

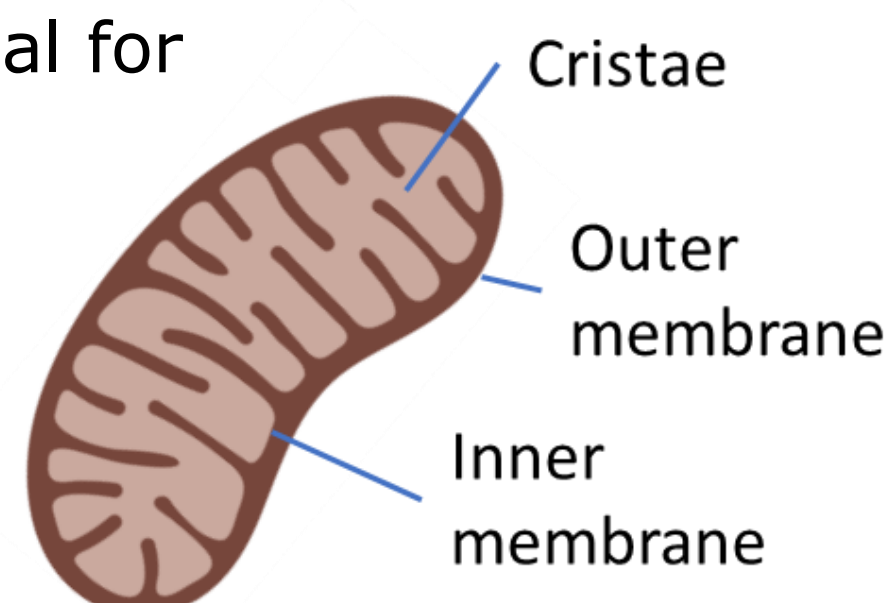
# The mitochondrial puzzle; identification of new pieces in mitochondrial dynamics

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## INTRODUCTION

- Mitochondria are dynamic organelles, essential for
  - Energy production
  - Calcium homeostasis
  - Apoptosis
  - ....

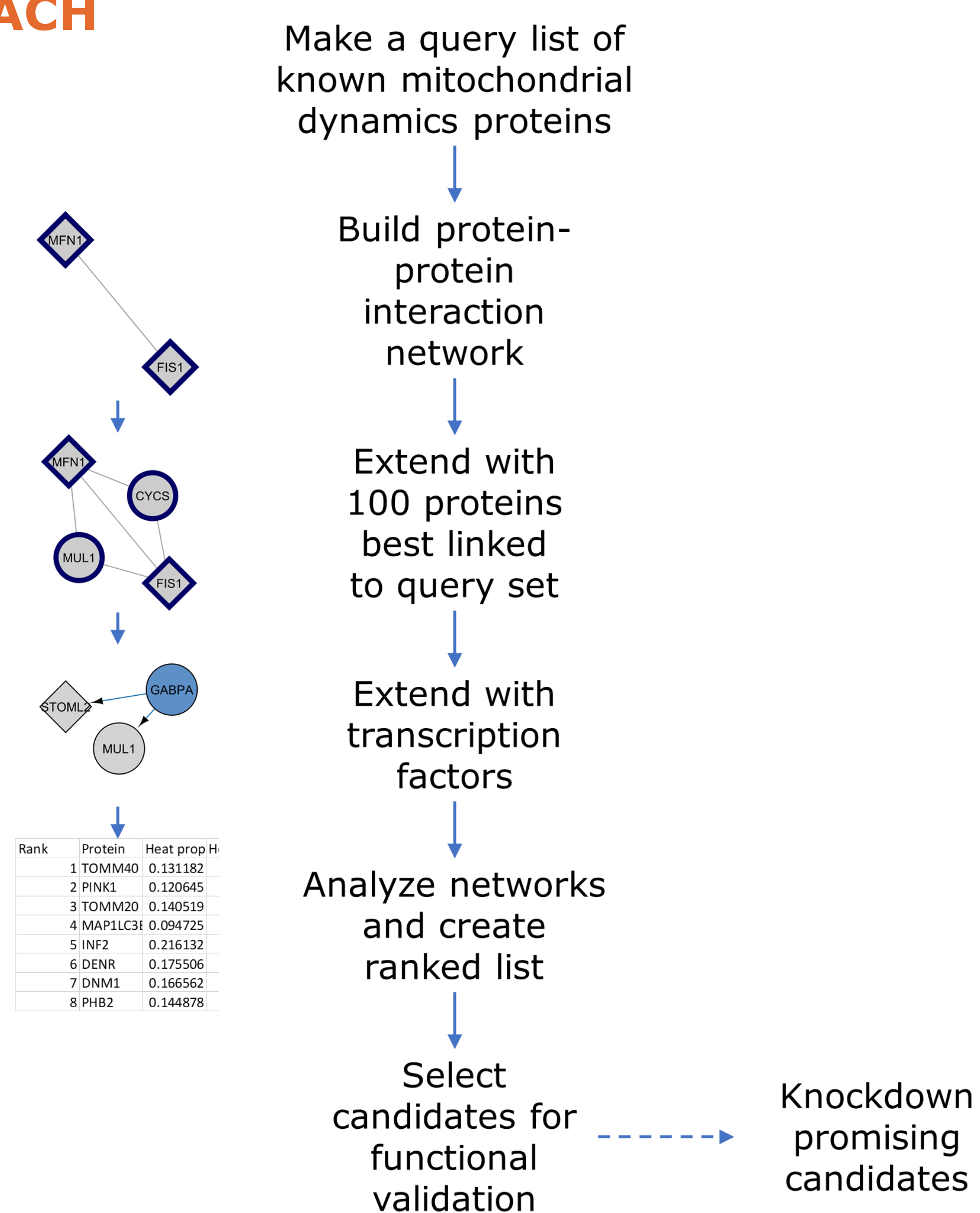


- Mitochondrial dynamics
  - Through fission and fusion
  - Defects involved in neurological disorders
    - Like Charcot-Marie-Tooth and Alzheimer's
  - Not all proteins involved identified
  - Hypothesis
    - The implementation of computational approaches will facilitate the identification of undiscovered mitochondrial dynamics proteins

## AIM

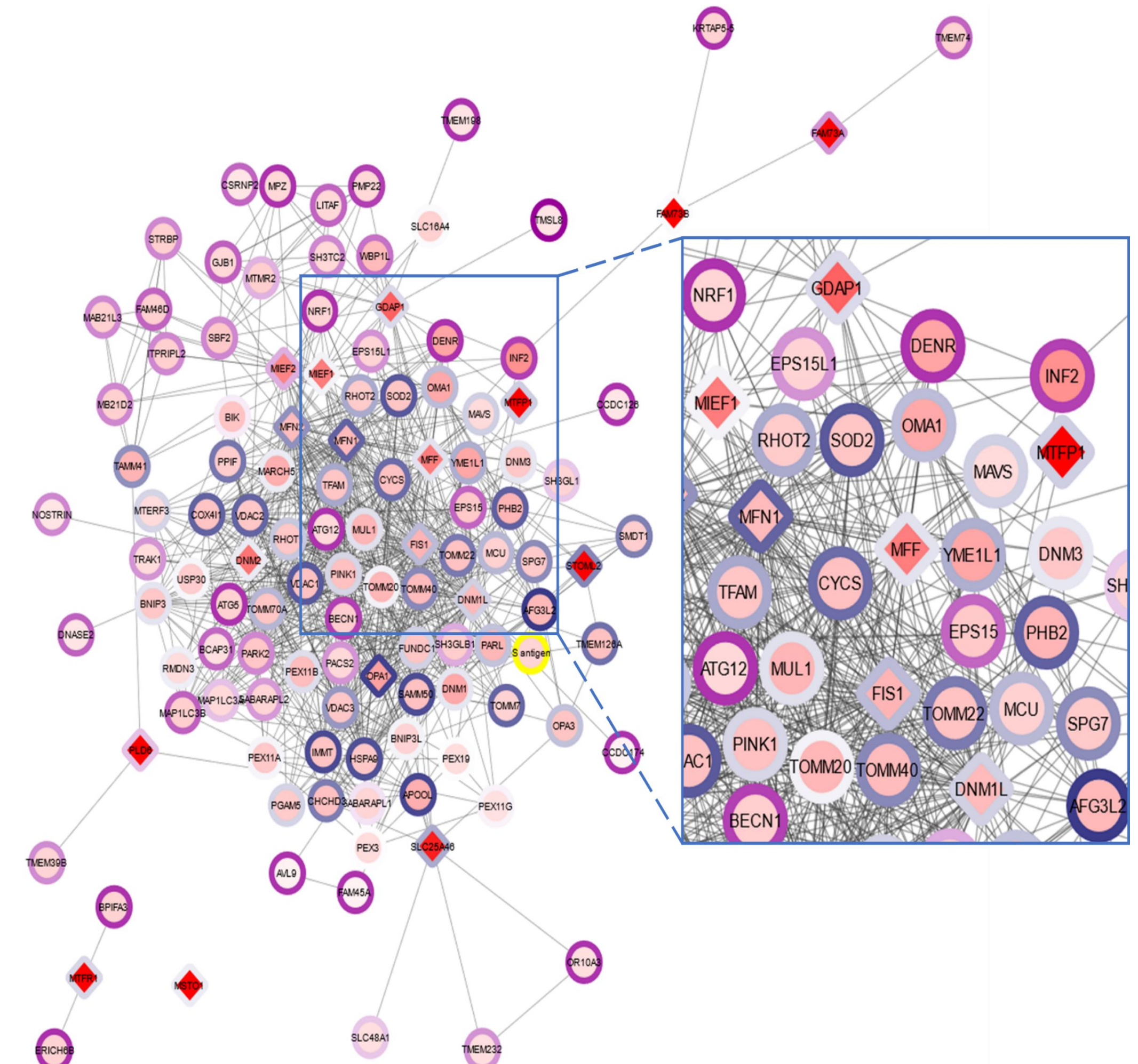
Apply a computational approach to identify novel mitochondrial dynamics proteins

## APPROACH



## PROTEIN-PROTEIN INTERACTIONS

- Extended protein-protein interaction network

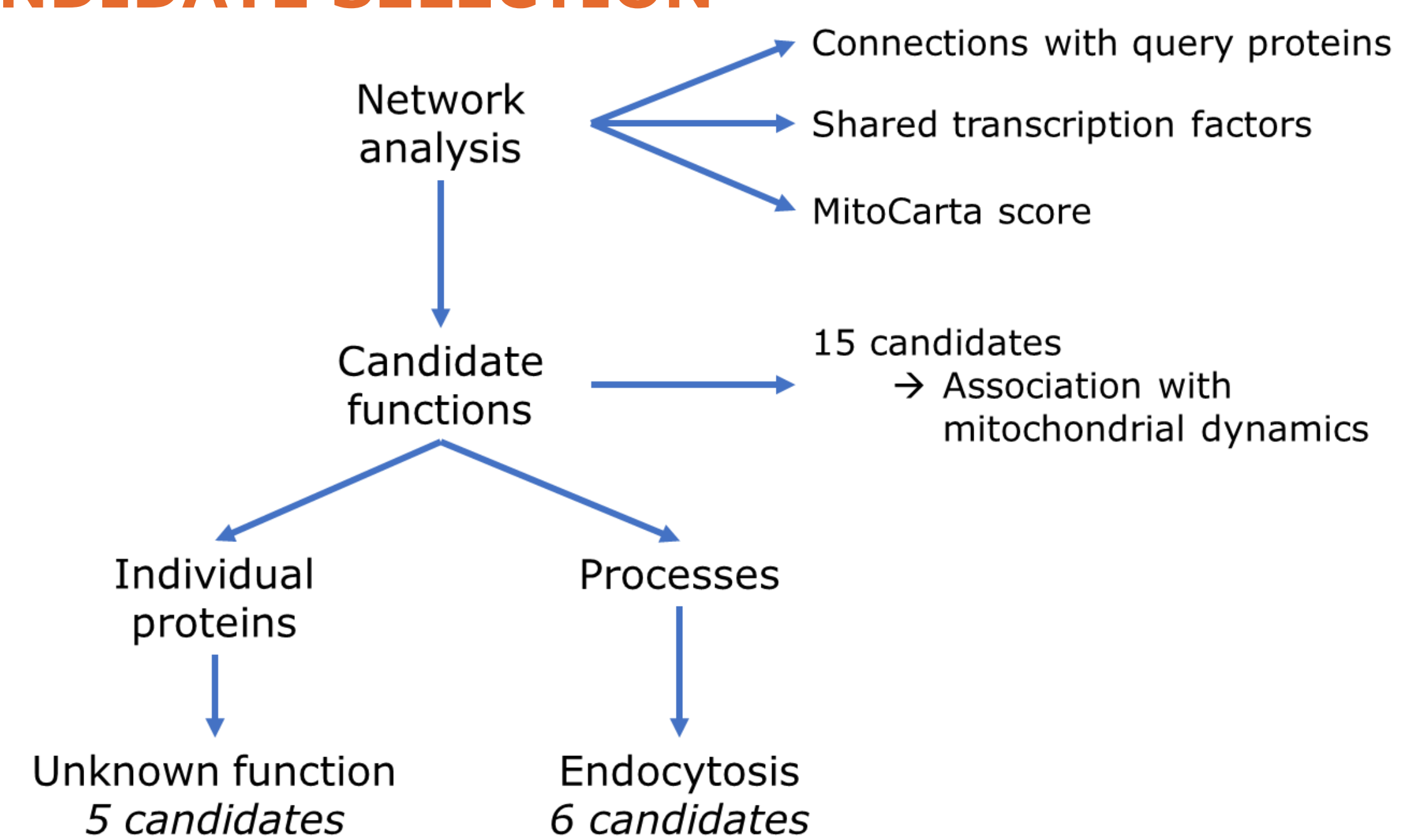


Protein-protein interaction network displaying the connections of expanded proteins (ellipse) with input proteins (diamond), with the heat propagation analysis visualized on the node (color gradient from red (score=1) to white (score=0)) where a high score is indicative of proteins more connected to the input. The MitoCarta2.0 score is visualized on the border, with a higher score indicative of mitochondrial localization (blue=positive, white=0 and purple=negative score).

- Validation

- Leave one out → 72% re-occurs upon extension
- Enrichment for mitochondrial proteins ( $p < 0.0001$ )

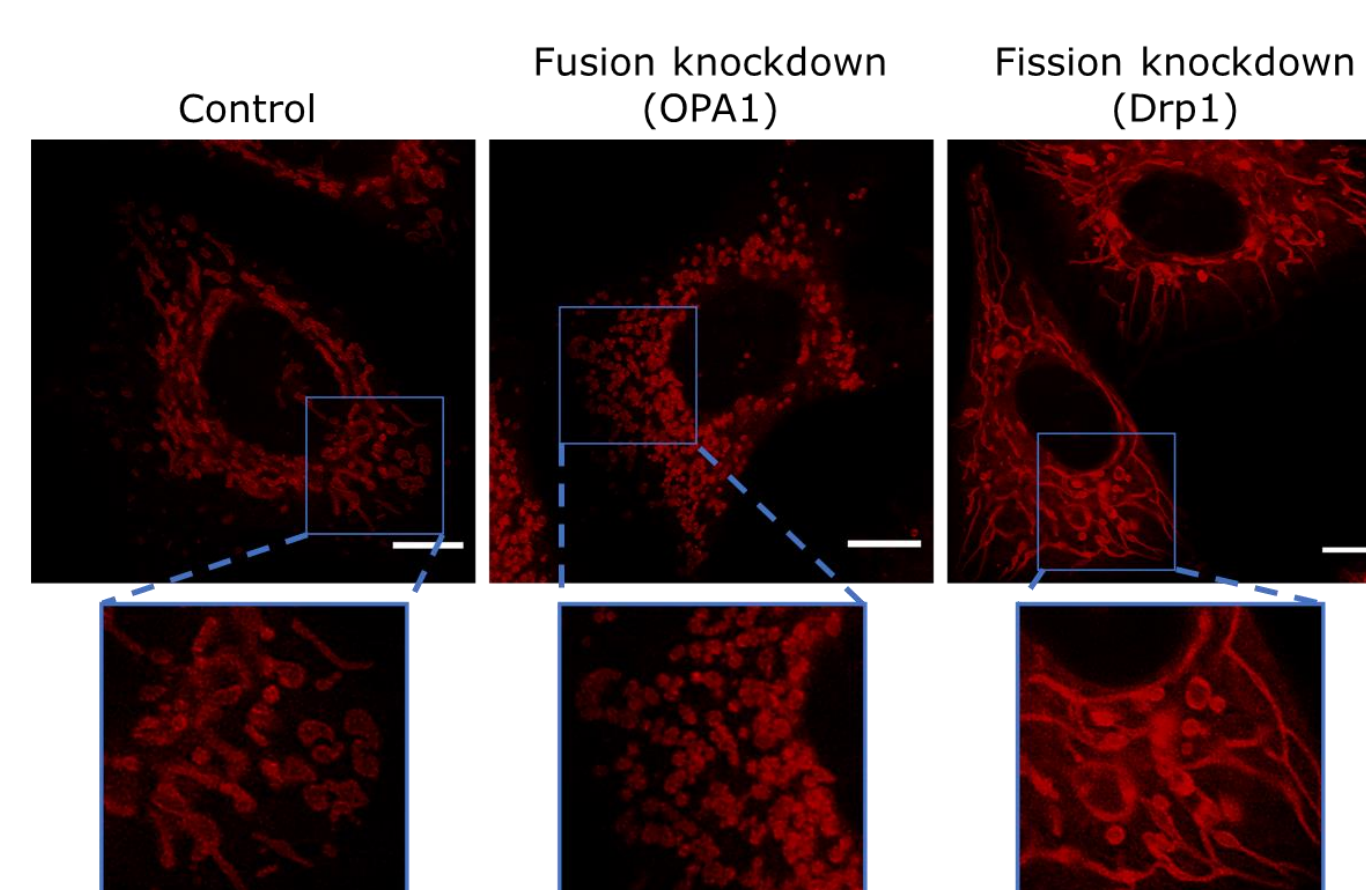
## CANDIDATE SELECTION



## GENE KNOCKDOWN

- esiRNA knockdown approach
- Expected morphology upon knockdown
  - Fusion → network fragmentation
  - Fission → network elongation
  - Knockdown efficiency >70%

Confocal images of control, OPA1 knockdown and Drp1 knockdown in HeLa cells stained with Mitotracker Red FM. OPA1 knockdown cells show a fragmented mitochondrial network compared to control, while Drp1 knockdown cells display a hyperfused mitochondrial network.



## DISCUSSION

- Prediction approach appears to work
  - Overrepresentation mitochondrial proteins
  - Prediction of associated mitochondrial dynamics proteins
- Functional validation necessary
  - Knockdown of promising candidates
  - Localization studies
  - To increase the understanding of mitochondrial dynamics