Cancer Therapeutics

Proteasome Inhibitors & Targeted Protein Degradation

Redirecting adaptive autophagy to enhance cancer therapy

VCU TechTransfer and Ventures
Office of the Vice President for Research and Innovation

Current proteasome inhibitor therapies for multiple myeloma and mantle cell lymphoma induce an adaptive autophagy response in cancer cells, which decreases their efficacy and limits their use in solid tumors.

Researchers at Virginia Commonwealth University have developed a novel therapeutic strategy that harnesses proteasome inhibitor-induced autophagy to selectively degrade resistance-associated proteins. Using Autophagy-Targeting Chimeras (AUTACs), this approach enhances cancer cell death and overcomes resistance, significantly improving the effectiveness of proteasome inhibitor-based treatments.

The Technology

This strategy leverages the interplay between proteasome inhibition and lysosome-mediated targeted protein degradation to eliminate key survival proteins such as Mcl-1, a major driver of resistance in cancer. Unlike traditional therapies that broadly inhibit autophagy, this technology redirects the process to degrade cancer-promoting proteins selectively, reducing off-target toxicity and enhancing therapeutic efficacy.

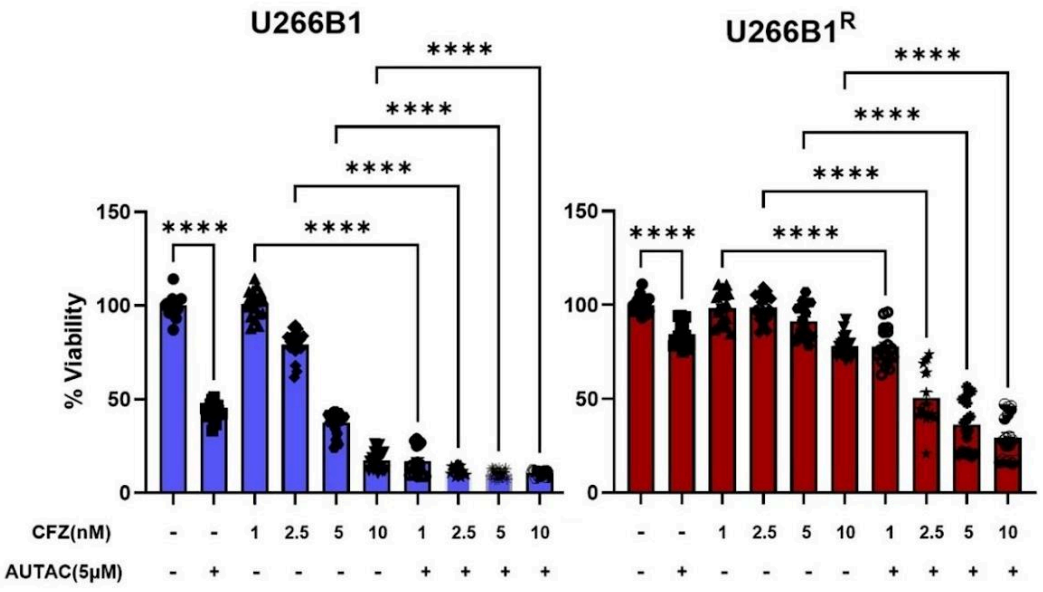

Figure 1. Mcl-1 AUTAC potentiates carfilzomib (CFZ)-induced cell death in wild-type (U266B1) and proteasome inhibitor-resistant (U266B1^R) multiple myeloma cell lines.

Benefits

- Increases efficacy of proteasome inhibitor treatments
- Overcomes proteasome inhibitor resistance
- Decreased cardiac toxicity
- Useful for multiple cancers

Applications

- Adjuvant therapy
- Targeted protein degradation

Patent Status:
Provisional Patent Application has been filed

License Status:
This technology is available for licensing to industry for further development and commercialization

Category:
Pharmacotherapeutics

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