FERRITIN-TARGETING PROTACS AND METHODS OF INDUCING PYROPTOSIS

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The Invention

UW-Madison researchers have developed ferritin-targeting proteolysis targeting chimeras (PROTACs) to establish an iron excess stress inside cancer cells. The PROTAC structure contains oleic acid for binding to ferritin dimer and the ligand of von Hippel-Lindau (VHL) E3 ligase, which is bridged by alkyl linkers. The researchers made an exemplary degrader (DeFer-2) through ternary complex formation, which efficiently and rapidly reduced the ferritin expression level in cancer cells, leading to a quick elevation of intracellular free iron content. After inducing iron overload stress with DeFer-2, the complex successfully triggered the caspase 3-GSDME-mediated pyroptosis in cancer cells.

Encouraged by the potent pyroptosis-inducing capacity, a tailored albumin-based nano-formulation was designed for in vivo DeFer-2 administration according to its structural and physicochemical characteristics. Notably, the resulting formulation (aDeFer-2) substantially inhibited tumor growth and prolonged the survival time of mice bearing B16F10 subcutaneous tumors with negligible adverse effects.

Tech Fields

- Research Tools : Other research tools
- Therapeutics & Vaccines : Oncology

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847