A Cellular Target Engagement Atlas of 100+ Drug Targets Validated by MICRO-TAG Platform

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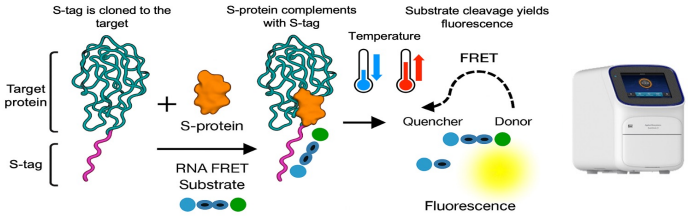
MICRO-TAG® measures target engagement across dynamic conformations in cells.
Atlas of 100+ target is now accessible through OTI.

Abstract

Systematic datasets describing cellular target engagement remain limited, particularly for structurally dynamic and difficult-to-assay drug targets. The MICRO-TAG® platform enables real-time, quantitative measurement of ligand-dependent target engagement in cells using temperature-series profiling. We present a cellular target engagement atlas of 100+ drug targets validated using MICRO-TAG, spanning both challenging and conventional classes, including enzymes, kinases, membrane proteins, transcription factors, and protein complexes. Baseline thermal profiles define assay conditions, while representative data capture ligand-induced stabilization and destabilization across diverse mechanisms.

This atlas provides a practical framework for configuring cellular target engagement assays and supports multiple applications, including hit validation and mechanism-of-action studies. It forms the foundation for the Open Target Initiative (OTI), which provides access to MICRO-TAG reagents and datasets for 100+ targets, enabling qualified researchers to expand cellular target engagement studies in early discovery.

Tackling Challenging Targets

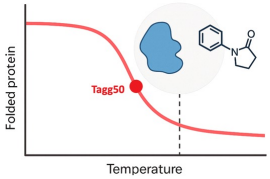


MICRO-TAG® is a fluorescence-based cellular target engagement platform that measures drug–target interactions directly in cells—critical for interrogating challenging targets.

These targets lack stable 3D structure outside cells and are defined by: • intrinsic disorder • transient interaction networks • shifting conformational ensembles (no single binding state) • multi-state ligand engagement • poor representation in static assays. MICRO-TAG® temperature series resolves this dynamic landscape in cells.

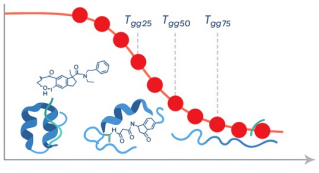
MICRO-TAG® Temperature Series Enables Deep Target Engagement

Conventional Cell Target Engagement



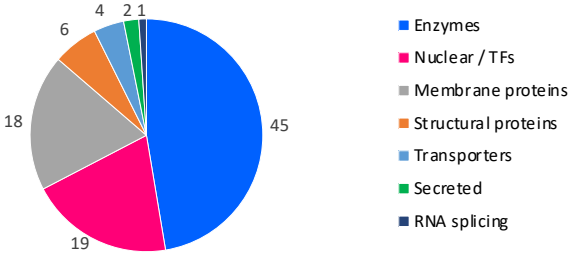
- **Ideal for well-behaved targets**
- Based on a single Tagg50;
- Drug-target interaction as a single conformation only;
- Misses important conformational states;
- End-point measurement;
- Prone to false positives and false negatives.

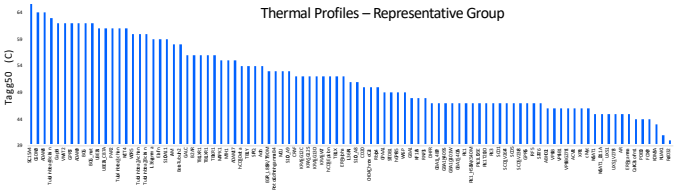
MICRO-TAG® Cell Target Engagement



- **Ideal for challenging drug targets**
- Reads multiple temperatures in series
- Reads drug-target engagement at various conformations of target;
- Gains deep mechanistic insight;
- Yields real-time target engagement data
- Yields partial and total EC50 measurements

Atlas of 100+ Drug Targets

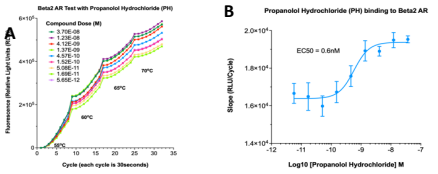




Key Insights from 100+ Drug Targets

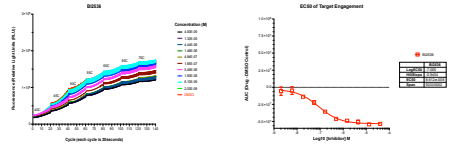
- Broad coverage across conventional and challenging targets
- Wide Tagg50 range defines diverse thermal behaviors
- Resolves distinct thermal fingerprints, capturing both stabilization and destabilization
- Enables cross-target comparison and key applications: hit validation, mechanism-of-action, target deconvolution, and challenging target interrogation

Example of B2AR



Real-time cellular temperature-series profiling of β2AR. (A) Temperature scanning profile of β2AR with propranolol hydrochloride (PH), showing ligand-dependent stabilization. **(B)** Quantification yields a total EC50 of 0.6 nM.

Example of PLK1



Real-time cellular temperature-series profiling of PLK1. (A) Temperature scanning profile of PLK1 withBI2536, showing ligand-induced de-stabilization. **(B)** Quantification yields a total EC50 of 86 nM.

Open Target Initiative (OTI)

Access to 100+ validated MICRO-TAG targets.
Generate real-time cellular engagement data.

- Reagents, target constructs and onboarding support
- Expand to new targets of interest
- Data remains with participant
- Qualified researchers invited to apply

Apply to Participate

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