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

- Healthy
- Aging or Risk Factors (Smoking and Obesity)
- Chronic Diseases (CHF and CKD)
- Genetic Diseases
- Acute Ischemia, Inflammation, and Death

Cell Dysfunction and Death

Mitochondria

Apoptosis

No ATP

Nucleus
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

- Renal disease
- Orphan mitochondrial diseases
- Heart failure
- Skeletal muscle disorders
- Atherosclerosis
- Metabolic and diabetic diseases
- Cardiovascular disease
- Neurodegeneration
- Ophthalmology

Dysfunctional Mitochondria
Bendavia
Therapeutic Potential

Renal disease

Heart failure

Atherosclerosis

Cardiovascular disease

Mitochondrial diseases

Skeletal muscle disorders

Metabolic and diabetic diseases

Ophthalmology

Neurodegeneration
Chronic Kidney Disease
Restores Renal Function in Animal Model

Eirin et al. ASN 2011

Hypertension

NORMAL  ARAS  ARAS+PTRA+vehicle  ARAS+PTRA+bendavia

JOURNAL OF THE AMERICAN HEART ASSOCIATION
Bendavia
Therapeutic Potential

- Renal disease
- Mitochondrial diseases
- Skeletal muscle disorders
- Metabolic and diabetic diseases
- Neurodegeneration
- Ophthalmology
- Cardiovascular disease
- Atherosclerosis
- Heart failure

Dysfunctional Mitochondria
Aging
Restores Muscle Function in Animal Model

Implements Maximal ATP Production
In Age

Control
Bendavia

Endurance Capacity

Control
Bendavia

Improves Maximal ATP Production

No apparent effect
of Bendavia on
normal muscle function

Marcinek et al. Aging Cell 2013
Bendavia
Therapeutic Potential

- Renal disease
- Mitochondrial diseases
- Skeletal muscle disorders
- Metabolic and diabetic diseases
- Neurodegeneration
- Ophthalmology & Diabetes

Dysfunctional Mitochondria

- Heart failure
- Atherosclerosis
- Cardiovascular disease
Diabetic Vision Loss
Reversed with Bendavia in Animal Model

Diabetic Diet Plus Streptozotocin (STZ)

Normal Diet

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