The Azrieli Faculty of Medicine
Bar-Ilan University

38th EPS European Peptide Symposium — 6 - 11th of September 2026 — Vienna, Austria

QVIT LAB

Targeted Inhibition of Fis1/Mfn1 Protein-Protein Interactions with Peptides Promotes Cardioprotection

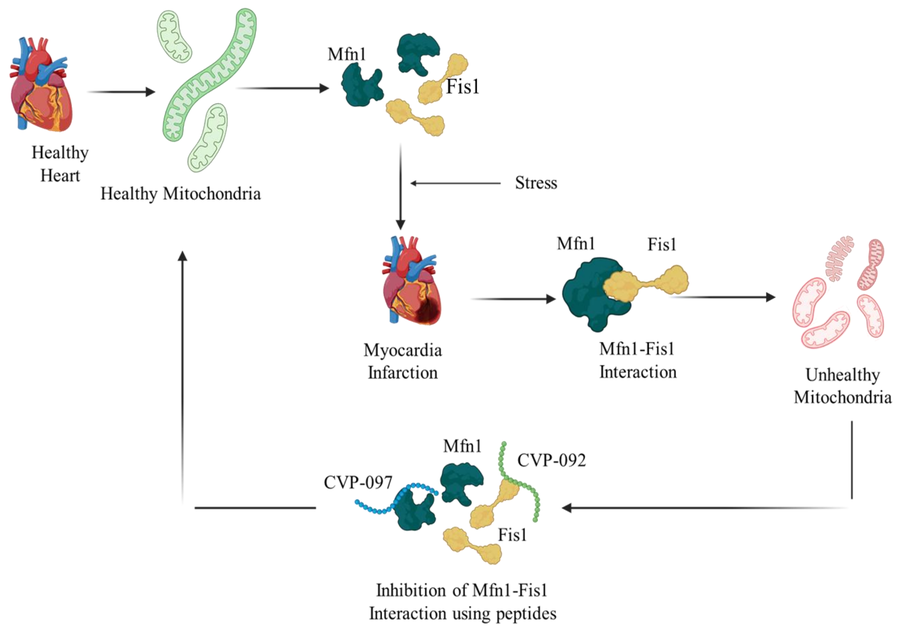
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Scientific Rationale

Pathological stress is proposed to favor Fis1-Mfn1 binding and suppress Mfn1-mediated mitochondrial fusion. CVP-097 was designed to bind Fis1; CVP-092 was designed to bind Mfn1.

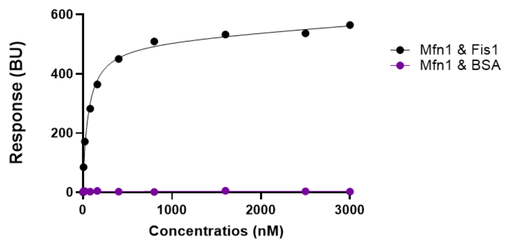


Question: Does selective inhibition of this protein-protein interaction preserve mitochondrial function during cellular stress?

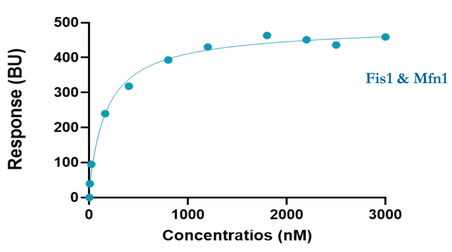
Results

Fis1-Mfn1 Interaction and Target Binding Confirmed

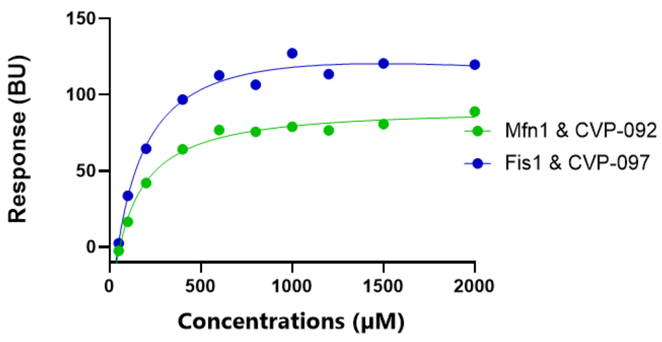
Mfn1 & Fis1 Interaction Mfn1 on Chip



Fis1 & Mfn1 Interaction Fis1 On Chip



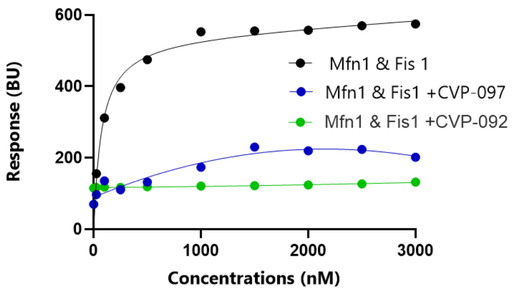
Peptide Protein Interaction



PPI	K_D (μM)
Mfn1 & Fis1 (Mfn1 on Chip)	0.060 ± 0.002
Fis1 & Mfn1 (Fis1 on Chip)	0.058±0.003
Mfn1 & BSA	undetectable binding
Fis1 & CVP-097	197± 16
Mfn1 & CVP-092	237±29

Experimental studies confirmed both Fis1-Mfn1 complex formation and the specific binding of CVP-092 and CVP-097 to their intended protein targets.

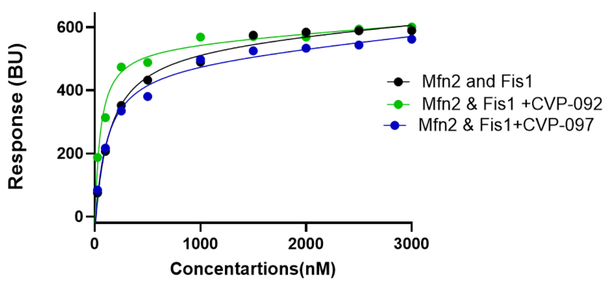
CVP-092 & CVP-097 Specifically Inhibit the Fis1-Mfn1 Interaction

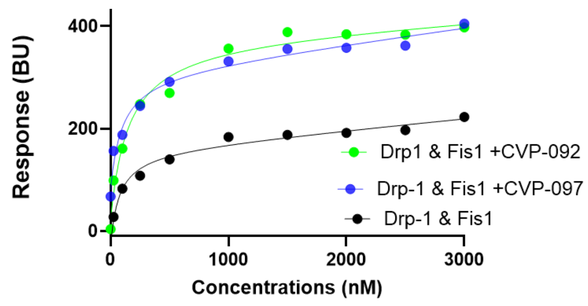


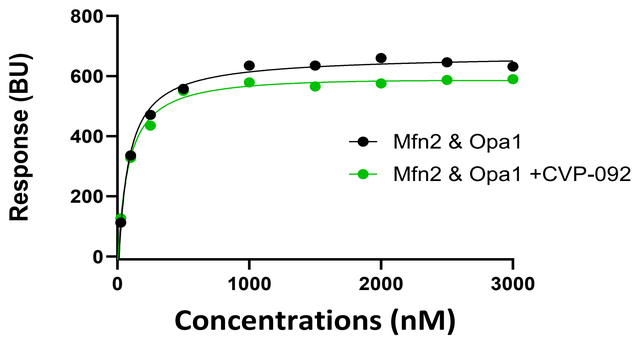
Competitive (PPI)	K_D (μM)
Mfn1 & Fis1	0.06 ± 0.002
Mfn1 & Fis1 + CVP-097	9.178 ± 0.18
Mfn1 & Fis1 + CVP-092	2.819 ± 0.26

Both CVP-092 and CVP-097 disrupted the Fis1-Mfn1 interaction, with CVP-097 producing a larger increase in K_D than CVP-092 (153-fold versus 47-fold, respectively).

Peptide Selectivity Study





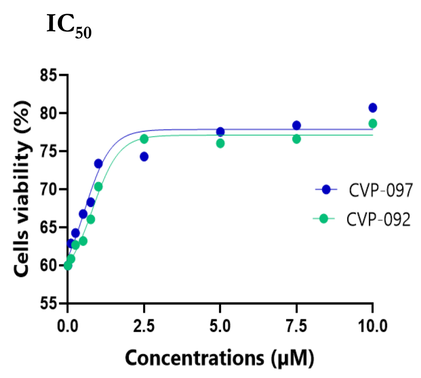


Competitive (PPI)	K_D (μM)
Mfn2 & Fis1	0.103 ± 0.002
Mfn2 & Fis1 + CVP-097	0.130± 0.024
Mfn2 & Fis1 + CVP-092	0.102 ± 0.032
Drp1 & Fis 1	0.072 ±0.010
Drp1 & Fis1 + CVP-097	0.095 ±0.020
Drp1 & Fis1 + CVP-092	0.153±0.018
Mfn2 & Opa1	0.068 ± 0.008
Fis1 & Opa1 + CVP-092	0.078 ± 0.010

CVP-092 and CVP-097 selectively disrupted the Fis1-Mfn1 interaction without affecting the other mitochondrial protein interactions tested.

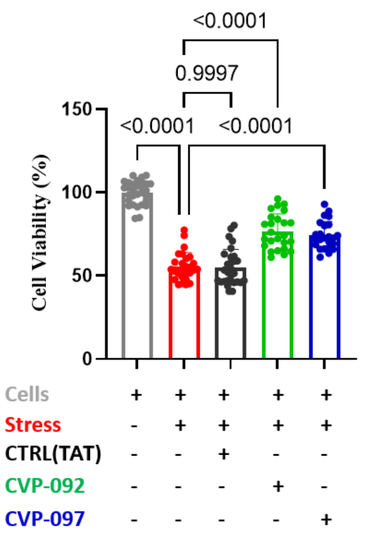
Peptides Protect H9c2 Cardiomyoblasts Under Chemical Ischemia Mimicry

IC_{50}

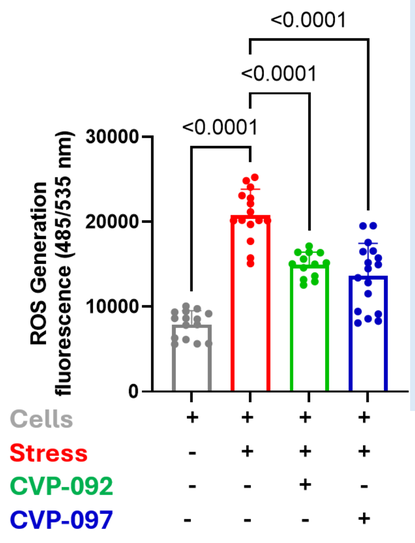


Peptides	IC_{50} (μM)
CVP-097	3.42± 0.60
CVP-092	3.76±0.49

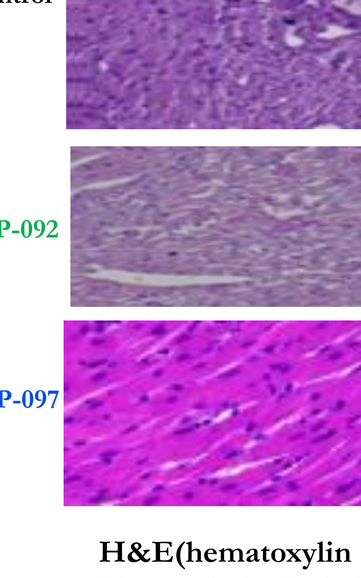
Cell Viability



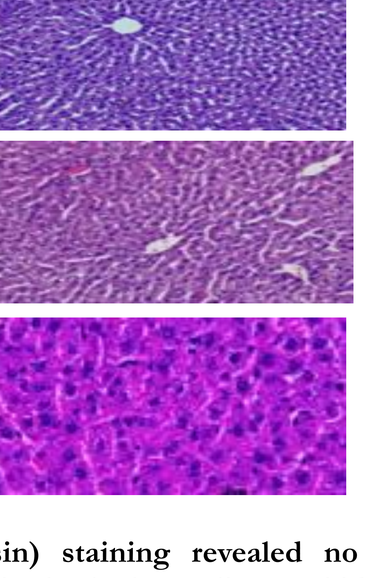
Reactive Oxygen Species



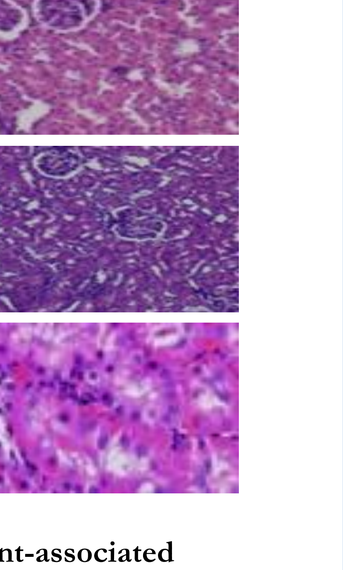
Mitochondrial Membrane Potential



LDH



ATP Level



CVP-092 and CVP-097 improved H9c2 cell viability and reduced stress-induced mitochondrial and cellular injury.

Peptides Show No Detectable Organ Toxicity

H&E(hematoxylin and eosin) staining revealed no treatment-associated histopathological abnormalities in the heart, liver, or kidney.

Take Home Message

1) CVP-097 and CVP-092 selectively weakened Fis1-Mfn1 binding, producing approximately 153-fold and 47-fold increases in apparent (KD), respectively.

2) Both peptides attenuated stress-induced H9c2 cell injury by improving viability, mitochondrial membrane potential, and ATP while reducing ROS and LDH release.

3) These findings support the Fis1-Mfn1 interface as a candidate therapeutic target; intracellular target engagement and in vivo cardioprotective efficacy remain to be established.

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