

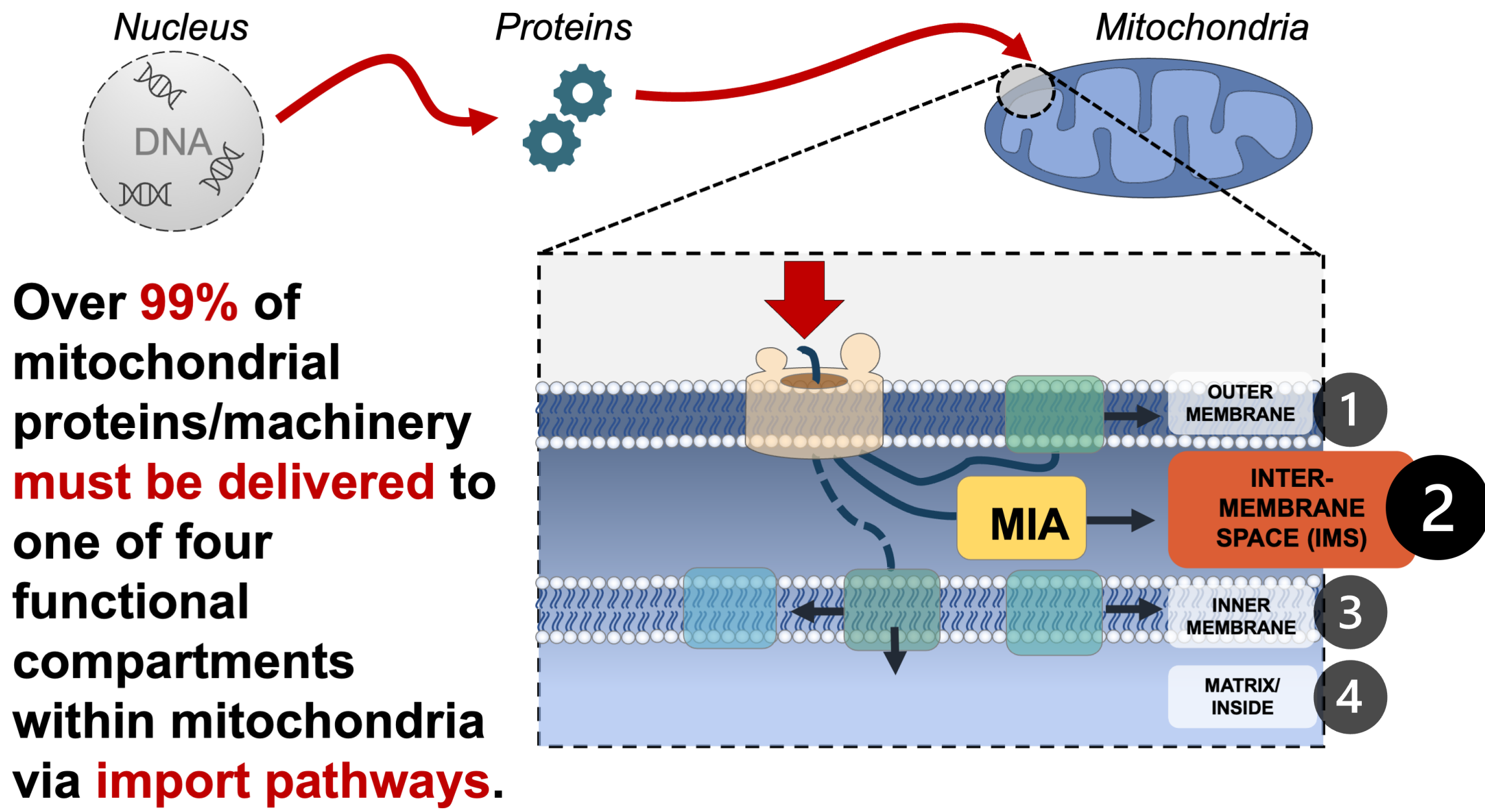
# Breaking into the Powerhouse:

## A peptide-based strategy to target mitochondrial biogenesis and fight cancer therapy resistance.

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### Project Background

Mitochondria are **cell powerhouses**, converting food into energy to fuel our body<sup>5</sup>.

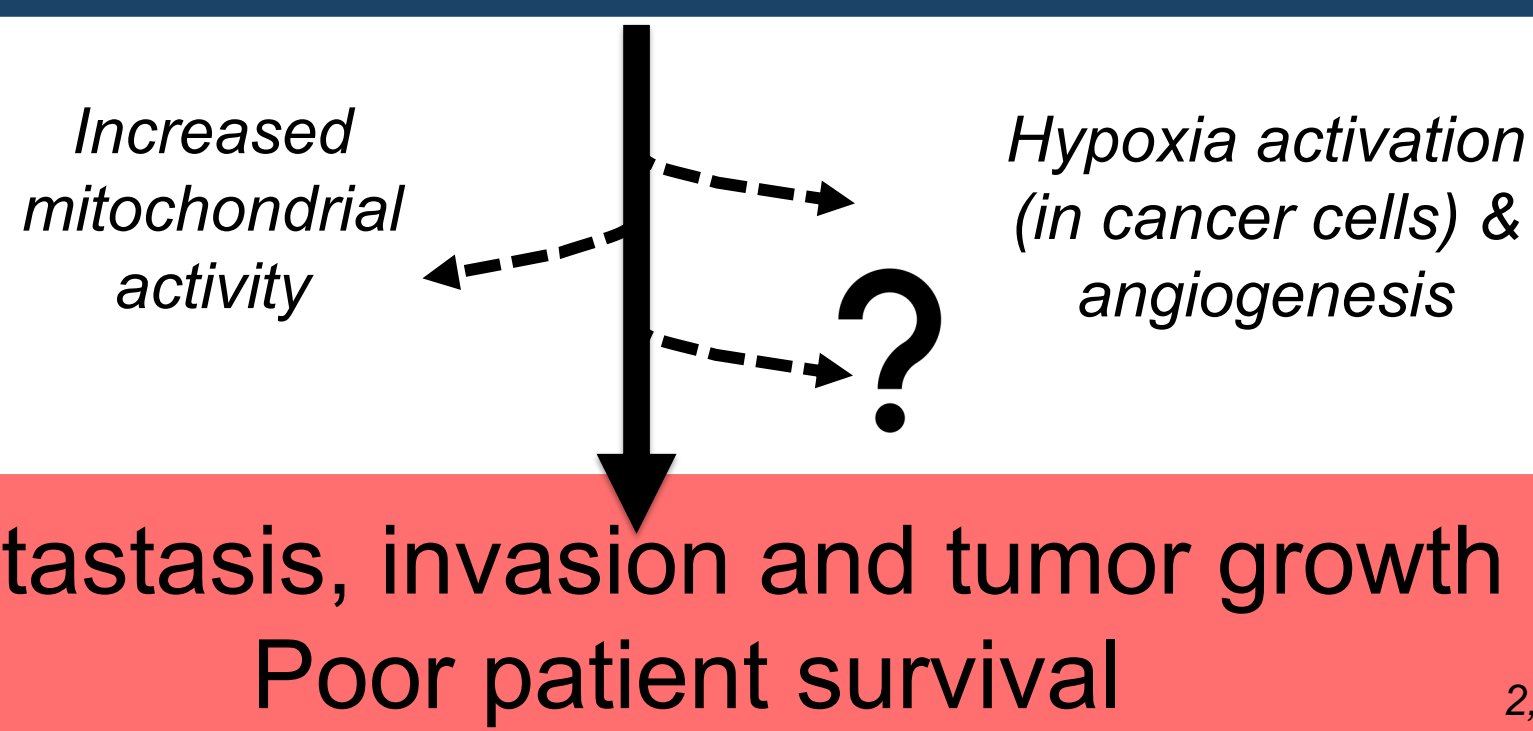


- The MIA40 pathway in the **IMS** **2** ensures proper folding and function of proteins entering the mitochondria<sup>1</sup>.
- The **MIA40 pathway is hyperactive in certain cancers**, including pancreatic, breast, lung, brain, and blood cancers<sup>1,2,3</sup>.
- Why cancer cells are reliant on this pathway remains unclear<sup>4</sup>.
- Cancer cells with an upregulated MIA40 pathway share characteristics with therapy-resistant cancer cells<sup>4</sup>.

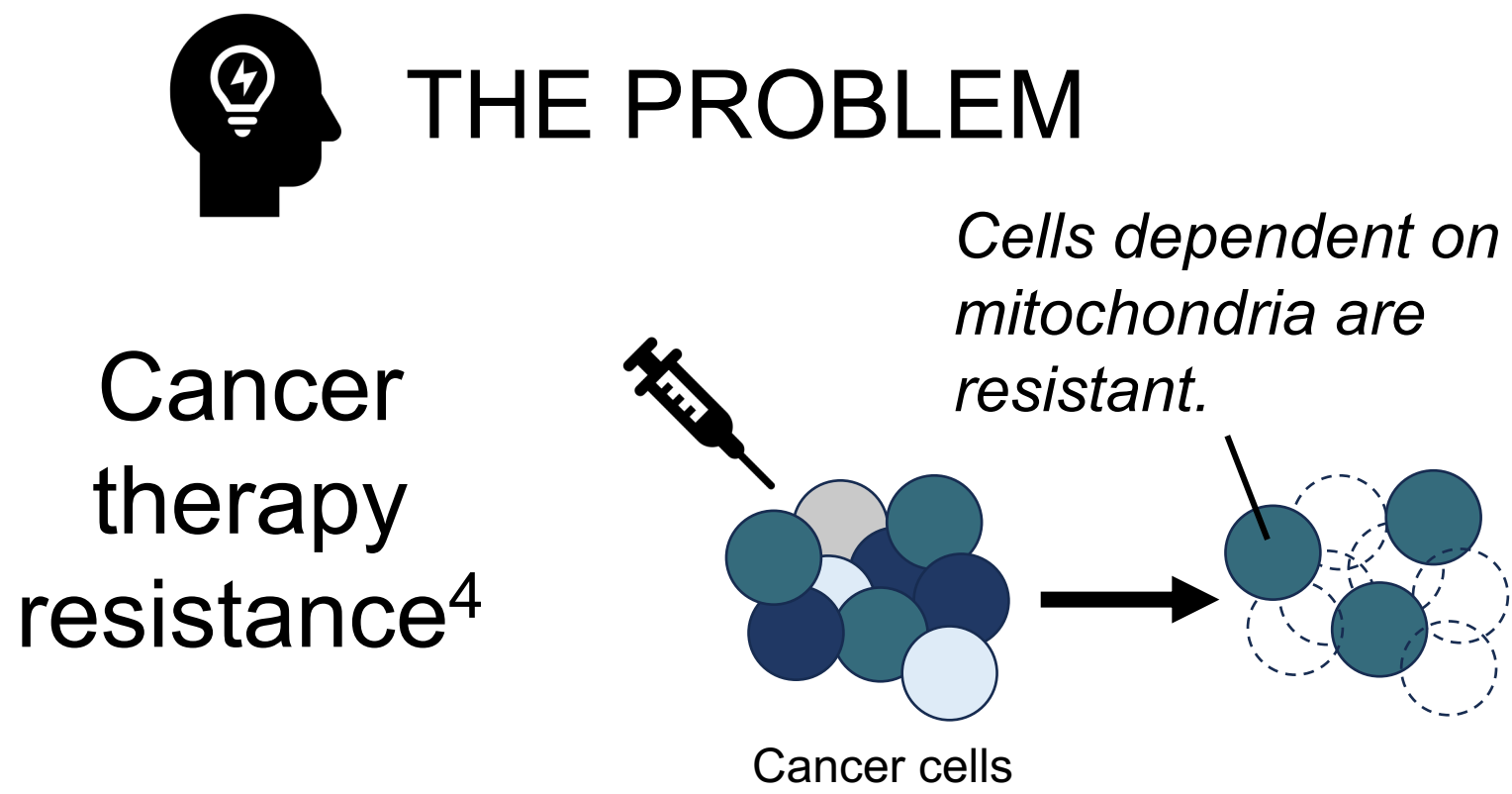
### Research Questions and Results

#### Question 1:

**Why** is the MIA40 pathway upregulated in cancer cells and **how** does it benefit them?



#### THE PROBLEM



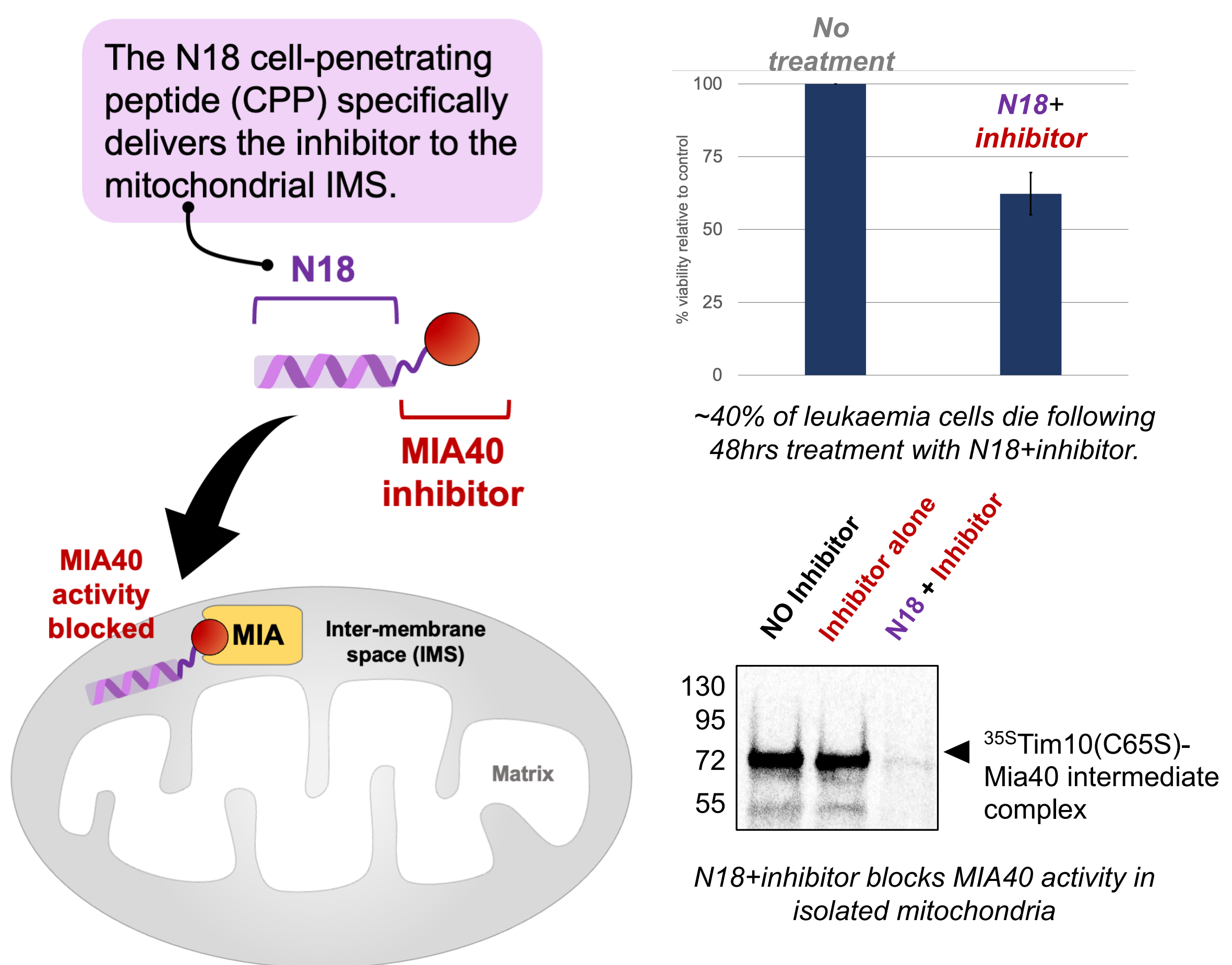
#### Question 2:

Can we exploit cancer cell dependency on mitochondria by **selectively blocking** a crucial mitochondrial pathway, **MIA40**, and **eradicate residual disease**?



#### THE SOLUTION

**Target** and **block cancer cells** with a MIA40 dependency using an in-house covalent, cell-penetrating peptide inhibitor<sup>6</sup>.



**Conclusion:** Blocking MIA40 disrupts cancer cells' dependency on mitochondria and eliminates them.

#### Future work:

- Using our MIA40 inhibitor as an investigative tool we can further explore the role of this pathway in cancer cells.
- Understanding and manipulating this pathway could be a game-changer in our fight against therapy-resistant cancers.

#### References:

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3. Thomas L, et al. *Cancer & Metabolism.* **2019**. 7.
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6. Murphy and Hartley. *Nat Rev Drug Discov.* **2018**. 17.



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