### **Bibliography Recommendation Report**

#### **Research Question**

Can we engineer or discover new pathways or mechanisms for mitochondria to sustain energy production independently of the traditional cellular substrates?

#### Introduction

Mitochondria, often referred to as the powerhouses of the cell, are critical for energy production through the process of oxidative phosphorylation (OXPHOS). Traditional cellular substrates such as glucose and fatty acids are metabolized to generate reducing equivalents (NADH and FADH2), which are then used by the electron transport chain (ETC) to create an electrochemical gradient that drives ATP synthesis. Exploring alternative pathways or mechanisms for mitochondrial energy production could have profound implications for treating metabolic disorders, neurodegenerative diseases, and conditions where traditional substrate metabolism is impaired.

#### **Recommended Sources**

# 1. Molecular and Supramolecular Structure of the Mitochondrial Oxidative Phosphorylation System: Implications for Pathology

- Source URL: Frontiers
- **Relevance**: This source discusses the molecular and supramolecular structures of the mitochondrial oxidative phosphorylation system. Understanding the current structure is crucial for engineering new pathways.
- **Reliability**: The article is published in a peer-reviewed journal, ensuring the reliability of the information.
- **Significance**: The detailed analysis of the OXPHOS system's structure could reveal potential targets for engineering new pathways or mechanisms for energy production.

# 2. Integrative Epigenomic and Transcriptomic Analyses Reveal Metabolic Switching by Intermittent Fasting in Brain

- Source URL: Geroscience
- **Relevance**: This study provides insights into how metabolic switching occurs in the brain during intermittent fasting, which could suggest alternative energy pathways.
- **Reliability**: Published in a reputable journal, the study's findings are based on rigorous epigenomic and transcriptomic analyses.
- **Significance**: Understanding how the brain adapts to intermittent fasting could lead to the discovery of new mitochondrial pathways for energy production.

# 3. Targetable Pathways for Alleviating Mitochondrial Dysfunction in Neurodegeneration of Metabolic and Non-metabolic Diseases

- Source URL: International Journal of Molecular Sciences
- **Relevance**: This article reviews pathways that can be targeted to alleviate mitochondrial dysfunction, which is relevant to engineering new energy production mechanisms.

- **Reliability**: The International Journal of Molecular Sciences is a well-regarded, peer-reviewed journal.
- **Significance**: The review could identify alternative pathways that bypass traditional substrate metabolism, which could be engineered for sustained energy production.

## 4. Can We Optimise the Exercise Training Prescription to Maximise Improvements in Mitochondria Function and Content?

- Source URL: Biochimica Biophysica Acta (BBA) General Subjects
- **Relevance**: This source explores the optimization of exercise training to enhance mitochondrial function, which may indirectly reveal new pathways for energy production.
- **Reliability**: The article is published in a reputable journal and provides a scientific approach to improving mitochondrial function.
- **Significance**: Insights from exercise physiology could inform the development of strategies to boost mitochondrial energy production through non-traditional substrates.

#### 5. Mitochondria-targeted Drugs for Diabetic Kidney Disease

- Source URL: Heliyon
- **Relevance**: This article discusses drugs targeting mitochondria for treating diabetic kidney disease, which may involve alternative energy pathways.
- **Reliability**: Heliyon is an open-access journal that publishes scientifically accurate and valuable research across various disciplines.
- **Significance**: The therapeutic approaches targeting mitochondria in this context could provide clues to new energy production mechanisms.

#### 6. Mitochondrial Quality Control and Mitohormesis

- Source URL: Nature
- **Relevance**: The concept of mitohormesis involves adaptive responses to mitochondrial stress, which could lead to the discovery of new energy production pathways.
- **Reliability**: Nature is one of the most prestigious scientific journals, ensuring the high reliability of the content.
- **Significance**: Understanding how mitochondria respond to stress and maintain quality control could reveal alternative mechanisms for energy production.

# 7. Warburg and Beyond: The Power of Mitochondrial Metabolism to Collaborate or Replace Fermentative Glycolysis in Cancer

- Source URL: Cancers (Basel)
- **Relevance**: This source discusses how mitochondrial metabolism can replace glycolysis in cancer, which is directly related to finding new energy production pathways.
- **Reliability**: The article is published in a peer-reviewed open-access journal, which supports the reliability of the information.
- **Significance**: Insights from cancer metabolism could lead to the discovery of alternative substrates or pathways for mitochondrial energy production.

### 8. Computational Framework for Analyzing and Simulating Mitochondrial ATP Synthesis

• Source URL: PubMed Central

- **Relevance**: This computational framework for analyzing mitochondrial ATP synthesis could be instrumental in modeling new pathways for energy production.
- **Reliability**: The framework is presented with detailed thermodynamic and kinetic principles, ensuring scientific rigor.
- **Significance**: The ability to simulate mitochondrial ATP synthesis could facilitate the engineering of new pathways for energy production.

### 9. Substrate Binding in the Mitochondrial ADP/ATP Carrier is a Step-wise Process Guiding the Structural Changes in the Transport Cycle

- Source URL: Nature Communications
- **Relevance**: Understanding the substrate binding process in the ADP/ATP carrier is crucial for engineering new energy production mechanisms.
- **Reliability**: Published in a high-impact journal, the study provides a detailed molecular analysis of the ADP/ATP carrier.
- **Significance**: Insights into the substrate binding and transport cycle could lead to the development of novel mitochondrial energy production pathways.

## 10. MFSD7C Switches Mitochondrial ATP Synthesis to Thermogenesis in Response to Heme

- Source URL: Nature Communications
- **Relevance**: This study shows how a protein can switch mitochondrial function from ATP synthesis to thermogenesis, which is relevant to alternative energy production.
- Reliability: The research is published in a reputable journal, adding to its credibility.
- **Significance**: The mechanism by which MFSD7C switches mitochondrial function could inspire new pathways for energy production.

#### **Conclusion**

The sources recommended in this report provide a comprehensive overview of current research related to mitochondrial function, energy production, and potential alternative pathways. They range from detailed molecular studies to broader reviews of mitochondrial bioenergetics and its role in disease. By examining these sources, researchers can gain insights into the current understanding of mitochondrial energy production and explore new avenues for engineering or discovering alternative pathways for sustaining energy production independently of traditional cellular substrates.