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Nrf2 Based Stapled Peptides for Sensitization of Cancers to Chemotherapeutics

Cell-permeable and stable stapled peptides inhibit Nrf2 by binding to MafG, effectively sensitizing non-small cell lung cancer cells for improved combinational chemotherapy outcomes.

Researchers at Purdue University have developed novel stapled peptides that sensitize cancer cells to chemotherapeutic agents. Increased levels of nuclear factor erythroid 2-related factor 2 (Nrf2) enhance resistance to chemotherapeutics, leading to a poor patient prognosis. A knockdown of Nrf2 has demonstrated a sensitization of cancer cells to chemotherapeutics. Current therapeutics with a similar target either have low potency, are not selective, are not cell permeable, or have a combination of these undesirable characteristics.

Purdue researchers have designed stapled peptides which inhibit Nrf2. The best molecule showed statistically significant inhibition of Nrf2 at 50 micromolar relative to DMSO. An additional dose response assay indicated the molecule may also be effective at lower doses. The researchers identified the mechanism of action of the stapled peptides. The peptide directly interacts with the transcription factor, small musculoaponeurotic fibrosarcoma G (MafG). Further studies validated that the peptides were capable of sensitizing non-small cell lung cancer cells to chemotherapeutics. Along with the peptide being cell permeable and proteolytically stable, these peptides are a candidate for combinational therapy with another chemotherapeutics.

Technology Validation: This technology has been validated using a luciferase assay, western blot, and MTT assay. These methods demonstrated that these novel stapled peptides inhibit Nrf2 by binding to MafG to sensitize non-small cell lung cancer cells to chemotherapies.

Advantages:

Technology ID
2023-PARK-69958

Category
Biotechnology & Life Sciences/Bioinformatics & Computational Biology
Artificial Intelligence & Machine Learning/AI Model Optimization & Acceleration Tools
Chemicals & Advanced Materials/Materials Processing & Manufacturing Technologies
Pharmaceuticals/Small Molecule Therapeutics

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-Cell permeable

-Proteolytic stability

-Sensitize cancer cells to known chemotherapuetics

Applications:

-Non-small cell lung cancer

-Chemotherapeutic

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Intellectual Property:

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