CellarisBio

PRODUCT WHITE PAPER

MICRO-TAG® Protein Complex Target Engagement Kit

Product Number: Cell-PPI-300

MICRO-TAG® Technology Overview

MICRO-TAG® is a fluorescence-based cellular target engagement platform built on split RNase S enzyme complementation. In the Protein Complex Target Engagement configuration, two proteins of interest are independently tagged: one protein is fused to the short, minimally perturbing MICRO-TAG peptide, while the interaction partner is fused to the complementary S-protein subunit. Functional proximity of the two tagged proteins enables enzyme reconstitution, resulting in cleavage of an RNA FRET substrate and generation of an amplified fluorescence signal.

This **dual-target design** converts **protein complex formation**—rather than single-protein stability—into a quantitative cellular engagement readout, enabling direct measurement of complex assembly, disruption or stabilization in native cellular environments.

Product in Snapshot

MICRO-TAG® Protein Complex Target Engagement Kit enables:

- Direct measurement of protein complex formation in cells
- Quantification of functional proximity between two defined protein partners
- Detection of compound-induced complex disruption, stabilization or induction
- Fluorescence-based detection on standard plate readers and real-time systems

Designed specifically for:

- Protein–protein interactions that define target function
- Ligand-induced recruitment events (e.g., adaptor binding)
- Mechanisms involving ternary or higher-order complexes

Core value:

- Reports functional protein complex engagement rather than isolated binding
- Operates in native cellular context without purified proteins
- Enables mechanism-aware evaluation of complex-modulating compounds

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Why Protein Complex Target Engagement + MICRO-TAG®

Many therapeutically relevant targets operate exclusively as part of protein complexes, where biological function depends on regulated protein–protein interactions. Conventional biochemical or reporter-based

PPI assays often rely on endpoint signals, purified components, artificial immobilization or indirect transcriptional outputs, limiting their ability to capture native complex dynamics.

The MICRO-TAG® Protein Complex Target Engagement workflow directly measures proximity-driven enzyme complementation between two tagged proteins in cells. This enables quantitative interrogation of **how ligands modulate protein complex formation**, stability and kinetics under physiologically relevant conditions.

Enzyme Complementation Chemistry and Signal

Detection chemistry:

- Split RNase S enzyme complementation
- 15-aa hydrophilic MICRO-TAG peptide fused to protein partner A
- Complementary S-protein fused to protein partner B

Complex-dependent behavior:

- Complex formed → tags in proximity → enzyme complements → high fluorescence
- Complex disrupted or absent → no proximity → no complementation → low fluorescence

Signal generation:

- Complemented RNase cleaves RNA FRET substrate
- Enzymatic amplification yields high signal-to-noise
- Multiple donor–quencher FRET pairs supported

Protein Complex Target Engagement Workflow

Workflow summary:

- Cells co-expressing two tagged protein partners are prepared under native conditions
- Test compounds are introduced to modulate protein–protein interactions
- Enzyme complementation reaction is initiated
- MICRO-TAG® fluorescence reports complex formation or disruption
- Engagement is quantified across dose or time or both

Functional logic:

- Disruptors reduce proximity-driven signal
- Stabilizers enhance or prolong signal
- Molecular glues induce signal from weak or transient interactions
- Degraders produce characteristic signal loss kinetics

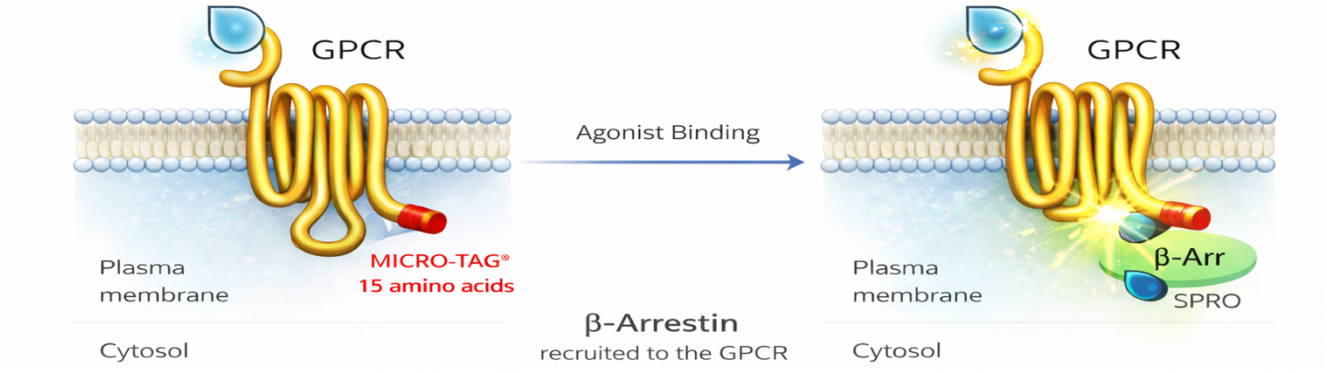

Figure 1. MICRO-TAG®–enabled protein complex target engagement workflow. Two proteins of interest (GPCR and β-Arrestin) are differentially tagged with the MICRO-TAG peptide and S-protein. Functional proximity of the proteins enables enzyme complementation and RNA FRET cleavage, generating a fluorescence signal that quantitatively reports protein complex formation and its modulation by small molecules.

Real-Time Detection and Instrument Compatibility

Compatible platforms:

- Standard fluorescence plate readers
- Programmable real-time fluorescence instruments

Practical benefits:

- No specialized imaging or biophysical instrumentation required
- Compatible with 96- and 384-well formats
- Scalable, automatable and HTS-ready

Quantitative Outputs

Supported readouts:

- Fluorescence intensity reflecting complex engagement
- Time-resolved engagement kinetics

- Dose–response profiles for complex modulation

Why this matters:

- Distinguishes direct complex modulation from downstream phenotypes
- Enables early mechanism confirmation
- Accelerates compound prioritization

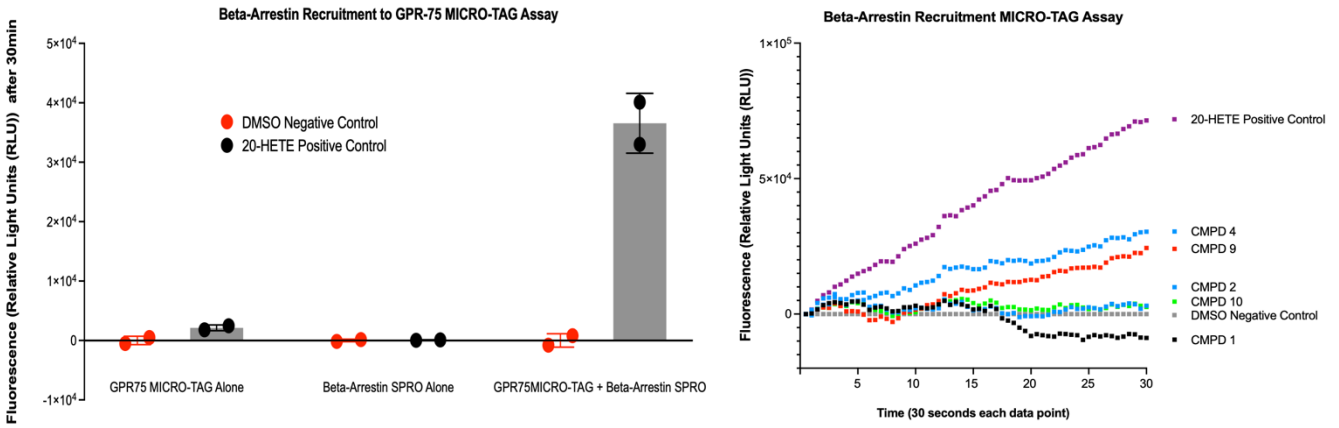

Figure 2. Small-molecule modulation of protein complex engagement. Representative engagement profiles illustrate compound-induced disruption, stabilization or induction of protein complexes as measured by MICRO-TAG® fluorescence, enabling direct comparison of functional mechanisms.

Therapeutic Modalities Supported

Compatible with most small-molecule modalities, including:

- PPI disruptors
- PPI stabilizers
- Molecular glues
- Targeted protein degraders (PROTACs and related bifunctionals)
- Allosteric modulators
- Neo-interaction inducers

Target Classes Supported

The MICRO-TAG® Protein Complex Target Engagement Kit is well suited for complexes involving:

- Transcription factors and co-regulators
- Membrane receptors and adaptor proteins (e.g., GPCR–β-arrestin)
- Kinase–scaffold interactions
- Chromatin remodeling complexes
- Structural and multiprotein assemblies
- Intrinsically disordered or context-dependent protein partners

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Kit Components

Included:

- Real-time–optimized RNA FRET substrate (200µl)
- S-protein enzyme complementation reagent (200µl)
- Assay buffers (10ml)
- Two positive control target plasmids (10µg)
- Inhibitor for positive control targets (10µl, 10mM DMSO stock)

Not included:

- Drug target construct (ordered separate from CellarisBio website)

Expandable:

- Custom construct design for user-defined protein pairs
- Stable cell line generation available

Applications

- Functional validation of protein–protein interactions
- Mechanism-of-action studies for molecular glues and degraders
- Screening and profiling of PPI modulators
- Target engagement confirmation for complex-dependent targets

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Summary

The MICRO-TAG® Protein Complex Target Engagement Kit enables direct, quantitative measurement of protein complex formation and modulation in cellular environments. By translating functional proximity into an amplified fluorescence signal, the platform provides a mechanism-aware approach for evaluating small-molecule modulation of protein complexes that are inaccessible to conventional assays.

Protocols

www.cellarisbio.com/protocols

References

Babic et al. *Real-Time Cellular Target Engagement Using MICRO-TAG Technology.* SLAS Discovery (2026).
