Advanced Nutritional Strategies for Optimal Health and Performance in Warfighters
Primary Funding

- Department of Defense - Combat Feeding Program, Natick, MA
- DARPA (Defense Advanced Research Project Agency)
- Quercegen Pharma
  - Gatorade Sports Science Institute
  - National Institute of Health (NIH)
  - National Cancer Institute (NCI)
  - American College of Sports Medicine Foundation
Optimal Health & Performance

MIND

NUTRITION

PHYSICAL ACTIVITY

BODY
Brain/ Muscle Food - Best Bets

- **Carbohydrates** – Good bet to delay mental and physical fatigue
  - Optimal doses vary widely and side effects can be serious in high doses, especially if combined with other stimulants

- **Caffeine** – Good bet to delay mental and physical fatigue

- **Quercetin** – Good evidence of a benefit on mental and physical fatigue

- **Curcumin** – Some evidence of faster performance recovery following muscle damage

- **Muscadine Extract** – Rising fast
Brain/ Muscle Food - Long Shots

• Tyrosine – Reasonable evidence of benefits on mental function, but not in athletes
• Ginseng – limited evidence of a benefit on cognitive function, but not physical performance
• Ginkgo Biloba – limited evidence on cognitive function but not physical performance
• Tea Catechins – good indirect evidence of a possible performance benefit, but no data of a specific benefit on mental or physical performance
Brain/ Muscle Food - **Losers**

- **Amino Acids** – mixed evidence, but preponderance of evidence does not support benefit.
- **Choline/DMAE** – no good evidence of a benefit.
- **Ephedrine/amphetamine** – evidence supports a performance benefit, but side effects are too great.
- **Omega-3 fatty acids** – good evidence for a role in brain development and cognition, but no evidence for improved mental/physical performance in adult exercisers.
Quercetin

- Flavonol consumption by U.S. adults is approximately 20-50 mg/day (quercetin 3/4s this amount)
- Apples, onions, berries, red grapes, black tea, and other fruits and vegetables are sources of quercetin. One large red apple has ~10 mg quercetin.
- Quercetin is readily absorbed with plasma half-lives of 6 to 12 hours.
Quercetin

Worldwide inexpensive GMP supply is in place.

Food Additive in Japan; Supplement in US; GRAS in US; FDA-notified GRAS in process
Hypothesized Mechanisms of Performance benefits of Quercetin

- **Central Nervous System**
  - Caffeine-like CNS stimulation
  - Increase in oxidative metabolism via increased mitochondria
  - Reduced oxidative stress & inflammation

- **Muscle**
  - Increased oxidative metabolism via increased mitochondria
  - Reduced oxidative stress & inflammation

![Diagram of the human body with a flowchart from Brain to Spinal Cord, then Muscle, leading to Performance]
Quercetin Can Increase Mitochondrial Number and Function in Muscle and Brain in rodents

- Ingestion of as little as 12.5 mg/kg in mice and rats (~875mg in humans) of quercetin for 7 days increased mitochondrial mass/capacity by 25 - 100% in skeletal **MUSCLE**, Liver, and **BRAIN**.
- Studies are ongoing in humans in my lab.
- Effects are lost after 7 days without Q.
Fig. 2A. mtDNA Muscle (Top) & Brain

- Fold Increase
- Placebo 12.5mg/kg/Q 25mg/kg/Q

Fig. 2B. Cyt.C Muscle (Top) & Brain

- Fold Increase
- Placebo 12.5mg/kg/Q 25mg/kg/Q

* indicates statistical significance.
Importance of Mitochondria

• Powerhouse of the cell
  – Oxygen consumption and ATP production
  – Regulates substrate utilization (fat vs carbohydrate)
  – Important regulator of cell death (apoptosis) and aging

• Most important limiting factor to endurance exercise performance
  – Increases VO2max, utilization of fat relative to carbohydrate, spares muscle and liver glycogen and increases lactate threshold
Health Effects of Mitochondria Loss/ Dysfunction

• Exercise intolerance
• Metabolic diseases
  – Obesity
  – Cardiovascular disease
  – Diabetes
• Neurodegenerative Diseases
  – Age-related Dementia
  – Alzheimer’s Disease
  – Frailty Syndrome
  – Sarcopenia (Cachexia/Wasting Syndrome)
Quercetin Can Increase VO$_2$max and Endurance Exercise Performance in rodents and humans

• 7d of Quercetin feeding was associated with
  - Increased endurance performance during force treadmill running and voluntary wheel running in sedentary mice
  - Increased VO$_2$max and endurance cycling in fit, but not highly trained, humans.

• Benefits are lost after 7 days without Q.
Maximal Exercise Capacity
Voluntary Wheel Running
Voluntary Wheel Running Apparatus - Test of 24 hr Physical Activity Patterns
**Treadmill run time to fatigue**

**Voluntary Wheel running**

![Bar graph showing % increase in treadmill run time to fatigue for Placebo, 12.5mg/kg/Q, and 25mg/kg/Q groups.](image)

![Line graph showing % increase in voluntary wheel running over days for Placebo and Quercetin (QU995) groups.](image)

- Placebo
- 12.5mg/kg/Q
- 25mg/kg/Q

- Placebo
- Quercetin (QU995)
Health Sciences Research Center
7-day Quercetin (1000mg/d) Increased Maximal Aerobic Power (~3.9% in Humans)

* p<0.05 vs. Baseline
# p<0.05 vs. Placebo

n = 12 subjects
7-day Quercetin (1000mg/d) Increased Endurance Cycling Capacity (~13% in Humans)

Time to Fatigue (min)

Baseline | Quercetin | Placebo

* p<0.05 vs. Baseline
# p<0.05 vs. Placebo

n = 12 subjects
Summary of Performance Studies

- Quercetin feedings of as little as 12.5mg/kg/d for 7 days is associated with:
  - ~30% - 100% increases in mitochondrial density/capacity in skeletal muscle, brain, and liver of mice and rats
  - Increased VO$_2$max and endurance capacity (both rodents and humans)
  - Faster recovery of performance following exercise-induced muscle-damage
  - Exercise training and Quercetin have synergistic benefits

- Biological mechanisms include pathways in both muscle and brain