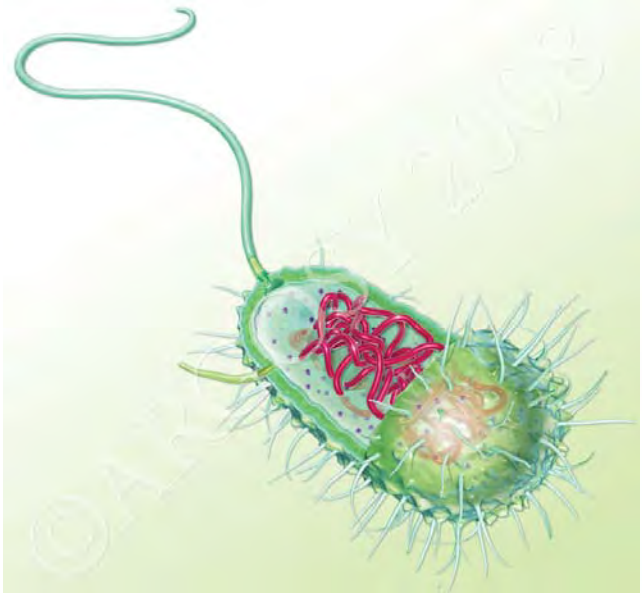
Stealth Peptides

Leading Mitochondrial Therapeutics

Mitochondria
Origin

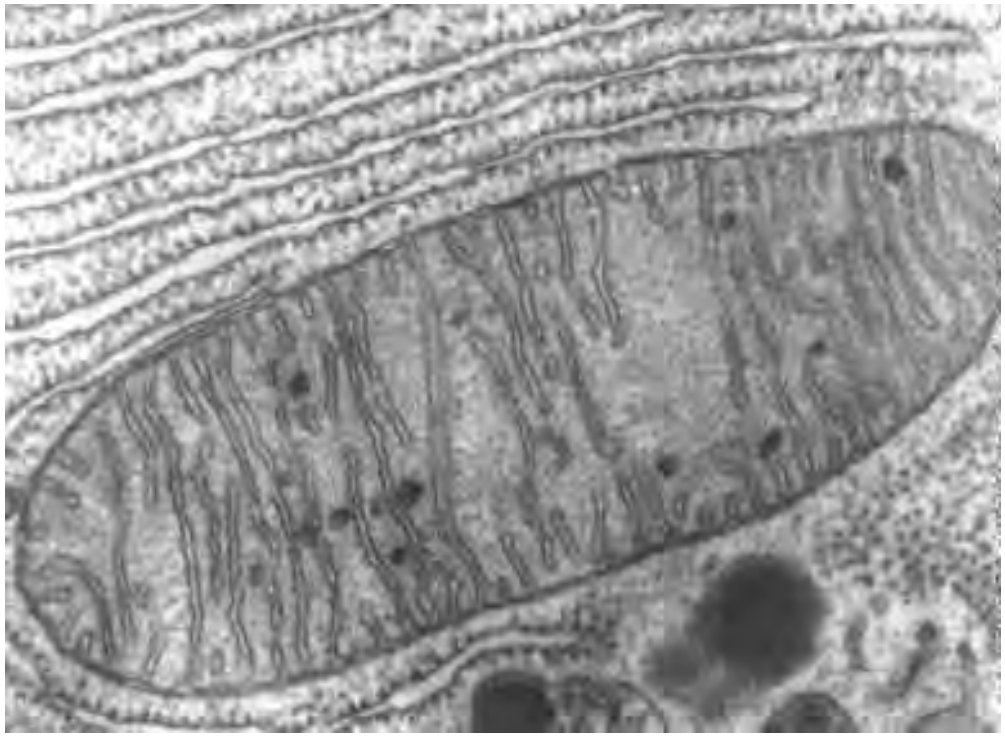
- Mitochondria primer
- Origins of mitochondria
  - Prokaryotic cells including bacteria
  - Eukaryotic cells



Mitochondria

Function

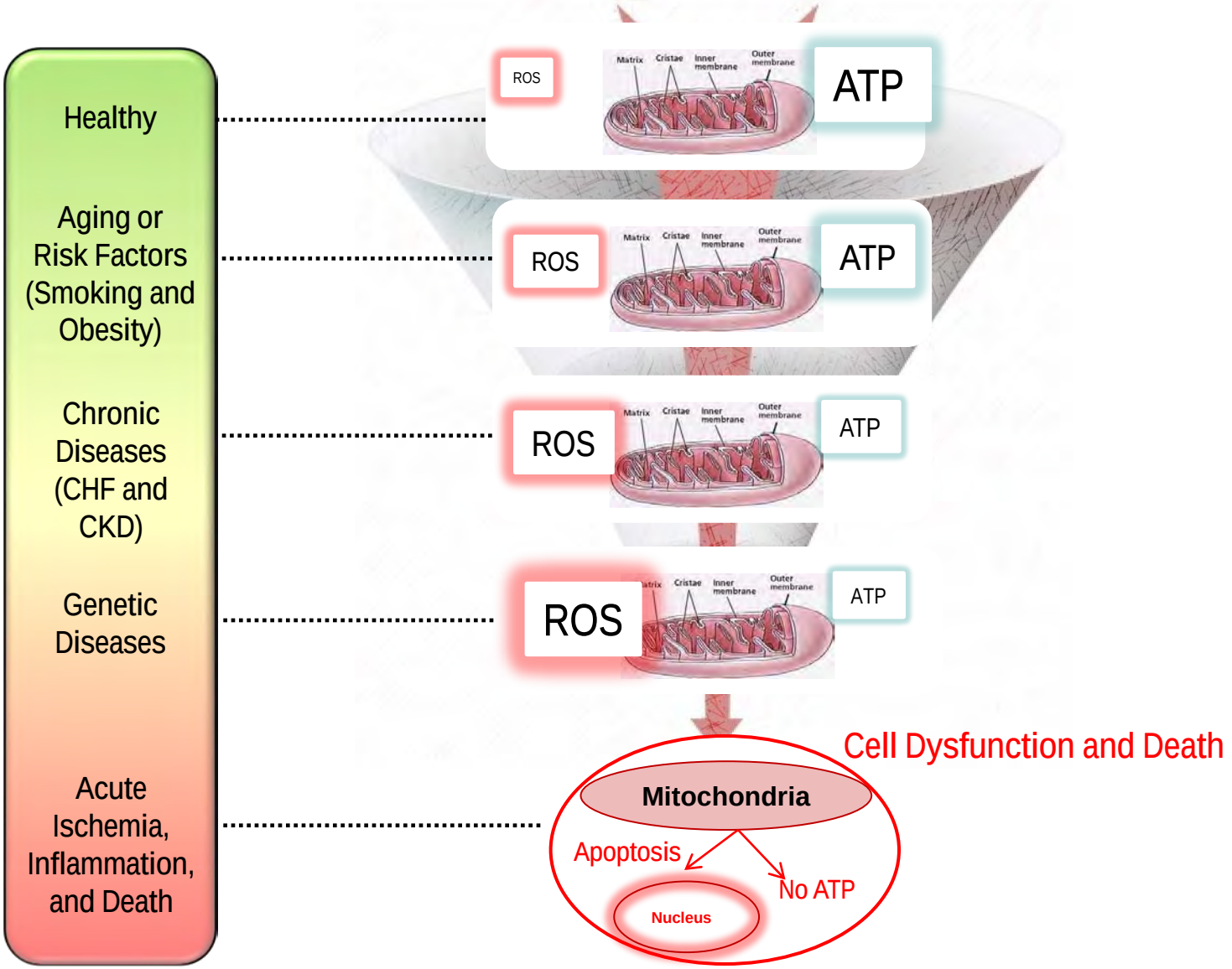
- **Mitochondria**
  - The organelle that produces energy in cells, often termed the “powerhouse of cells”
- Mitochondria produce energy or **ATP** using energy from food
- Primary source of **ROS**, initiates apoptosis or cellular death



Continuum of Mitochondrial Dysfunction

Disease Progression

Progression of Disease



Mitochondria

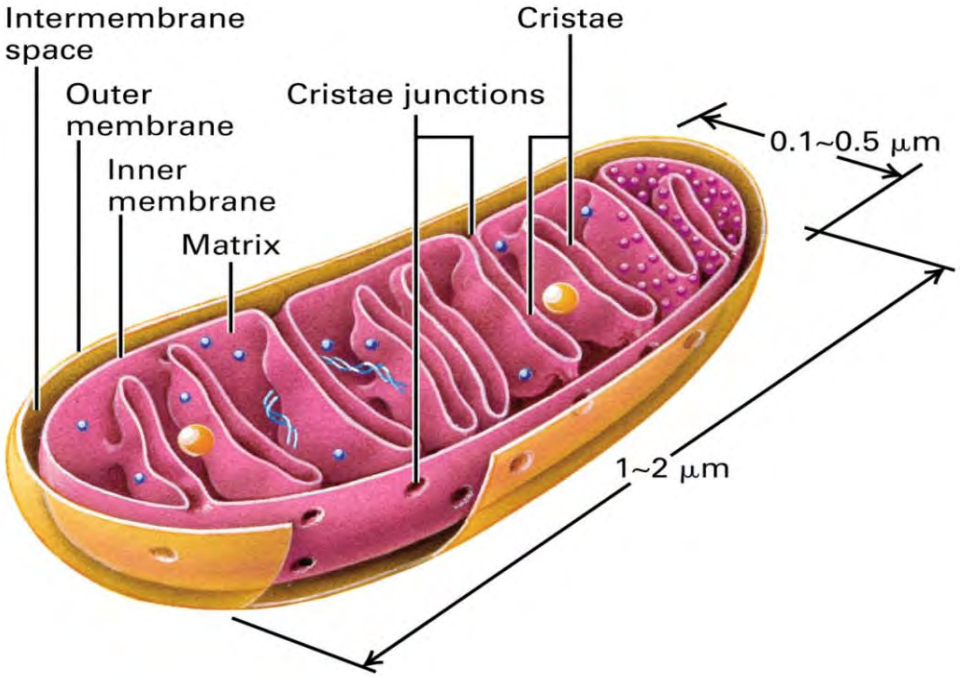
Role in Disease

- Diseased mitochondria produce excess **ROS** and lack **ATP** stores
  - Vicious cycle of disease progression
- Heart failure
- Autism
- Orphan mitochondrial diseases
- Inflammation and sepsis
- Neurodegeneration
- Diabetes
- Ophthalmology
- Kidney disease

Mitochondria

Therapeutic Hurdles

- Challenges to treating mitochondria
  - Cellular and outer mitochondrial membrane penetration
  - Reduced membrane potential in disease
  - Mitochondrial toxicity
- Critical need for therapies to overcome these hurdles



Bendavia

First-in-Class Mitochondrial Targeted Compound

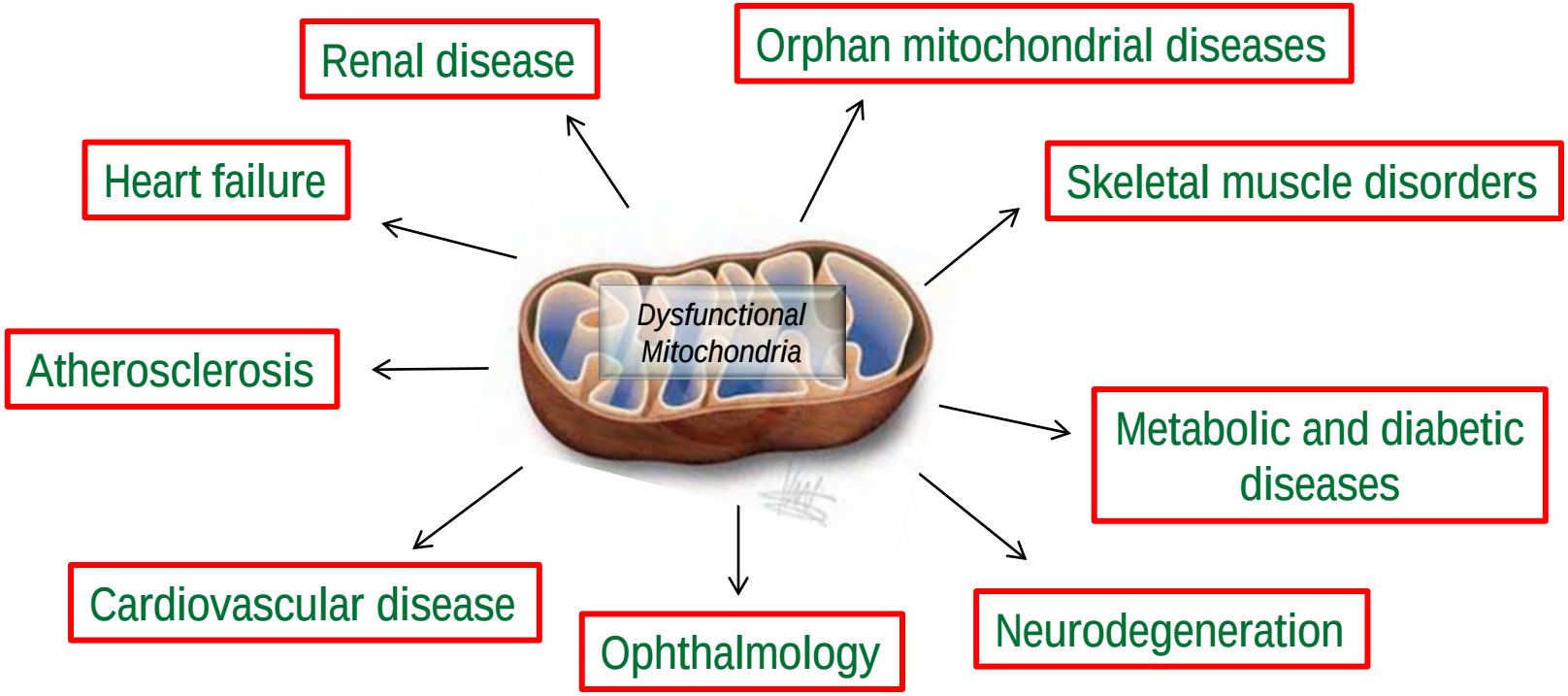
- Targets cardiolipin, found exclusively in the inner mitochondrial membrane
  - Restores **ATP**
  - Prevents the formation of **ROS**
- No apparent effect in healthy mitochondria
- Ongoing and planned Phase 2 clinical trials
  - ACS study, led by Dr. Michael Gibson
  - CKD study, led by Dr. Stephen Textor
  - DME study, led by Dr. Jeffrey Heier

What's in a name?

Bendavia is named after the German physician, Dr. Carl Benda. In 1898, Dr. Benda coined the term "mitochondria," which was derived from the Greek terms "mitos" (thread) and "chondros" (granules), which describe the appearance of the mitochondrion as viewed during early cellular development.

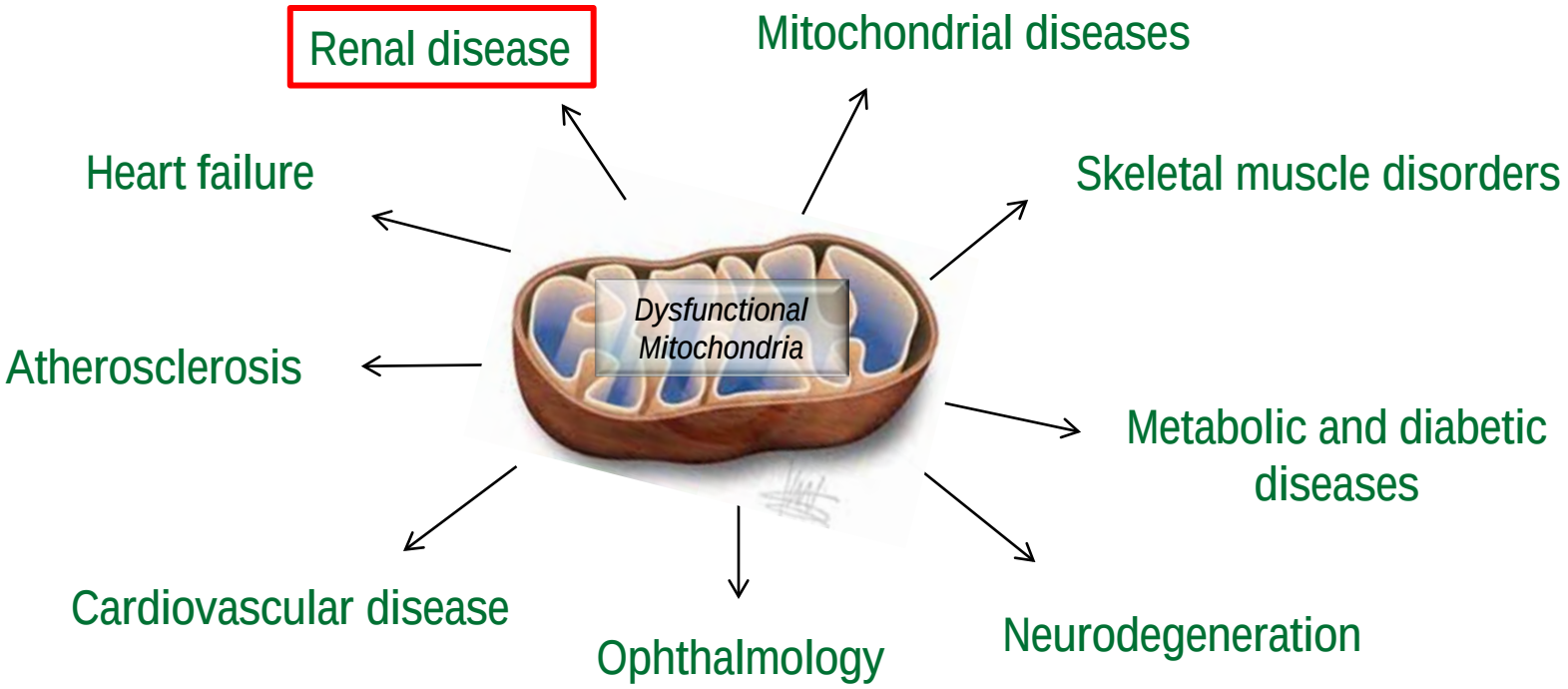
Bendavia

Therapeutic Potential



Bendavia

Therapeutic Potential



Chronic Kidney Disease

Restores Renal Function in Animal Model

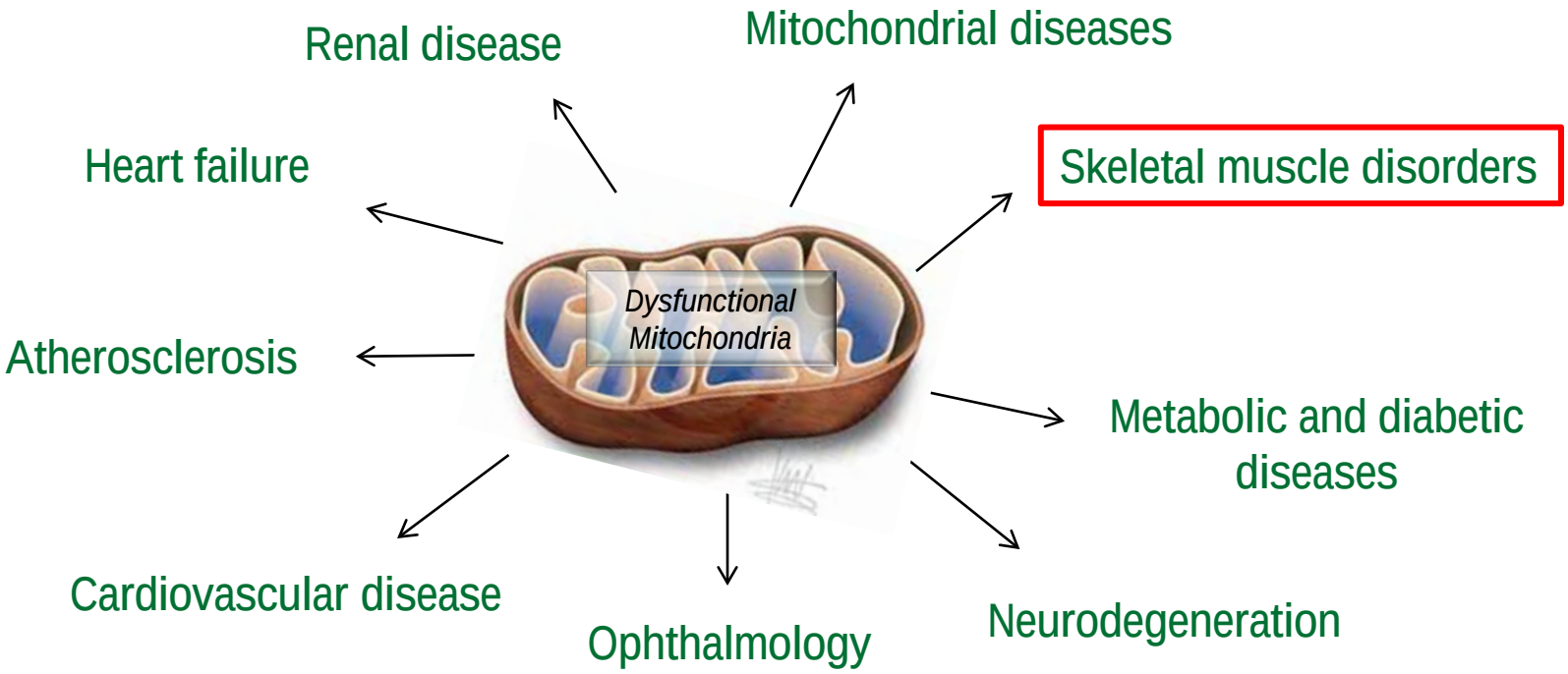
Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION

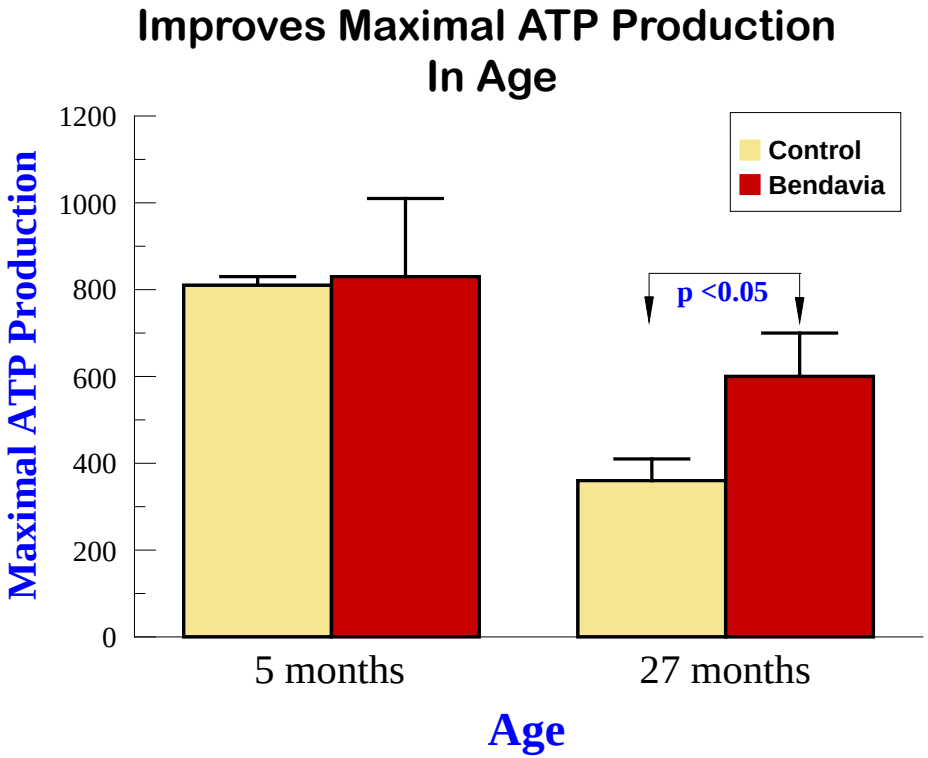
Eirin et al. *ASN* 2011

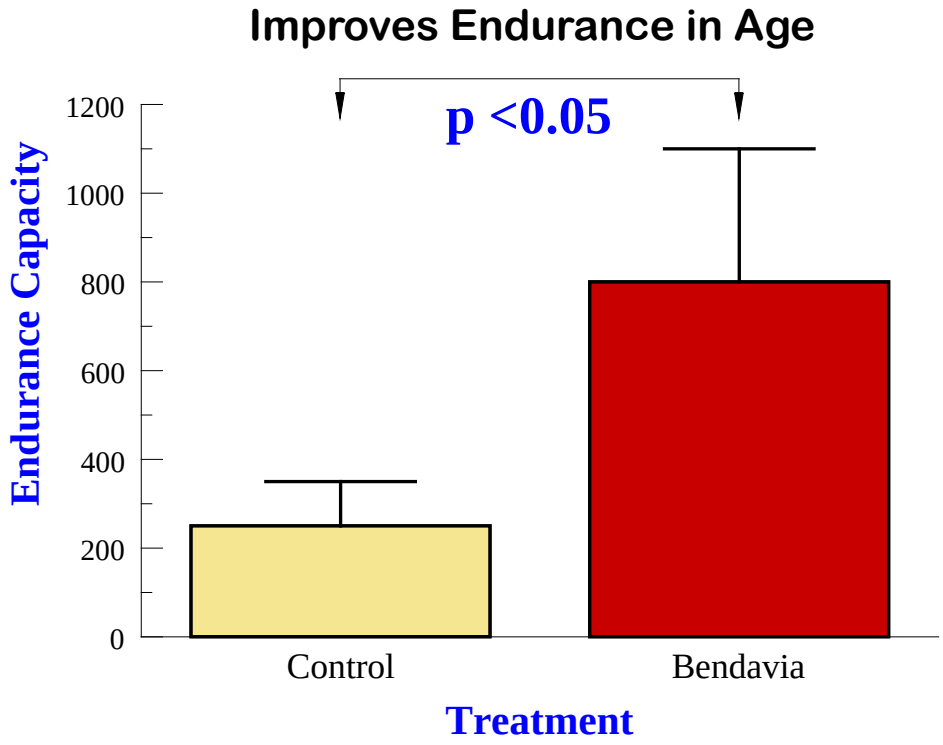
Bendavia

Therapeutic Potential



Aging
Restores Muscle Function in Animal Model



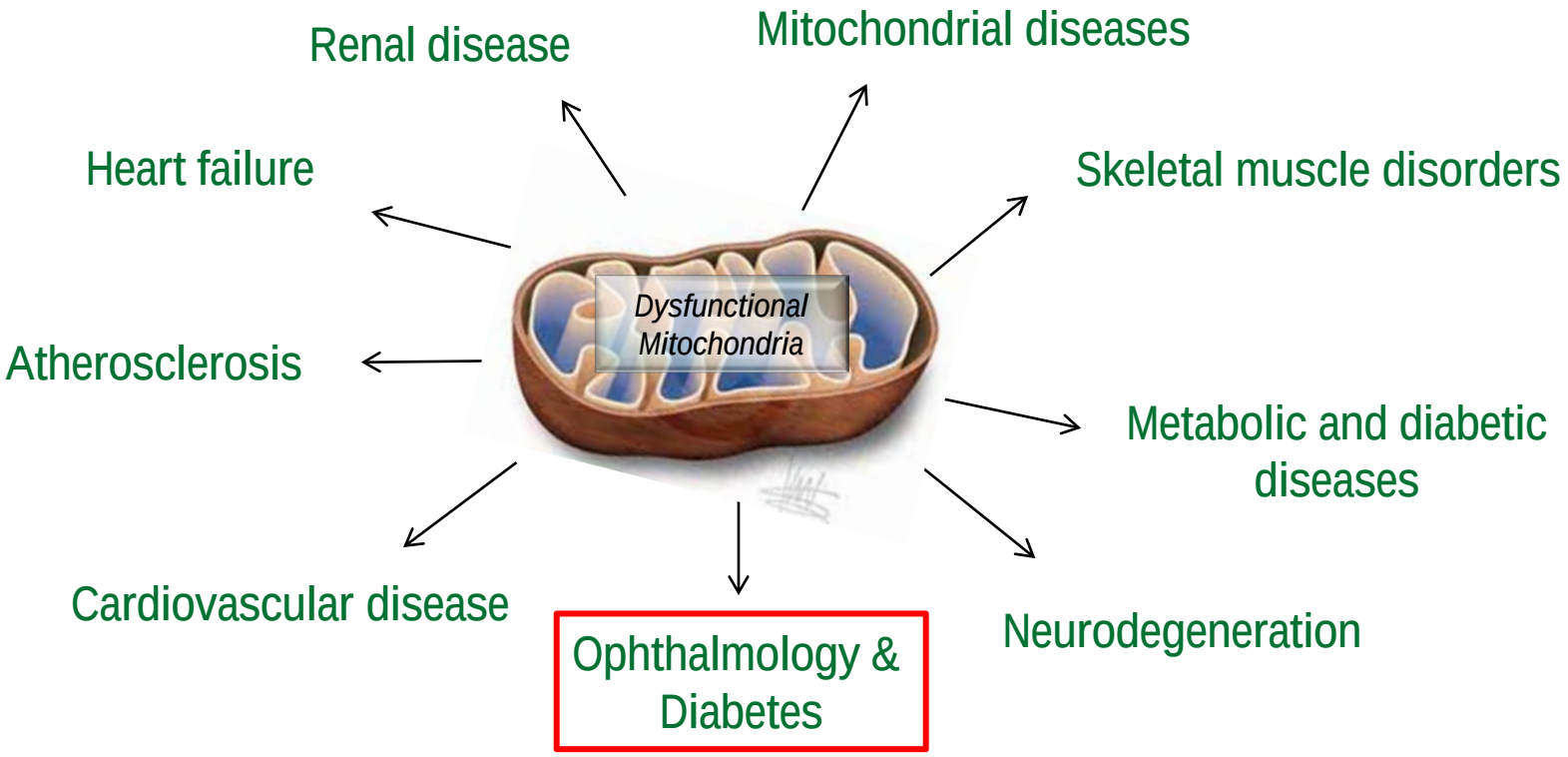


No apparent effect of Bendavia on normal muscle function

Marcinek et al. *Aging Cell* 2013

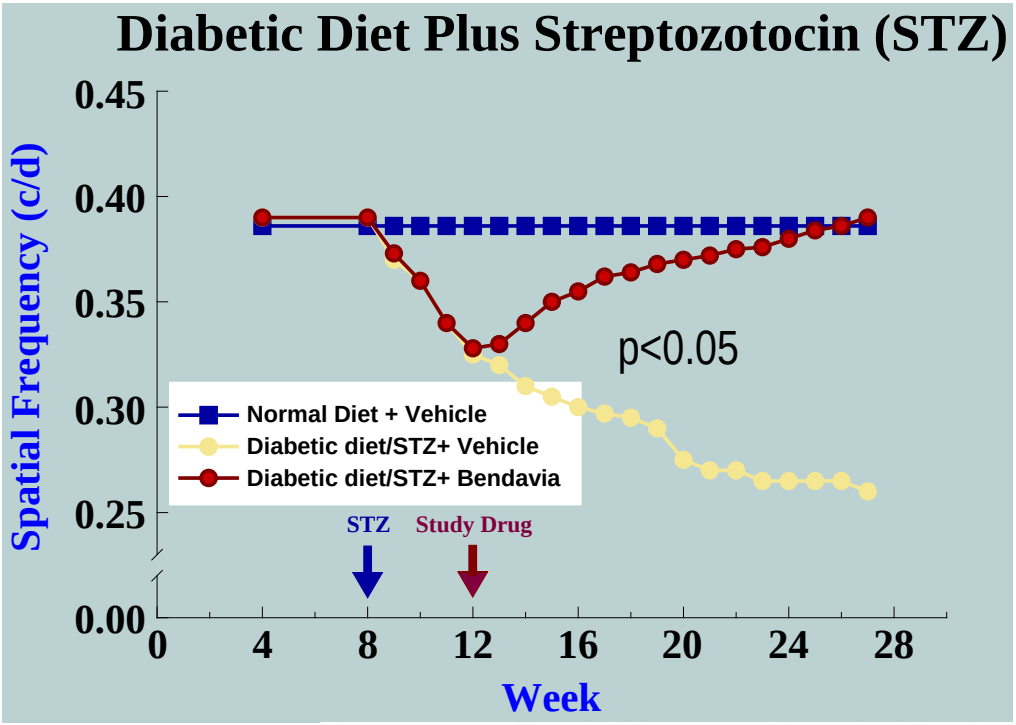
Bendavia

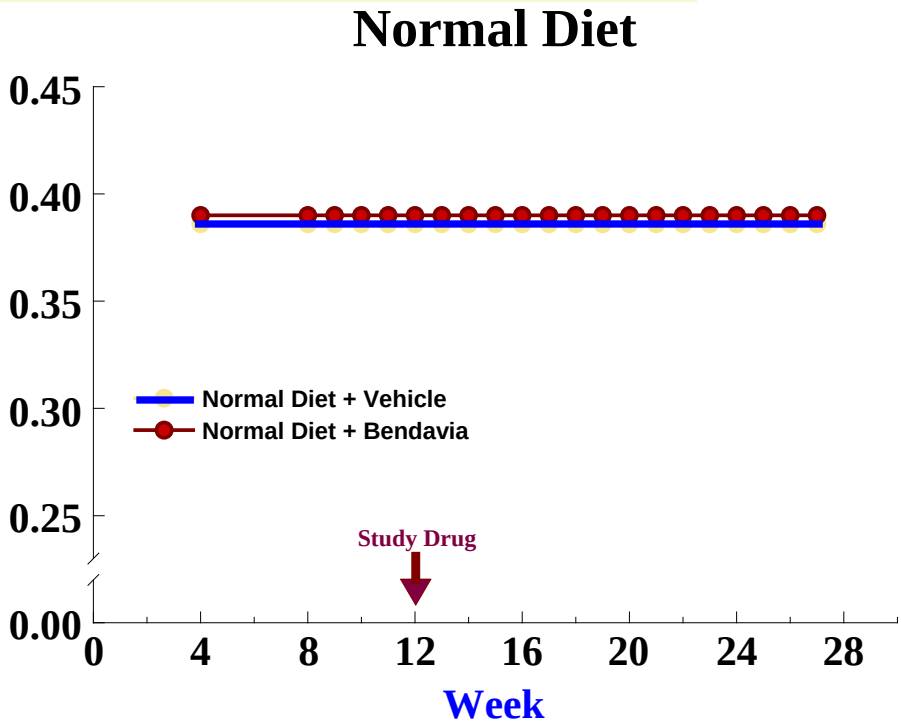
Therapeutic Potential

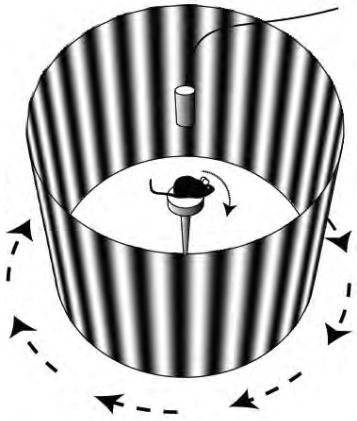


Diabetic Vision Loss

Reversed with Bendavia in Animal Model







No apparent effect of Bendavia on blood glucose or body weight

Alam et al. *ADA* 2012

Summary

Mitochondria and Bendavia

- Everyone has mitochondrial disease
  - The continuum from aging to genetic mitochondrial diseases
- The continuum of mitochondrial dysfunction features increased **ROS** and decreased **ATP**
- Bendavia appears to restore **ATP** levels and prevents **ROS** formation, without affecting healthy mitochondria
  - More than 100-peer reviewed papers and abstracts
  - More than 300 patients and volunteers of clinical experience with Bendavia
- No apparent effect in normal, healthy mitochondria

Stealth Peptides