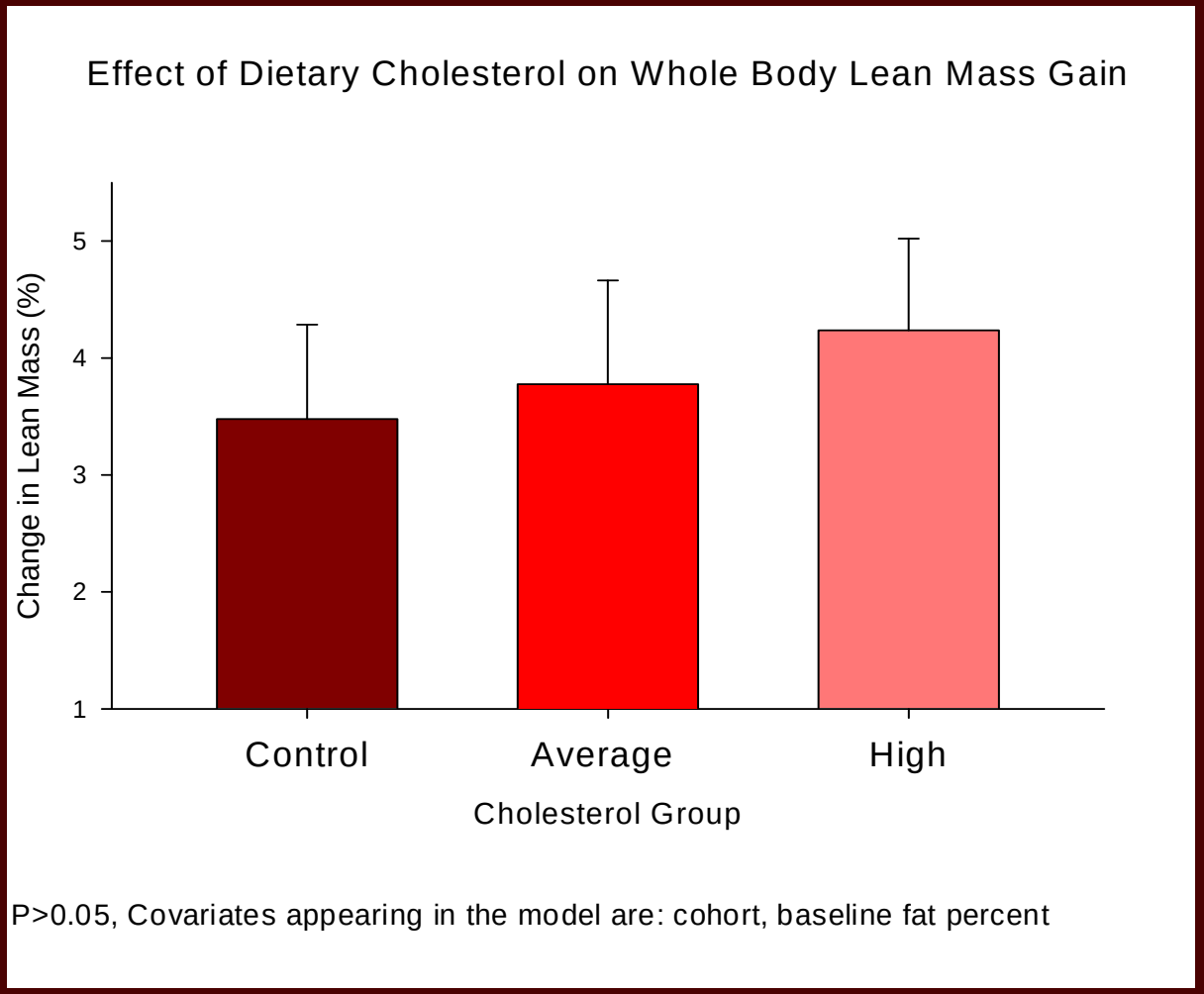
- Women and men, age 50-69, generally healthy, blood cholesterol <215 mg/dl
- 12 weeks of RET (same design as MERET II) using Keiser RET equipment

Funded by: U.S. Poultry and Egg Association

Resistance Training and Dietary Cholesterol

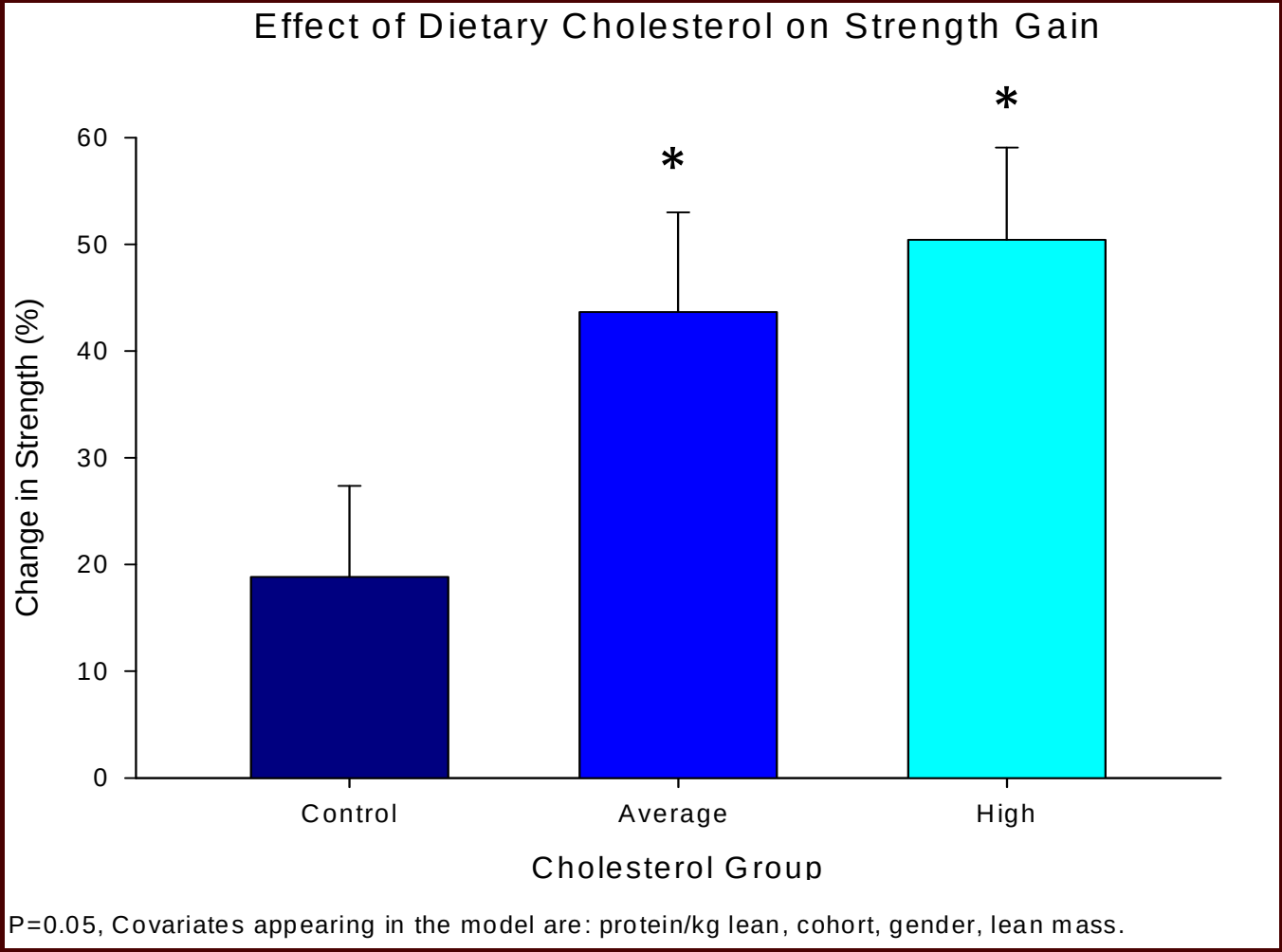
- Randomize N=36 to zero, ~200 or 600 mg supplemental cholesterol daily (N=12/group)
- Food cholesterol restricted to <200 mg
- Double-Blind administration in a protein drink
- Daily food intake log (Nutribase software)

Lean Mass Gain



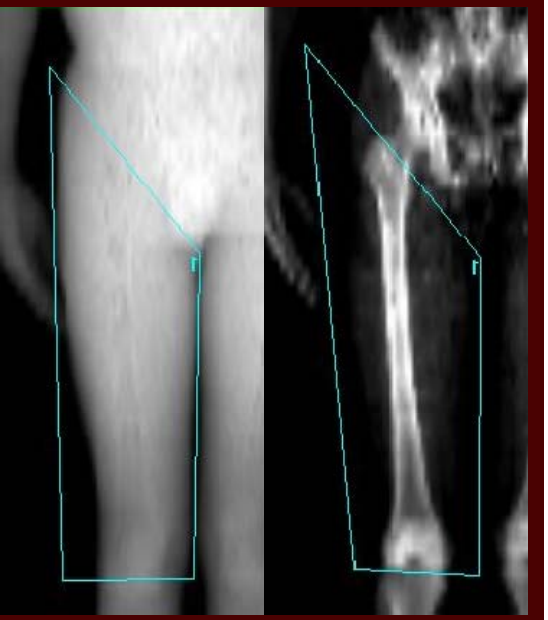
P>0.05, Covariates appearing in the model are: cohort, baseline fat percent

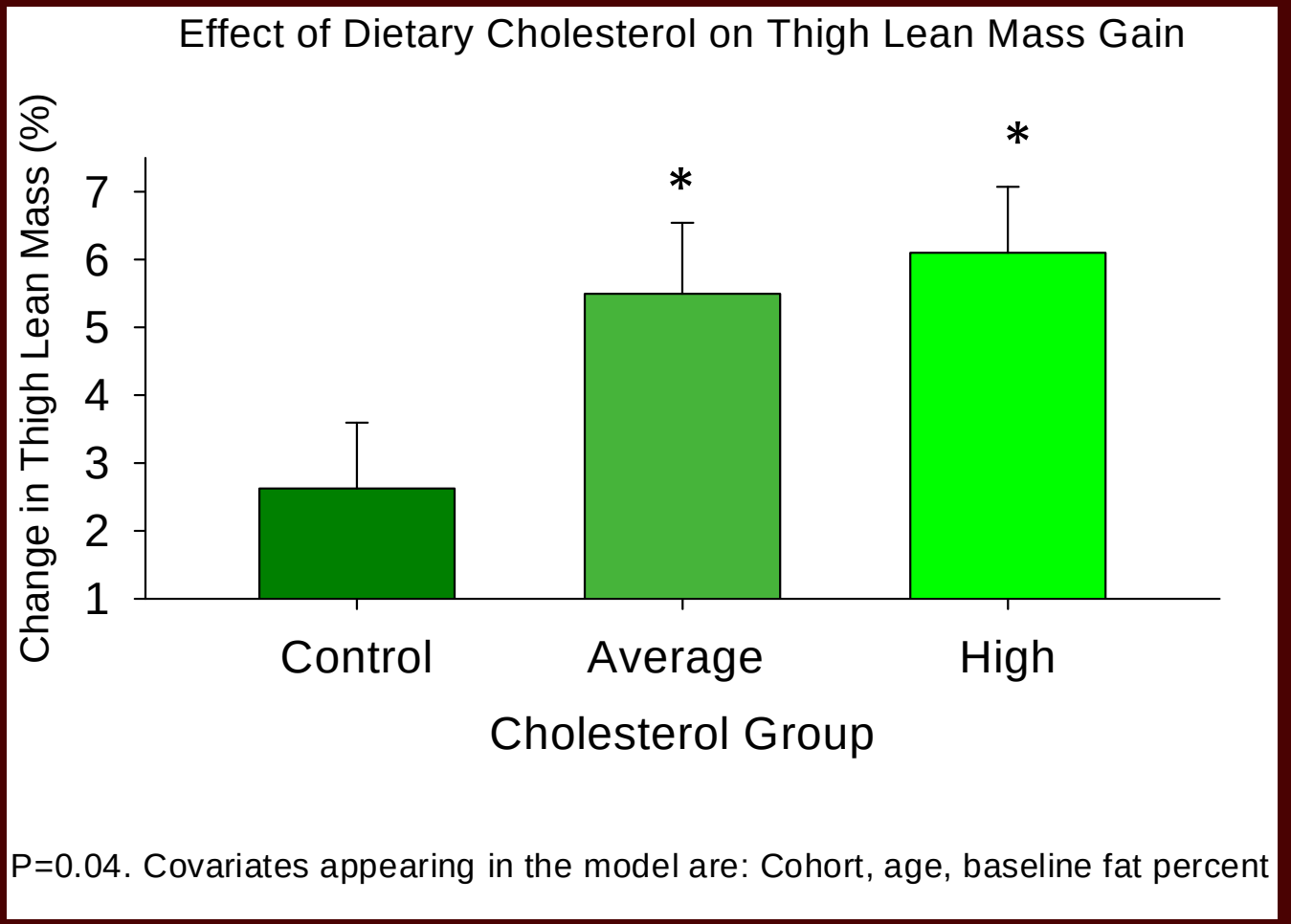
Strength Gain



P=0.05, Covariates appearing in the model are: protein/kg lean, cohort, gender, lean mass.

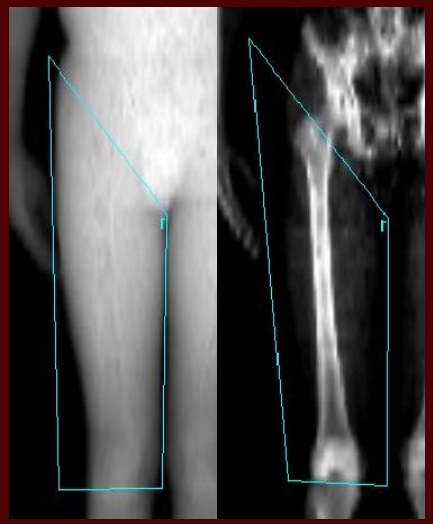
Thigh Muscle Gain

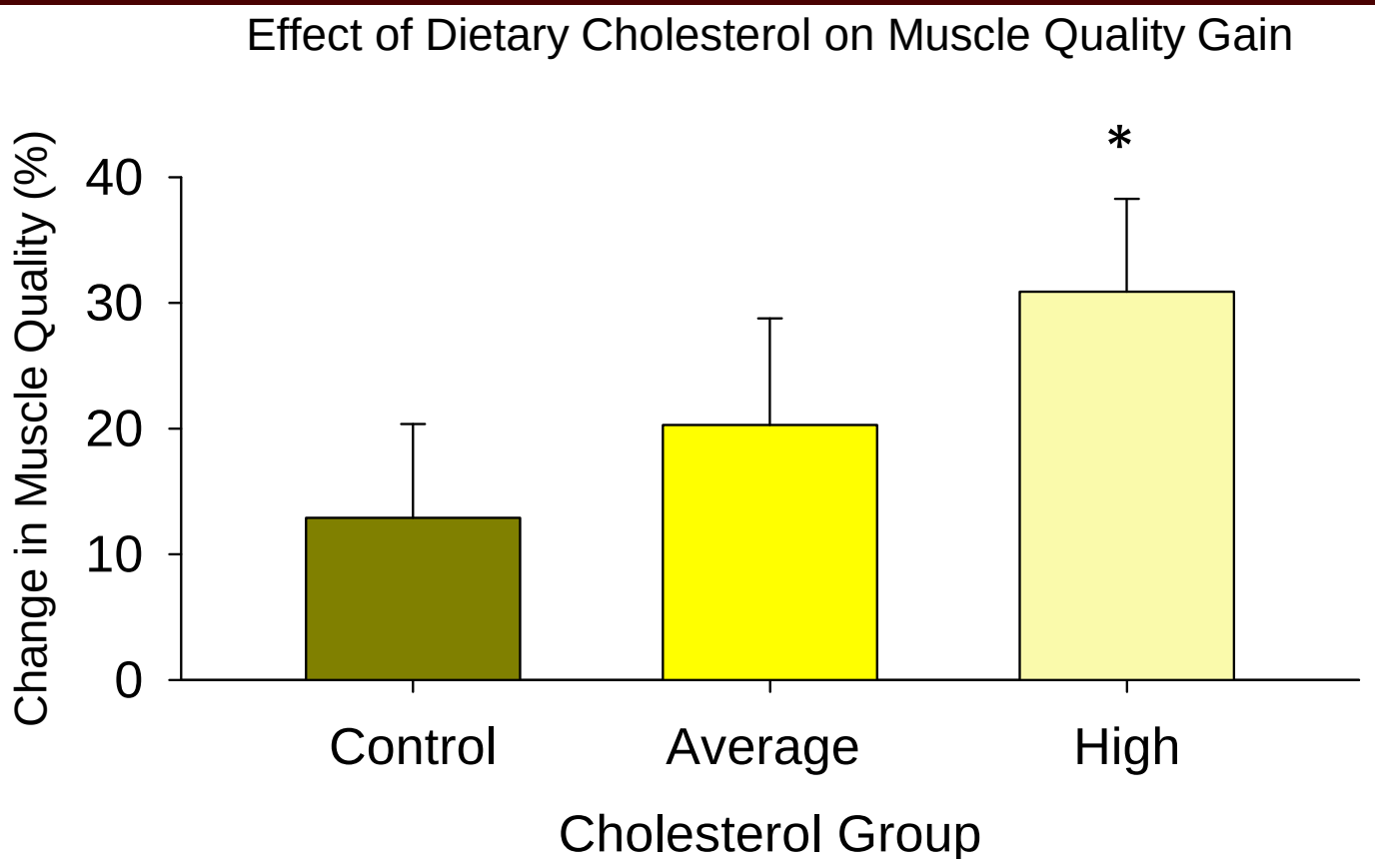




P=0.04. Covariates appearing in the model are: Cohort, age, baseline fat percent

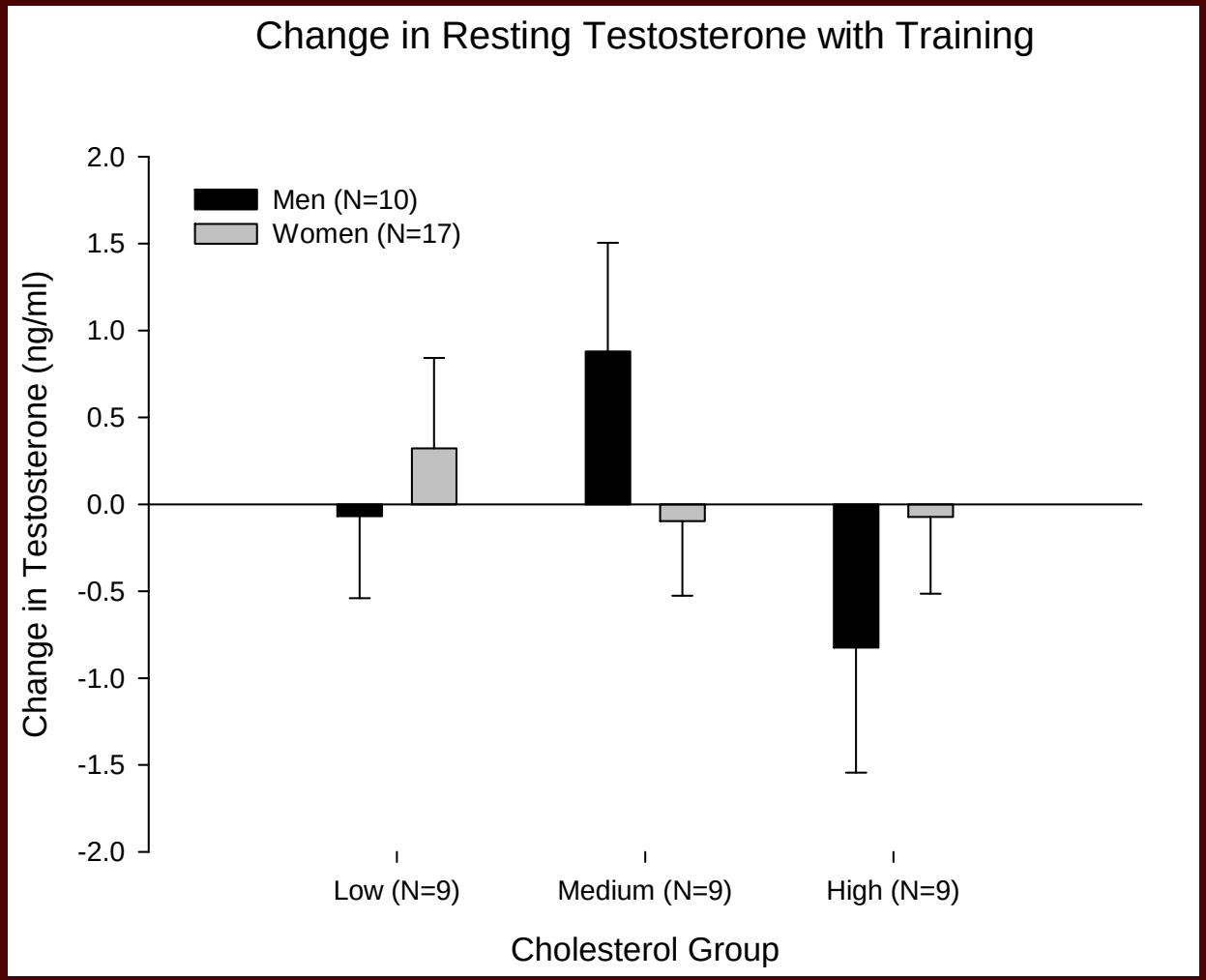
Muscle Quality Gain



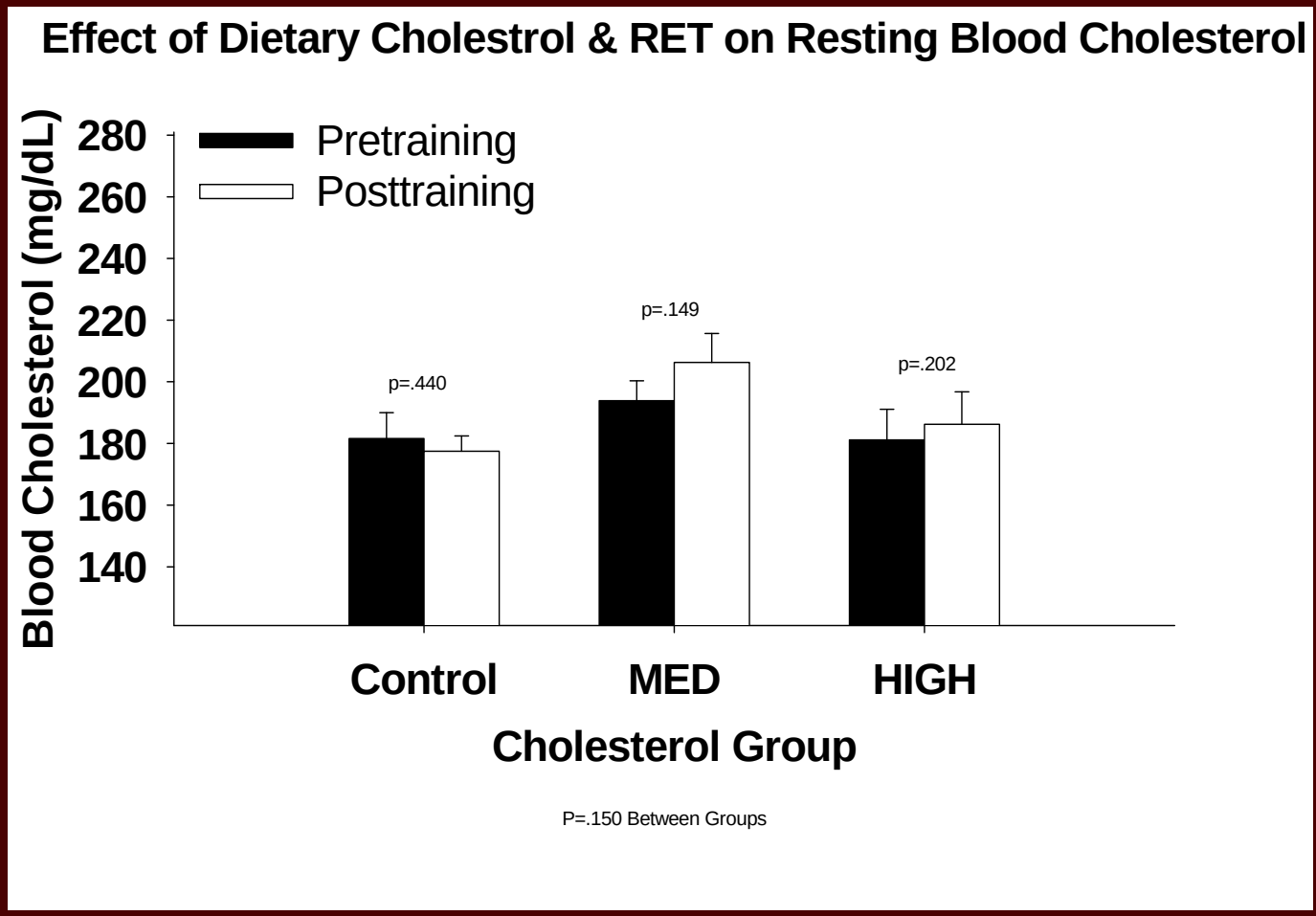


P>0.05, Covariates appearing in the model are: protein/kg lean, gender, lean mass.

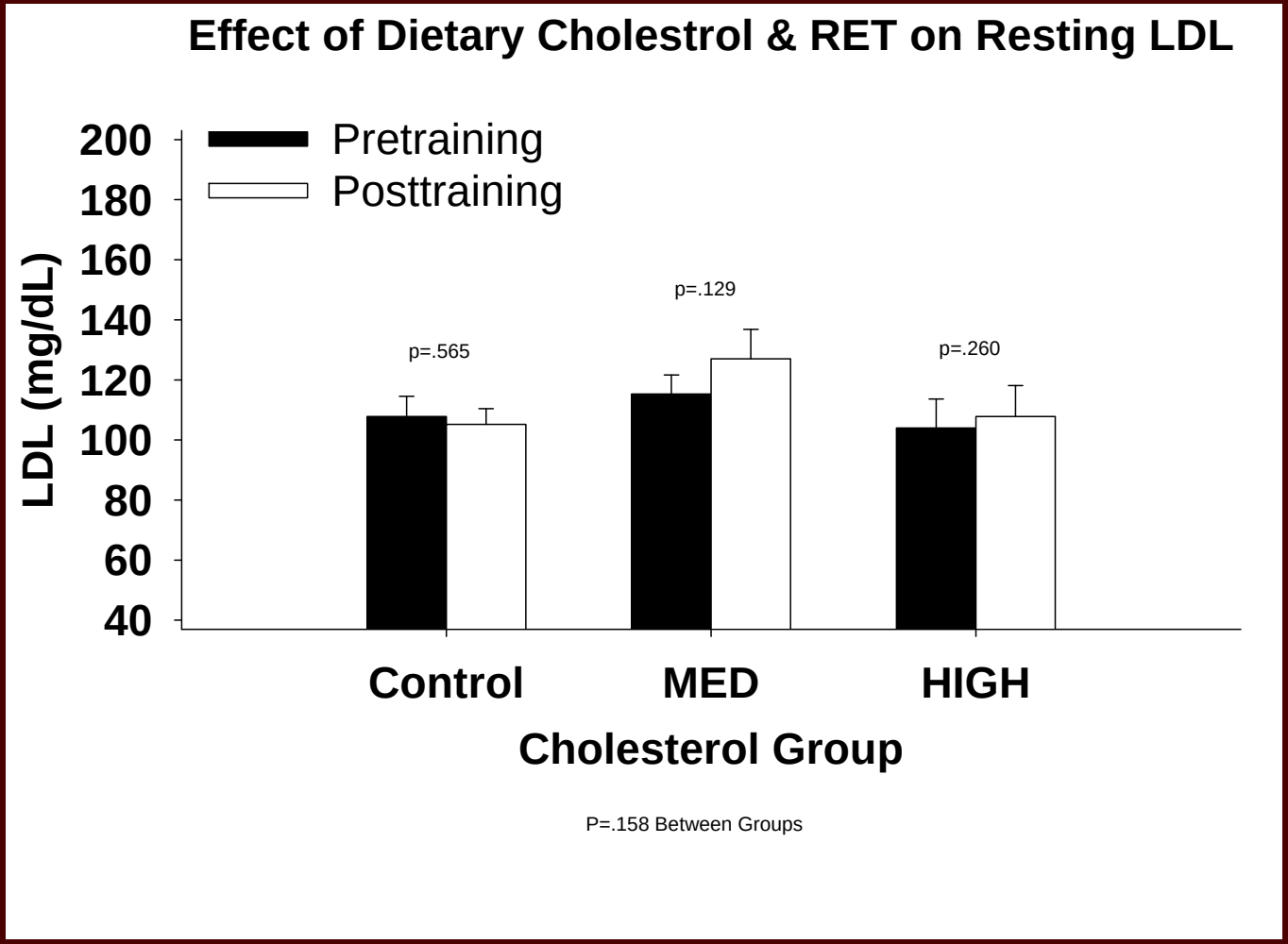
Testosterone



Dietary and Blood Cholesterol

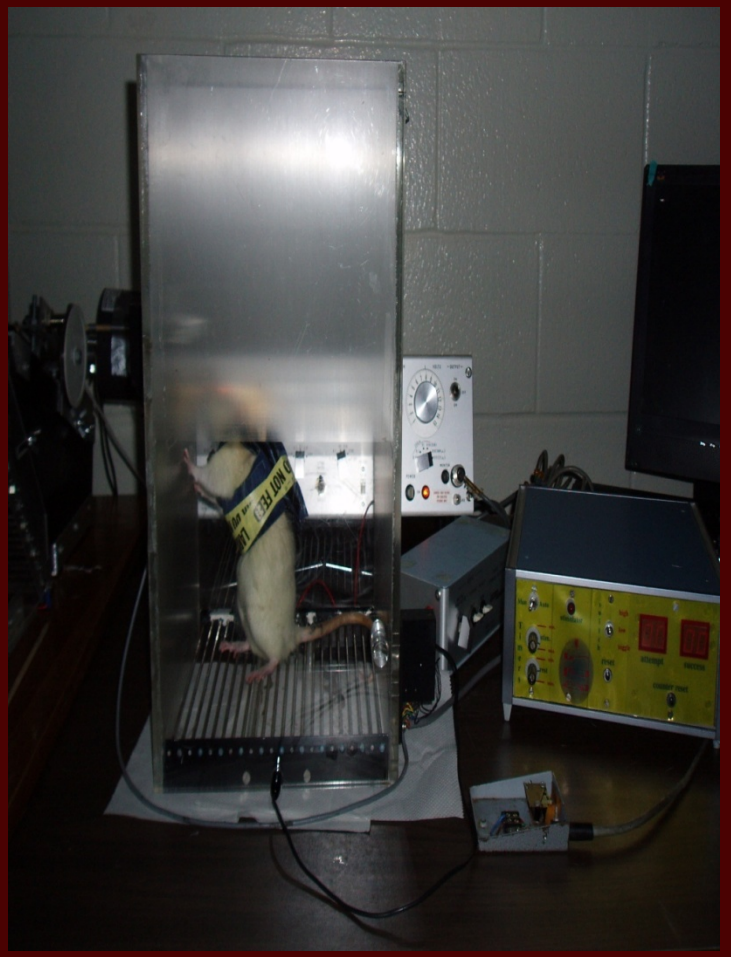


Dietary Cholesterol and LDL



Cholesterol, Hypertrophy in Rats

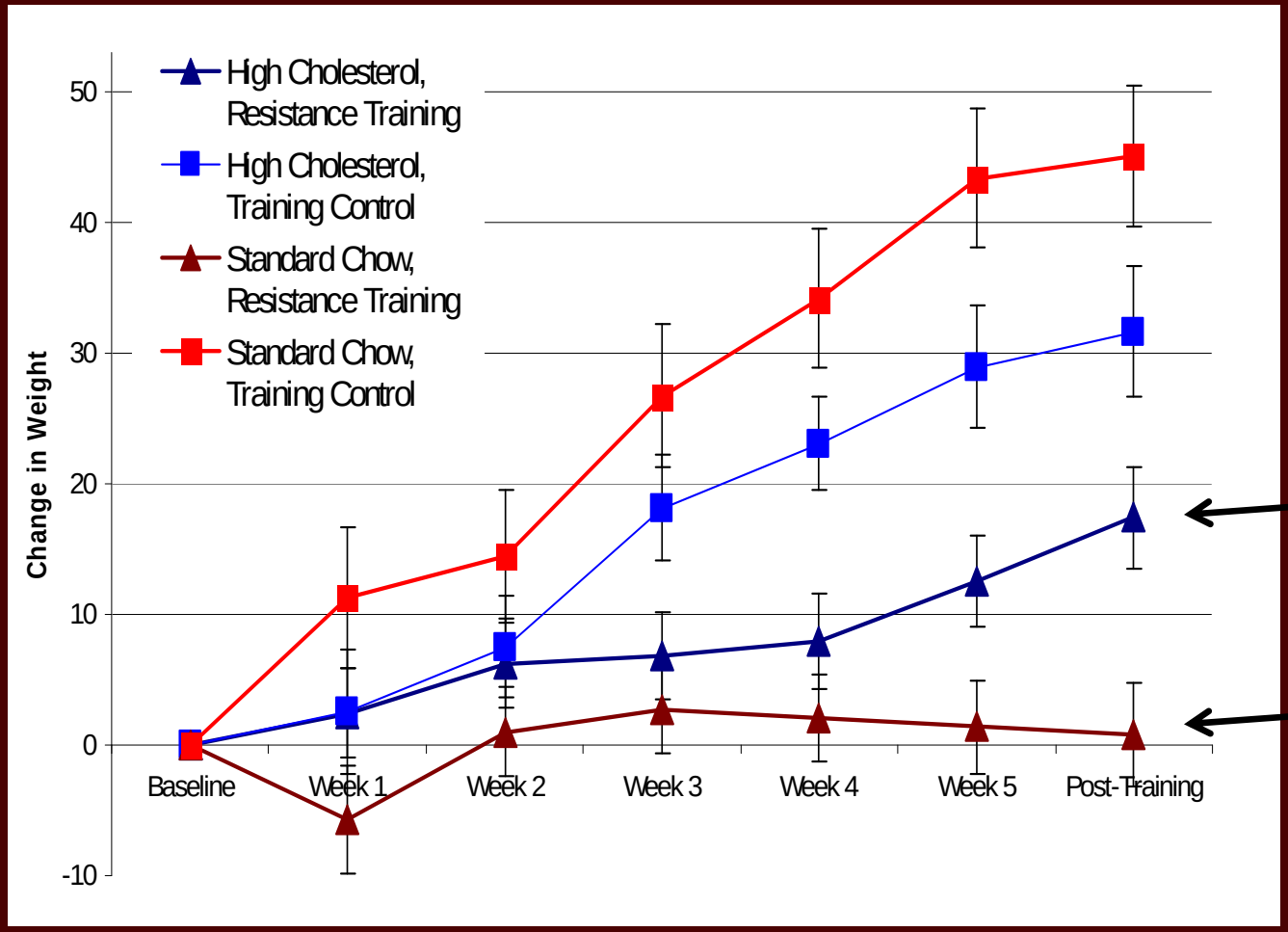
Purpose: Develop a parallel model in rats to accelerate discovery of the mechanisms of cholesterol effects on muscle hypertrophy

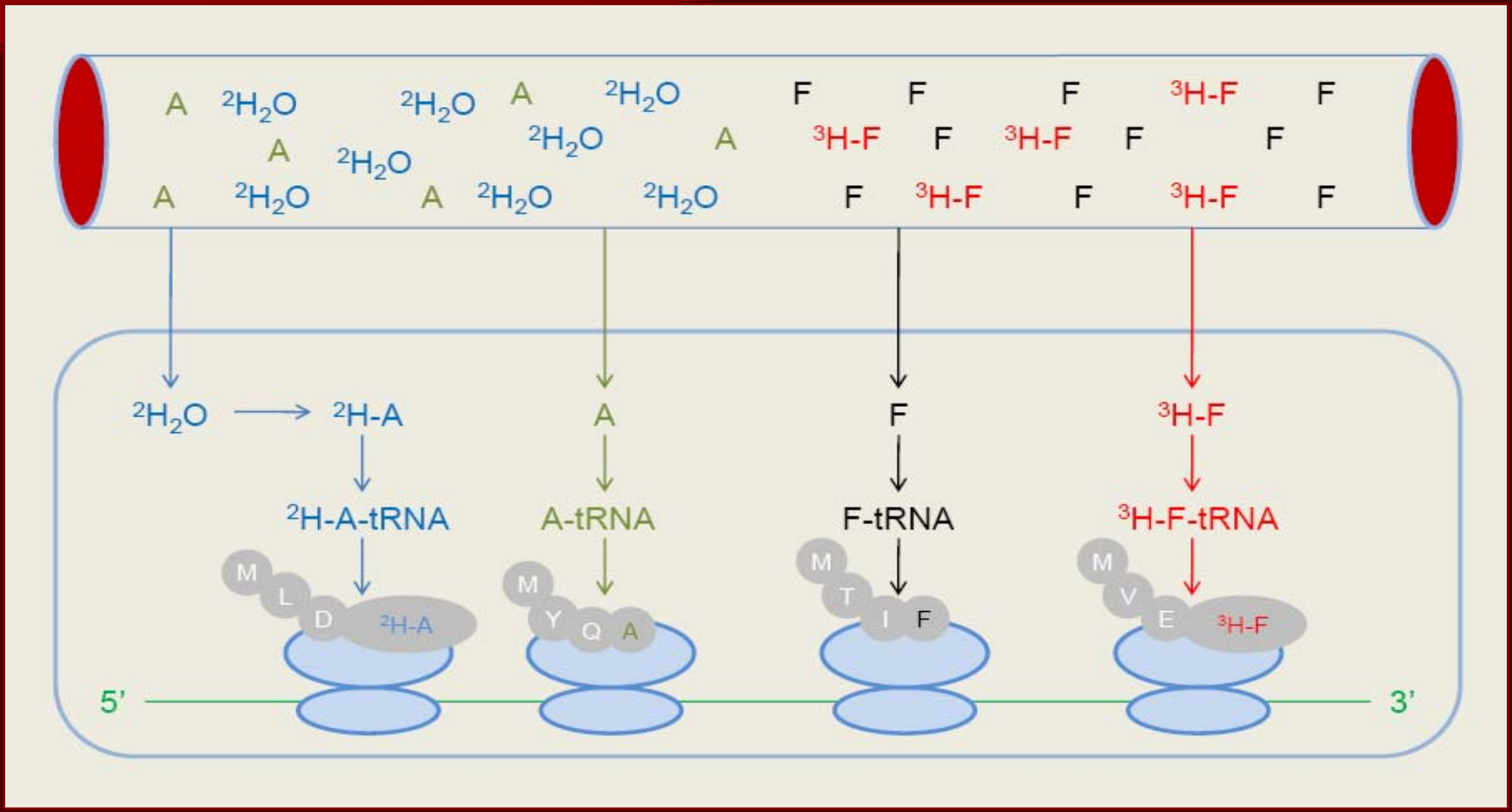


Training Paradigm

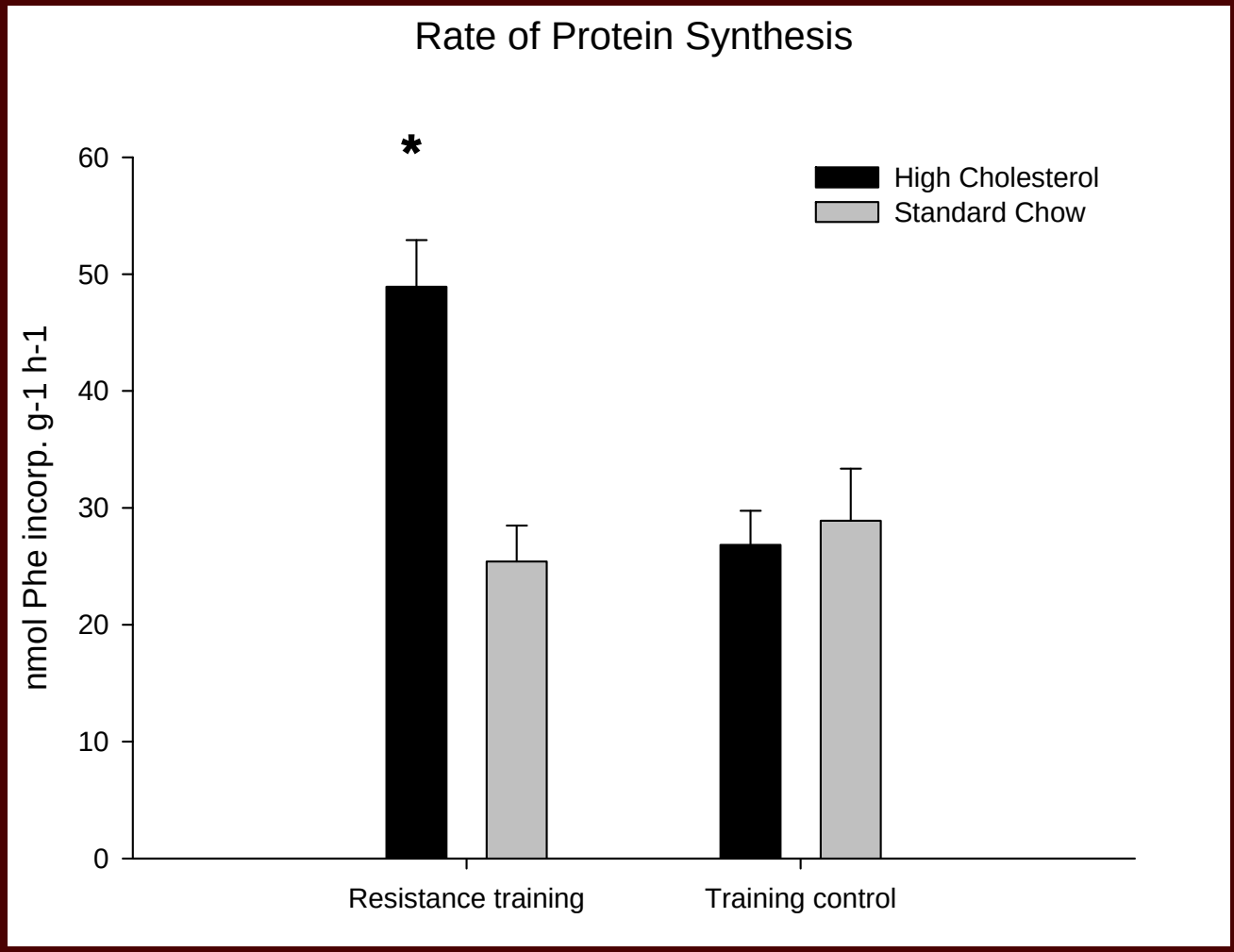
- Resistance Trained and Control
  - operant conditioning
  - 15 training sessions (3/week)
  - Randomized to standard chow and standard chow + 10X cholesterol
- Resistance Trained
  - Progressive resistance training (80g – 410 g)
  - Start at 50 reps and decreased to 16 (final session)
- Training Control
  - Non-weighted vest
  - Matched reps and electrical stimulation as RT

Weight Gain

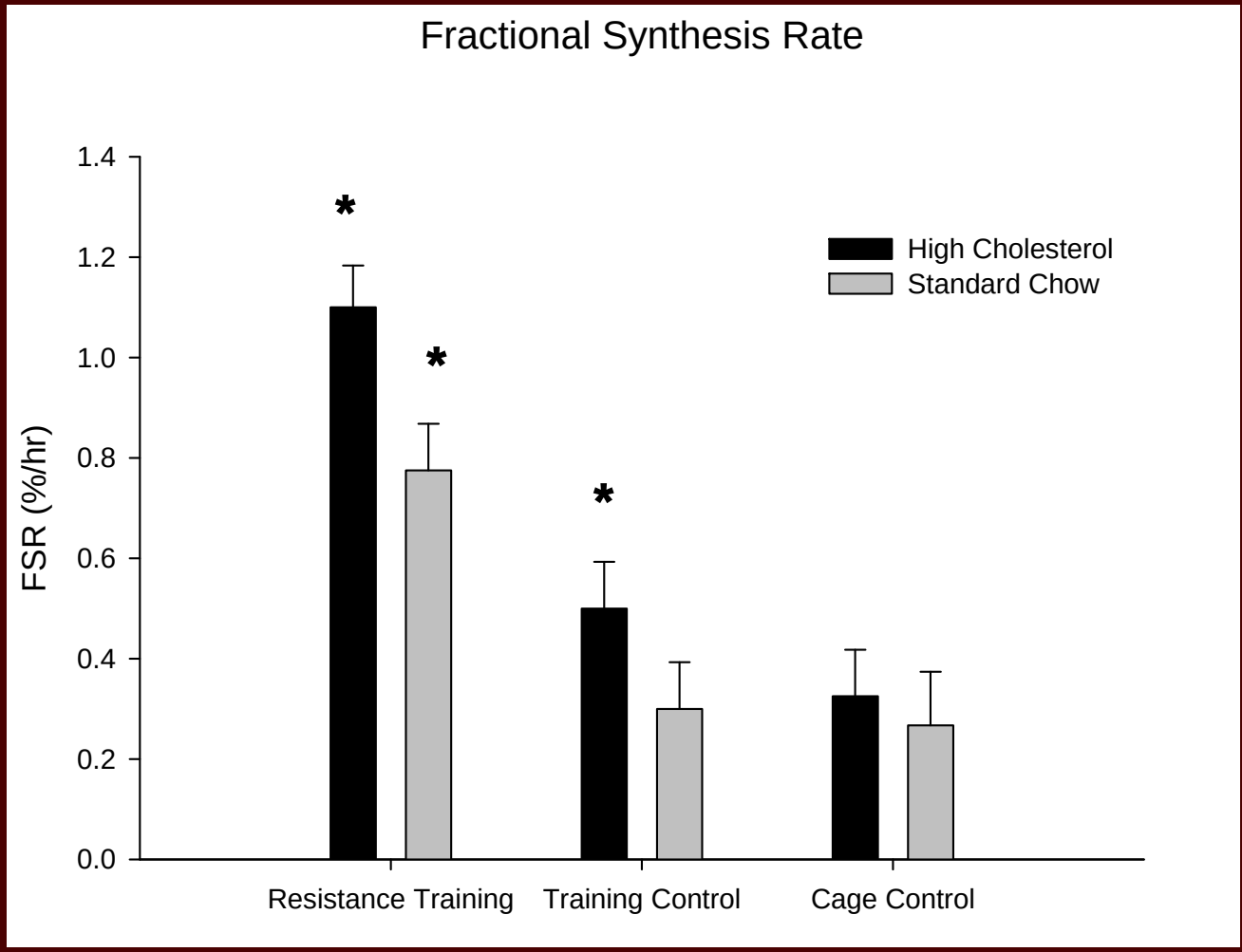

High Cholesterol, Resistance Training
High Cholesterol, Training Control
Standard Chow, Resistance Training
Standard Chow, Training Control
Change in Weight
50
40
30
20
10
0
-10
Baseline
Week 1
Week 2
Week 3
Week 4
Week 5
Post-Training
+4.9% lean
-0.7% lean


A
^2H_2O
^2H_2O
A
^2H_2O
F
F
F
^3H-F
F
A
^2H_2O
^3H-F
F
^3H-F
F
F
A
^2H_2O
A
^2H_2O
^2H_2O
F
^3H-F
F
^3H-F
F
^2H_2O
^2H-A
A
F
^3H-F
^2H-A-tRNA
A-tRNA
F-tRNA
^3H-F-tRNA
M
L
D
^2H-A
M
Y
Q
A
M
T
I
F
M
V
E
^3H-F
5’
3’

Rate of Muscle Protein Synthesis



Fractional Muscle Protein Synthesis Rate



New Studies

- Elite powerlifters: 8 weeks, ~10 whole eggs per day vs equivalent egg white
  - Mass and performance outcomes
- Muscle damage follow up with deuterium measures of protein synthesis

Conclusions

- Dietary Cholesterol positively affects muscle responses with resistance training in rats and humans
- The mechanism appears at least partly due to both increased protein synthesis and enhanced inflammatory response

Questions?

- Have cattle drives diminished over the years? What impact does sedentary cattle have on the nutritional value of the meat?

Acknowledgements

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