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Antibody-Targeted Molecular Glue Degraders for Selective Cancer Therapy

Stanford researchers have developed degrader-antibody conjugates that deliver hyper-potent molecular glue degraders directly to tumor cells. The design combines the targeting precision of antibodies with the catalytic potency of targeted protein degradation, acting selectively on cancer cells that express a defined tumor antigen.

Many potent degraders act across a wide range of cell types, which can limit their therapeutic window and expose healthy tissue to unwanted activity. The Stanford team conjugates optimized molecular glues to antibodies that recognize antigens enriched on tumor cells. The antibody restricts payload delivery to antigen-positive cells, where the molecular glue drives degradation of its target protein. Confining degrader activity to tumor cells is designed to widen the therapeutic index and spare normal tissue relative to untargeted degrader or small molecule approaches. The approach is modular, so a single degrader payload can be paired with different antibodies to address a range of tumor antigens, and the antibody format can be matched to the target and indication.

Stage of Development
Research – in vitro

Applications

- Targeted treatment of cancers with high expression of a defined tumor antigen
- Antibody-directed delivery of targeted protein degraders (degrader-antibody conjugates)
- Modular payload approach pairing molecular glue degraders with antibodies against multiple tumor antigens

- Precision oncology programs seeking a wider therapeutic index than untargeted degraders or small molecules

Advantages

- Improved selectivity through antibody-directed delivery to antigen-positive tumor cells
- High potency from hyper-potent molecular glue degrader payloads
- Wider therapeutic index and greater sparing of normal tissue than untargeted degrader or small molecule approaches
- Modular design compatible with multiple antibodies and tumor antigens
- Novel combination of targeted protein degradation and antibody delivery

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