# Selective Bfl-1 Peptides

Technology #18607

## Applications

Peptide inhibitors of Bfl-1, an anti-apoptotic protein, allow for selective targeting of Bfl-1 dependent cancer cells in therapeutic treatment. Selective peptides may also be used as Bfl-1-detection reagents. This allows for cellular profiling for anti-apoptotic protein dependency, thus potentially acting as a diagnostic tool for stratifying patients.

## Problem Addressed

Many cancer cells overexpress anti-apoptotic Bcl-2 family proteins that confer resistance to chemotherapy treatment. Selective inhibitors of Bcl-2 are available in clinic to treat Bcl-2 dependent cancers. However, such tools are missing for Bfl-1. Selective inhibitors allow for selective targeting of Bfl-1 dependent cancer cells while limiting systemic toxicity.

## Technology

Selective peptide inhibitors of Bfl-1 were identified by screening for sequence variants of the BH3 motif of PUMA, a highly potent binder of Bcl-2 family members. Peptides were designed using computational analysis followed by experimental screening that identified peptides with high affinity for Bfl-1 yet weakened interactions with other anti-apoptotic proteins. The lead peptide inhibitors are >100-fold selective for binding to Bfl-1 binding over other anti-apoptotic proteins of Bcl-2 family. Selectivity towards Bfl-1 was further augmented by modifying the peptide inhibitors with electrophiles to allow for covalent interaction in the binding pocket of Bfl-1. The selectivity of the peptide Bfl-1 inhibitors in a cellular context was confirmed by the relative mitochondrial depolarization or cytochrome-c release after peptide treatment of Bfl-1 dependent cells vs. other anti-apoptotic protein dependent cells.

## Advantages

- The peptide inhibitors are potent and selective towards Bfl-1 with >100-fold selectivity over other anti-apoptotic proteins
- The peptide inhibitors can also be used as diagnostic tools to profile cells for Bfl-1 dependency

## Categories For This Invention:

Life Sciences
Clinical Applications
Oncology
Diagnostics
Protein
Research Tools
Protein & Protein Chemistry

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Screening Assays
Therapeutics
Peptide

## Intellectual Property:

Selective Bfl-1 peptides
US Patent Pending
2019-0185531

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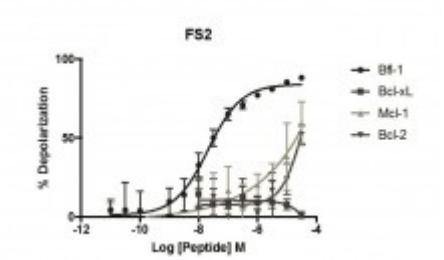
## Publications:

Epistatic Mutations in PUMA BH3 Drive an Alternate Binding Mode to Potently and Selectively Inhibit Anti-apoptotic Bfl-1.
Elife
2017 Jun 8;6. pii: e25541. doi: 10.7554/eLife.25541.

## External Links:

Keating Lab
https://keatinglab.mit.edu/

## Image Gallery:

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