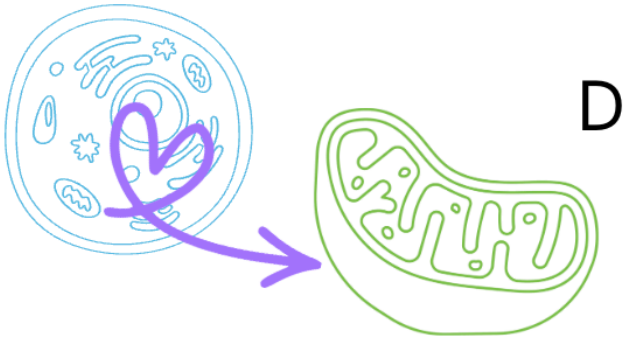
# BARTH SYNDROME

Barth Syndrome Foundation®

Caused by changes in *TAFAZZIN* gene



Decreased energy output

Cardiomyopathy

Neutropenia/infection

Muscle weakness

Feeding/GI issues

Growth delay

Exercise intolerance

# Mitochondria Structure

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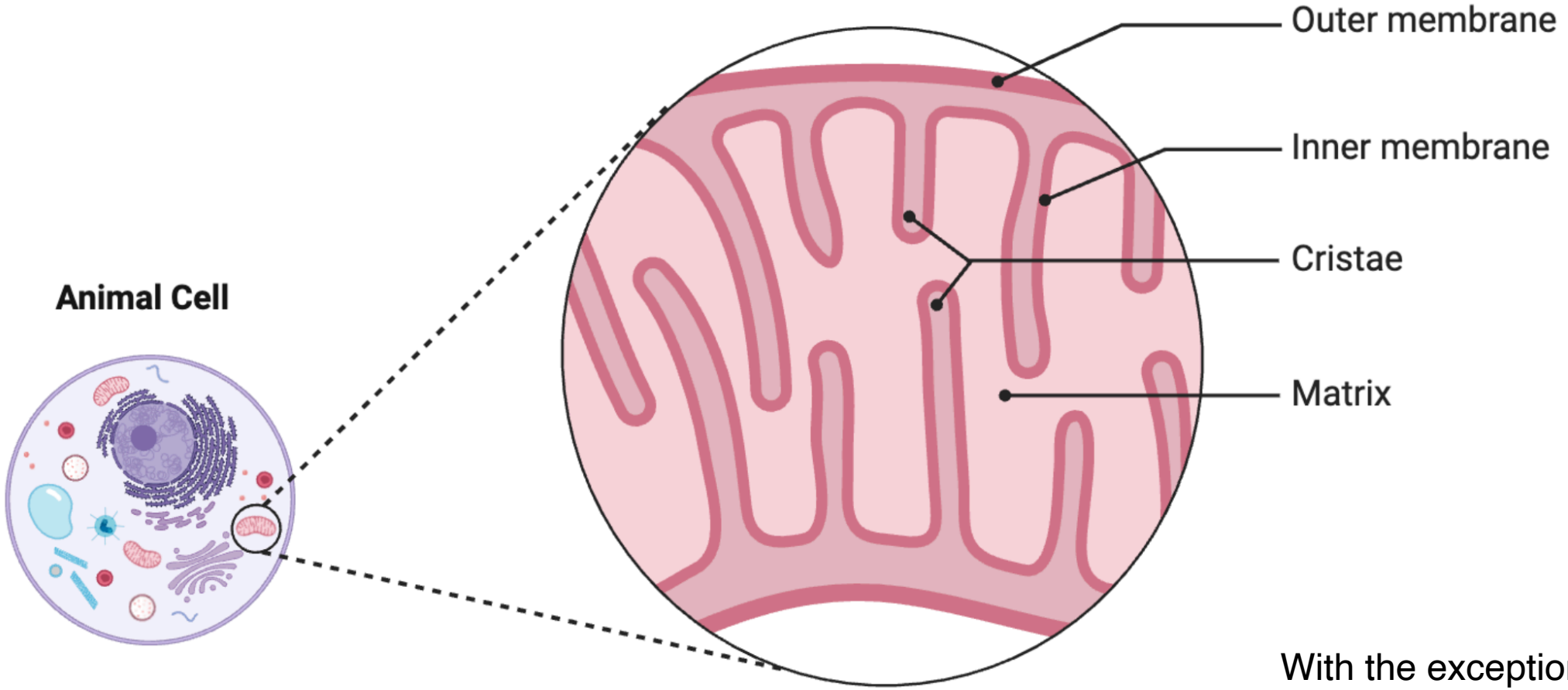


With the exception of red blood cells, every cell in the body has an army of special structures called mitochondria. The job of mitochondria is to produce the majority of energy (i.e. battery power) that cells need to do their jobs.

# BARTH SYNDROME: CARDIOLIPIN ISSUES

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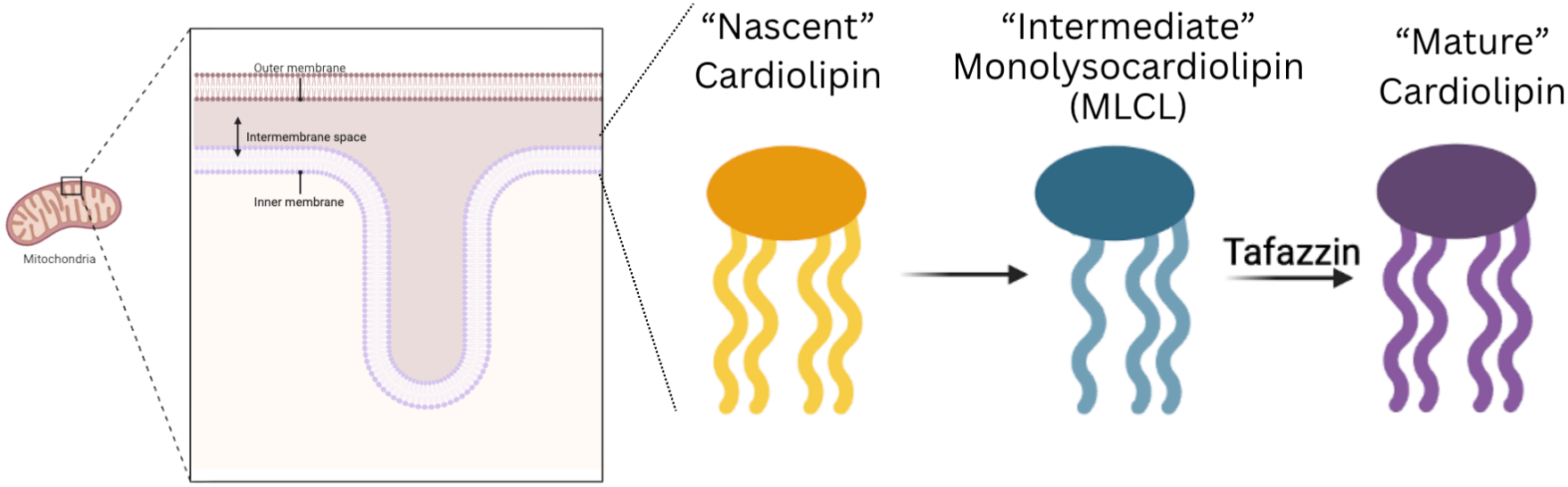
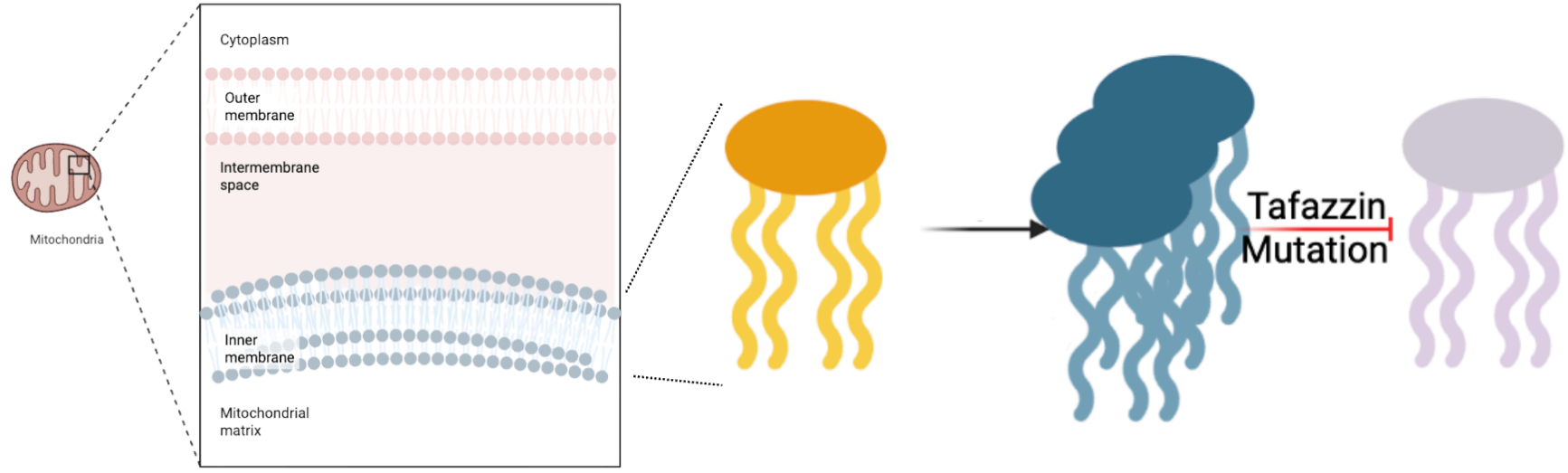
## Non-Barth




## Barth syndrome




In Barth syndrome, MLCL "piles up" instead of mature cardiolipin. The MLCL pileup changes the shape of the mitochondria and makes energy production far less efficient, which in turn makes it hard for cells to do their jobs. Cells in organs that use a lot of energy (heart/skeletal muscle) are most impacted.

# BARTH SYNDROME: HOW ELAMIPRETIDE WORKS

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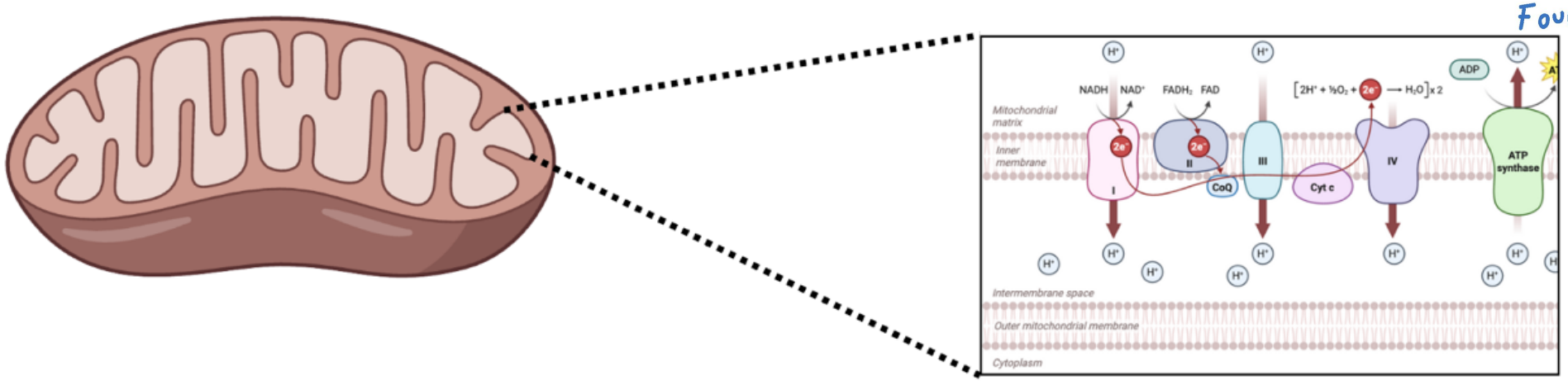
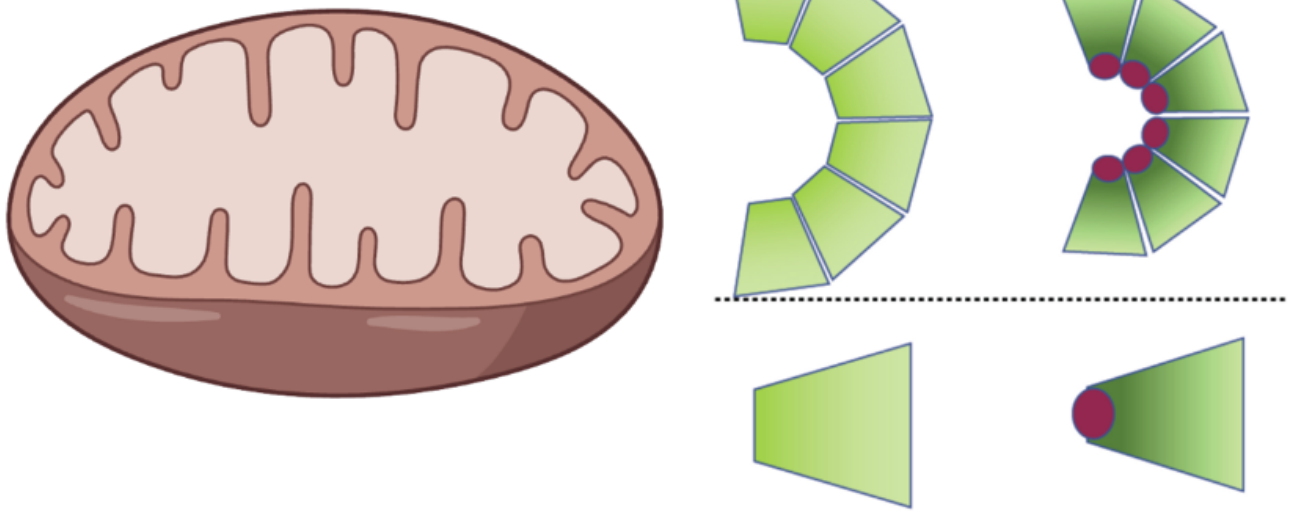
Non-Barth




Barth syndrome



Elamipretide works by restoring the shape of mitochondria so that the machinery that make cellular energy (ATP) can work together better

● Elamipretide

*Szeto (2018) Protein & Peptide Letters, 25, 1-16*

# Road Map for Drug Development

Barth Syndrome Foundation®

Idea

Discovery Research

FDA INTERACT Meeting

Preclinical Research

FDA IND Submission

Clinical Research

FDA NDA Submission

Approval

Idea

Discovery Research

FDA INTERACT Meeting

Preclinical Research

FDA IND Submission

Clinical Research

FDA NDA Submission

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# Elamipretide

2004

Dr. Hazel Szeto  Dr. Peter Schiller

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2014

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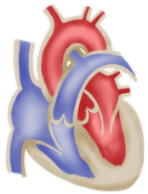
Stealth BIOTHERAPEUTICS

2018 → 2021



TAZPOWER

Phase 1-3 Clinical Trials

# Elamipretide's Road Map for Drug Development

Barth Syndrome Foundation®

## 2021

- Data weren't perfect but showed efficacy
- Bounced to 4 different divisions at FDA
- FDA refused to file NDA

## 2022

- FDA workshop with experts and advocacy
- New protocol designs rejected
- FDA said improved heart function supported accelerated approval path

## 2023

- FDA reverses guidance on accelerated approval
- BSF submits petition to FDA with ~20k signatures asking for FDA review

## 2024

- NDA accepted but filed with standard review
- Assigned priority review
- 10-6 vote by AdComm for elamipretide efficacy

## 2025

- PDUFA date extended twice
- CRL issued by FDA in May
- Path forward would not include infants