# Article information:

Functional E3 ligase hotspots and resistance mechanisms to small-molecule degraders | Nature Chemical Biology  
<https://www.nature.com/articles/s41589-022-01177-2>

# Article summary:

1. Proximity-inducing pharmacology is a therapeutic paradigm that uses small molecules to induce interactions between proteins.

2. Targeted protein degradation (TPD) is one of the most powerful embodiments of this approach, using small-molecule ‘degraders’ to induce the molecular proximity between an E3 ubiquitin ligase and a protein of interest (POI).

3. This article explores functional hotspots in E3 ligases that dictate degrader efficacy, leveraging human haploid genetics and deep mutational scanning (DMS) libraries to identify these hotspots.

# Article rating:

Appears well balanced: The article presents the information in a reliable and balanced way, without biases and prejudices. The claims made in the article are well supported and, where applicable, all sides of the argument are given opportunity to present their point of view. The article appears trustworthy and reliable.

# Article analysis:

The article provides a comprehensive overview of the current state of research on targeted protein degradation (TPD), which is a promising therapeutic paradigm for treating diseases. The authors provide an in-depth analysis of the various aspects involved in TPD, such as the role of E3 ubiquitin ligases, substrate receptors, and small-molecule degraders. They also discuss how structural biology has been instrumental in shaping understanding of TPD and how it can be used to inform predictive computational models.

The article is generally well written and provides a thorough overview of the topic at hand. It does not appear to be biased or one-sided, as it presents both sides equally and does not make any unsupported claims or omit any points of consideration. Furthermore, it does not contain any promotional content or partiality towards any particular viewpoint or opinion. The authors have also noted potential risks associated with TPD, such as resistance acquisition due to mutations in substrate receptors or ternary complex assembly defects.

In conclusion, this article appears to be trustworthy and reliable overall, providing an unbiased overview of targeted protein degradation with detailed insights into its various components and potential risks associated with it.

# Topics for further research:

* Targeted protein degradation mechanism
* E3 ubiquitin ligase structure
* Substrate receptor function
* Small-molecule degrader design
* Structural biology of TPD
* Computational modeling of TPD

# Report location:

<https://www.fullpicture.app/item/4231f94ef5c8923243cf89d7e226c016>