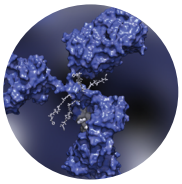
Targeted Protein Degrader Safety



Our Mission

To advance efficient and effective translational safety assessment to maximize the therapeutic potential of targeted protein degraders for patients, by an international network of multi-partite, multi-stakeholder experts.

Chairs

Public Chair
Dr. Lyn Jones (Dana-Farber Cancer Institute)

Private Chairs
Dr. Ruth Roberts (ApconiX)
Dr. Mira Pavkovic (Bayer AG)

HESI Staff

Dr. Lucilia Mouriès (lmouries@hesiglobal.org)
Ms. Connie Mitchell (cmitchell@hesiglobal.org)
Dr. Raegan O'Lone (rolone@hesiglobal.org)

Webpage

https://hesiglobal.org/targeted-protein-degrader-safety/

2022 Committee Highlights

Participating Organizations
2 government/regulatory agencies,
2 academic/research institutes,
20 industry

Publications
1 publication

Scientific Meetings and Trainings
1 meeting

- HESI PROTACs and Molecular Glues Safety Workshop (virtual; 200 attendees)

Outreach
1 oral presentation, 1 networking event

Safety Pharmacology Society Annual Meeting
- *Targeted Protein Degraders: Introduction and Potential Safety Challenges*. Connie Mitchell (HESI).

5th Targeted Protein Degradation Summit
- The committee held an event for committee members attending this meeting or local to the area to meet in person.

Geographic Representation
Denmark, France, Germany, Switzerland, United Kingdom, United States

Working Groups

NEW **Cereblon-related Safety Challenges.** This group is exploring challenges related to cereblon-mediated protein degradation and mapping current tools employed to evaluate those challenges (e.g., teratogenicity).

NEW **Study Design Challenges**. This group is discussing assays and models used to evaluate safety and highlight specific differences for heterobifunctional degraders and molecular glue degraders compared to traditional small molecules.

Areas of Focus for 2023

- Continued public sector outreach.
- Creation of points-to-consider framework for safety assessment.
- The committee will be organizing a session at the Society of Toxicology 2023 Annual Meeting entitled "*Targeted protein degradation therapeutics: opportunities and challenges*".

Strategic Impact Areas

Enhanced efficiency and accuracy in safety assessment practice
This committee is focused on advancing safety assessment to maximize the therapeutic potential of targeted protein degraders for patients.

Catalysis of new science
Heterobifunctional degraders and molecular glues are a newer class of therapeutics that require special safety considerations compared to small molecules. This is a new committee at HESI, launched in December 2021, based on the needs expressed by stakeholders at the HESI workshop held in October 2021.

Enhancement of the societal knowledge base on human biological processes of relevance for protecting human health
While these molecules are being developed as therapeutics, the underlying biology of the degradation pathways are sometimes unknown. This committee is also exploring what is known about specific endogenous processes, such as the role of cereblon, compared to small molecules.

Increasing the audiences for collaborative safety science
Within this new committee, HESI is entering an emerging field where there is a need for collaborative approaches to better understand safety challenges. While TPDs are largely being developed for cancer applications, this group included new participants this year, with expertise in applications such as infectious diseases and agricultural biotechnology.

Publications

Published

Jones et al. 2022. Targeted protein degraders: a call for collective action to advance safety assessment. *Nature Reviews Drug Discovery.* https://doi.org/10.1038/d41573-022-00055-9.

Participating Organizations

Government/Regulatory Agencies

National Institutes of Health (NIH),
National Institute of Allergy and Infectious Diseases (NIAID)
US Food and Drug Administration (FDA)

Academic/Research Institutes

Broad Institute of MIT and Harvard
Dana-Farber Cancer Institute

Industry

AbbVie
Amgen
ApconiX
Bayer
Bristol-Myers Squibb
C4 Therapeutics
Foghorn Therapeutics
Genentech/Roche
Janssen Pharmaceuticals
Kymera Therapeutics
LEO Pharma
Merck & Co,
Merck Healthcare KGaA
Novartis Pharmaceuticals
Oerth Bio
Pfizer, Inc.
Sanofi
Schrodinger
Takeda Pharmaceutical Company, Ltd.
UCB Biopharma SPRL