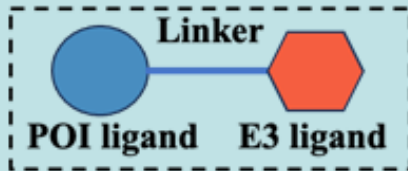
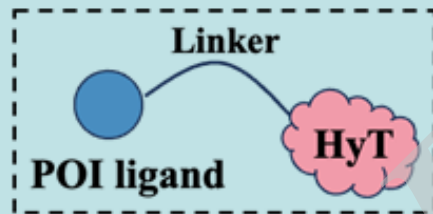


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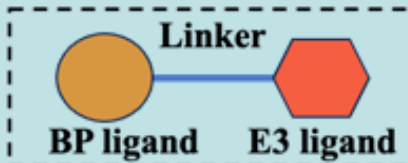
Exploiting targeted degradation of cyclins and cyclin-dependent kinases for cancer therapeutics: a review

Key words: Cyclin-dependent kinase (CDK); Cyclin; Protein degrader; Targeted protein degradation

Hydrophobic tag degrader

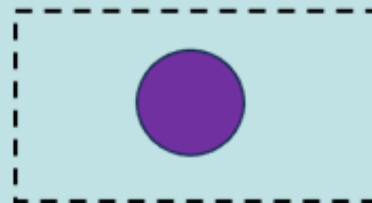


PROTAC

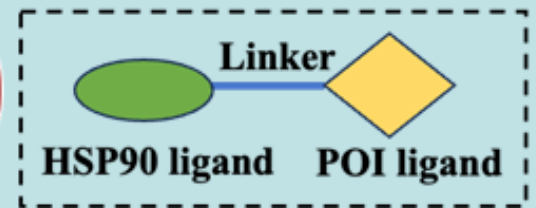


Molecular glue

Molecular glue



HEMTAC



Targeted degradation
of cyclins and CDKs
via proteasome

Research Summary

CDKs and cyclins play critical roles in cancer, representing compelling therapeutic targets in oncology. Better understanding their mechanism and function will provide important insights for the development of targeted anti-cancer therapy.

This review synthesizes current knowledge on targeted protein degradation, with emphasis on CDK/cyclin degraders, their molecular mechanisms, and therapeutic applications. CDK/cyclin degraders not only provide novel tools for biomedical research but also represent a bright future in pharmaceutical development.

Highlights

- **Overview of strategies and advances in targeted protein degradation of CDK and cyclins for cancer therapeutics**
- **In-depth mechanistic and structural analyses of proteolysis-targeting chimeras, HSP90-mediated targeting chimeras, hydrophobic tag-based protein degraders, and molecular glues**
- **State-of-the-art summary of proteasome-dependent CDK/cyclin degrader development**
- **Insights into future research pathways of CDK/cyclin degrader development and therapeutic implementation**

List of figures and tables

Figure 1 | Working mechanisms of proteolysis-targeting chimera (PROTAC), heat shock protein 90 (HSP90)-mediated targeting chimera (HEMTAC) and hydrophobic tag (HyT)

Figure 2 | Working mechanisms of molecular glue degraders

Figure 3 | Molecular structures of selective proteolysis-targeting chimeras (PROTACs) that target cyclin-dependent kinase 2 (CDK2)

Figure 4 | Molecular structures of selective proteolysis-targeting chimeras (PROTACs) and heat shock protein 90 (HSP90)-mediated targeting chimeras (HEMTACs) that target cyclin-dependent kinase 4/6 (CDK4/6)

Figure 5 | Molecular structures of selective degraders against cyclin-dependent kinase 8/19 (CDK8/19), CDK7, and CDK9/Cyclin

Figure 6 | Molecular structures of the selective molecular glue of Cyclin K and proteolysis-targeting chimeras (PROTACs) that target either cyclin-dependent kinase 12/13 (CDK12/13) or CDK17

Figure 7 | Cell cycle regulatory cyclin-dependent kinase (CDK)/cyclin complexes and their reported degraders

Table 1 | Comparison among inhibitors and various proteasome-dependent chemical degraders

Future perspectives

- **Unfilled gaps in CDK and cyclin biology**
- **Advantages of targeted protein degradation over conventional protein inhibition**
- **Potential of PROTACs to improve selectivity for CDK targets**
- **Strategies and challenges in heterofunctional CDK degrader design**
- **Bioavailability challenges for protein degraders**
- **Underdeveloped fields for degraders targeting CDK and cyclin**