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. Over 99% of mitochondrial proteins/machinery must be delivered to one of four functional compartments within mitochondria via import pathways.

The MIA40 pathway in the IMS ensures proper folding and function of proteins entering the mitochondria.

The MIA40 pathway is hyperactive in certain cancers, including pancreatic, breast, lung, brain, and blood cancers.

Why cancer cells are reliant on this pathway remains unclear.

Cancer cells with an upregulated MIA40 pathway share characteristics with therapy-resistant cancer cells.

Research Questions and Results

Question 1: Why is the MIA40 pathway upregulated in cancer cells and how does it benefit them?

Increased mitochondrial activity

Hypoxia activation (in cancer cells) & angiogenesis

Metastasis, invasion and tumor growth

Poor patient survival

Question 2: Can we exploit cancer cell dependency on mitochondria by selectively blocking a crucial mitochondrial pathway, MIA40, and eradicate residual disease?

THE PROBLEM

Cancer therapy resistance

Cells dependent on mitochondria are resistant.

THE SOLUTION

Target and block cancer cells with a MIA40 dependency using an in-house covalent, cell-penetrating peptide inhibitor.

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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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