Perspective

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PROTACs in Cancer Therapy: Targeted Protein Degradation for Next-Generation Oncology

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Introduction

Cancer therapy has traditionally relied on strategies such as chemotherapy, radiation, and targeted small-molecule inhibitors. While these approaches have improved survival, many tumors develop resistance due to genetic mutations, compensatory signaling, or protein overexpression. Proteolysis-targeting chimeras (PROTACs) represent an innovative therapeutic approach that leverages the cell's ubiquitin-proteasome system to selectively degrade disease-causing proteins [1-5]. By targeting proteins for destruction rather than inhibition, PROTACs offer a promising avenue for overcoming drug resistance and expanding the therapeutic landscape in oncology.

Discussion

PROTACs are bifunctional molecules composed of three key elements: a ligand that binds the protein of interest, a ligand that recruits an E3 ubiquitin ligase, and a linker connecting the two. Once the PROTAC brings the target protein into proximity with the E3 ligase, the protein is ubiquitinated and subsequently degraded by the proteasome. This catalytic mechanism allows a single PROTAC molecule to induce degradation of multiple target protein copies, providing sustained therapeutic effects even at low concentrations.

In cancer therapy, PROTACs have shown promise against traditionally "undruggable" targets, including transcription factors, scaffold proteins, and signaling molecules that lack enzymatic activity. For instance, PROTACs targeting androgen receptor (AR) in prostate cancer or estrogen receptor (ER) in breast cancer have demonstrated efficacy in preclinical models, including tumors resistant to conventional inhibitors. Similarly, PROTACs designed against oncogenic kinases, such as BCR-ABL or BET family proteins, show potential for overcoming resistance to tyrosine kinase inhibitors and epigenetic therapies.

The advantages of PROTACs include specificity, the ability to target proteins previously considered inaccessible, and the potential for reduced side effects due to selective degradation rather than systemic inhibition. However, challenges remain, including optimizing cell permeability, oral bioavailability, metabolic stability, and minimizing off-target degradation. Clinical development is ongoing, with several PROTAC candidates entering early-phase trials, providing important insights into pharmacokinetics, efficacy, and safety.

Conclusion

PROTACs represent a groundbreaking strategy in cancer therapy, offering targeted protein degradation as an alternative to traditional inhibition. By expanding the range of druggable targets and addressing resistance mechanisms, PROTACs hold significant potential to improve outcomes for patients with refractory or resistant cancers. Ongoing research and clinical development will determine the broader applicability of this technology, positioning PROTACs as a transformative approach in next-generation oncology therapeutics.

References

1. Middleton JD (1968) A Method to Evaluate Skin Moistrizers in Vivo Brit. J Dermatology 80: 437-450.
2. Li L, MacMary S, Sainthillier JM, Nouveau S, de Lacharriere O, et al. (2006) Age-related changes of the cutaneous microcirculation in vivo. Gerontology 52: 142-153.
3. Wang J, Kuesten C, Mayne J, Majmudar G, Pappas TN, et al. (2021) Human Skin Gloss Perception Based on Texture Statistics. IEEE Trans Image Process. 30: 3610-3622.
4. Gupta R, Badhe Y, Rai B, Mitragotri S (2020) Molecular mechanism of the skin permeation enhancing effect of ethanol: a molecular dynamics study. RSC Adv 10: 12234-12248.
5. Bukhari SNA, Roswandi NL, Waqas M, Habib H, Hussain F, et al. (2018) Hyaluronic acid, a promising skin rejuvenating biomedicine: A review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. Int J Biol Macromol 120: 1682-1695.