Skeletal Muscle Adaptation(s): From the Field to the Lab and Clinic

Bite of Science - Orlando

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The Gameplan

- **Skeletal Muscle and Exercise Research!**
  - Athletics/Rehabilitation, Aging, Metabolism
- **To take you from the Field to the Lab and Clinic**
  - Highlight my path from the West Coast to East Coast
The Field
The Field Meets the Lab

Effects of High Dose Fish Oil Supplementation on Delayed Onset Muscle Soreness (DOMS) and Inflammatory Markers
The Lab

Colin Jackson
NSAID Consumption

- Americans spend over 2.5 billion dollars on Over-the-Counter NSAIDs per year
- Top two = Ibuprofen, Acetaminophen
- Heart and COX-2 - Celebrex, Vioxx
- What happens to Skeletal muscle?
  - Blunted normal response in protein synthesis in young men and women after resistance training
COX-Inhibitors and Skeletal Muscle

Muscle Atrophy

Muscle Growth

Acute RE Drugs ↓ PGF$_{2\alpha}$ and FSR

PGE$_2$ Receptor

PGF$_{2\alpha}$ Receptor

Phospholipid

PLA$_2$

Arachadonic Acid

PGH$_2$

PGE$_2$ Synthase

PGF$_{2\alpha}$ Synthase

PGE$_2$

PGF$_{2\alpha}$
**Aging Training Study**

**Resistance Training Program**
3 x 10 Knee Ext, 3d/wk 3mo

**Drug Consumption**
Acetaminophen (4,000mg)
Ibuprofen (1,200mg)

**Pre and Post Training Measurements**
- Screening
- Muscle Size - MRI
- Muscle Strength
- Biopsy

**Drugs Stimulate 25-50% Increases in Muscle Mass and Strength Above Placebo**
Mechanism Underlying Muscle Growth?

1. Identified and Measured 21 Components Associated with Muscle Growth:
   - 7 Enzymes, 2 Receptors (PG)
   - 3 Growth Regulators
   - 4 Atrophy Regulators
   - 5 Inflammatory Regulators

Focus on 3 Components
Proposed Mechanism #1

**Muscle Atrophy**

- **Placebo**
- **Acetaminophen**
- **Ibuprofen**

**Muscle Growth**

- **PGF_{2\alpha} Rec**
- **PGF_{2\alpha} Rec**
- **PGF_{2\alpha} Rec**

**Phospholipid**

- **PLA_{2}**

**Arachidonic Acid**

**PGH_{2}**

- **PGE_{2} Synthase**
- **PGF_{2\alpha} Synthase**

**PGE_{2}**

**PGF_{2\alpha}**

**COX-Inhibitors**
Mechanism Underlying Muscle Growth?

IL-6 Stimulates Net Skeletal Muscle Loss
MuRF-1 is an E3 Ubiquitin Ligase that Contributes to Skeletal Muscle Proteolysis

Trappe et al. 2013 AJPReg
Proposed Mechanism of Action

Drugs $\downarrow$

PGE$_2$

EP4

Not Known if this Occurs in Human Skeletal Muscle

Drugs $\downarrow$

IL-6

MuRF-1

Proteolysis

Net Muscle Loss
1. Development of *ex vivo* Methodology
Ex Vivo Study

Analysis

IL-6 and MuRF-1 mRNA Expression

Pre
Ex Vivo Study

Confirm PGE Stimulates IL-6 and MuRF-1 Transcription in Human Skeletal Muscle
Proposed Mechanism #2

- **PGE\(_2\) Receptor**
- **PGF\(_{2\alpha}\) Receptor**
- **Phospholipid**
- **Arachadonic Acid**
- **COX-Inhibitors**
- **IL-6**
- **MuRF-1**

**Muscle Atrophy**
- **Muscle Growth**

**Fold Change**
- Pre
- Post

**Bar Graphs**
- Placebo
- Acetaminophen
- Ibuprofen

**Chemical Reactions**
- **PGE\(_2\) Synthase**
- **PGF\(_{2\alpha}\) Synthase**
- **PGE\(_2\)**
- **PGF\(_{2\alpha}\)**
NSAID Study Summary

- PGF$_{2\alpha}$ receptor: an activator of skeletal muscle protein synthesis
- IL-6 and MuRF-1: mediators of skeletal muscle loss
- COX-inhibitor drug consumption produced an environment that:
  - Promoted protein synthesis
  - Reduced protein breakdown
Muscle Meets Metabolism
Peripheral Insulin Resistance

Inactivity  
Caloric Excess

Obesity/T2D

Peripheral  
Insulin  
Resistance

Impaired Glucose Uptake  
Altered FA Metabolism  
Oxidative Stress

?
MIRAGE-Skeletal Muscle Lipid and Insulin Resistance and Aging

6 Month Intervention

- Education Control (CON)
- Diet-Induced Weight Loss (DIWL)
- Diet-Induced Weight Loss + Exercise (WLEX)

VO2max
DEXA
Muscle CSA-MRI

Hyp-Eug Clamp MB X 2

Hyp-Eug Clamp MB X 2

VO2max
DEXA
Muscle CSA-MRI

Abs Change GIR (mg/FFMkg/min)
Take Home Message

- Questions and a Hypothesis
- Finding the answers
  - Pubmed/Google Scholar
  - Create your own solution
  - Acquire the skills so you can answer
- Building a Building
- Creating Opportunities - Who moved my cheese
Questions?

ED FISCHER 08

Yes, yes, yes - now, seriously - what can we do to improve our health?

1. Exercise
2. Exercise
3. Exercise
4. Exercise
5. Exercise
6. Exercise
7. Exercise
8. etc.

EXERCISE: THE KEY