

ACTT : Expanding the protein degradation field

The Problem

- Targeted Protein Degraders are a new class of drugs that promises to revolutionise the treatments of many diseases – TPDs allows us to target the 'undruggable'.
- E3 ligase warheads are the cornerstone of protein degrader (PD) technology.
- The vast majority of current PD technology utilises two E3 warheads VHL and Cereblon, limiting the targets that can be degraded.

The Solution

- The Australian Centre for Targeted Therapeutics (ACTT), based at WEHI, seeks develop **four** new E3 ligase warheads, drawing from the remaining pool of >600 E3 ligases, and **two** novel TPDs against transcription factors in oncology.
- E3s will be selected for spatial, temporal and disease association, to improve selectivity and reduce toxicity.
- We have technologies and expertise to enable development of the next generation of TPDs.

Our Program

- Progress: Two screening campaign completed with medicinal chemistry underway; screens against remaining targets in progress.
- Goal: To develop four novel E3 ligase targeting moieties enabling lead candidates to be developed. This platform technology will enable partnerships and co-development with investors with their own preferred targets/indications. Additionally, ACTT aims to develop target binders of our own, one common and one rare cancer.

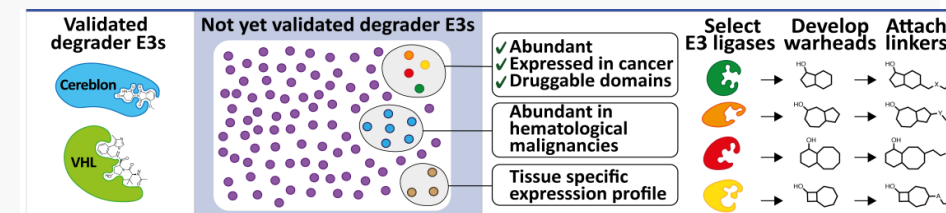
Target E3 ligase selection criteria

Degradative E3 ligase

Tissue expression: broad vs. specific

Disease association: yes/no

Available and amenable binding pockets not interfering with activity



Example cancer-specific E3 ligase warhead workflow

Our Team

Dr Joanne Boag, Centre Director
Dr Bernard Lechtenberg, E3W Lead
Dr Bekky Feltham, Target Biology Lead
Dr Nicole Trainor, Medicinal Chemistry Lead

Janet Yeo, PhD, Business Development Manager
yeo.j@wehi.edu.au