Assessing Cellular Target Engagement with MICRO-TAG®: ARID1B as an "Undruggable" Case Study

Huarui Cui[1], Silvia Escudero[1], Julie Di Bernardo[1], Marina Nelen[1], Ivan Babic[2], Elmar Nurmemmedov[2]

[1]*Foghorn Therapeutics, Watertown, MA* | [2]*CellarisBio, San Diego, CA*

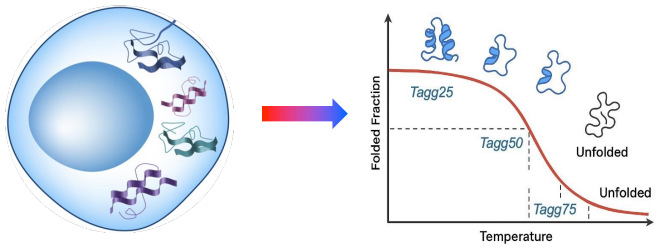
Abstract

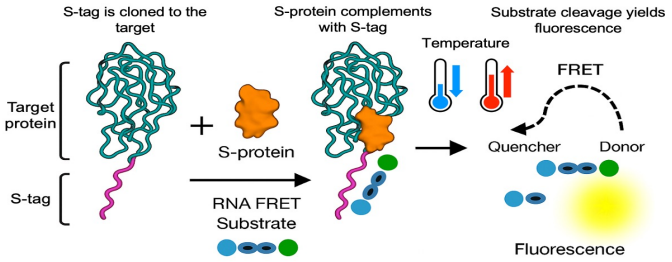
MICRO-TAG® is a real-time Cellular Target Engagement (CTE) technology designed to measure drug–target interactions directly in cells, including for challenging and traditionally 'undruggable' proteins. By enabling quantitative, temperature-series measurements, MICRO-TAG® provides insight into whether and how compounds engage their intended targets in a cellular environment.

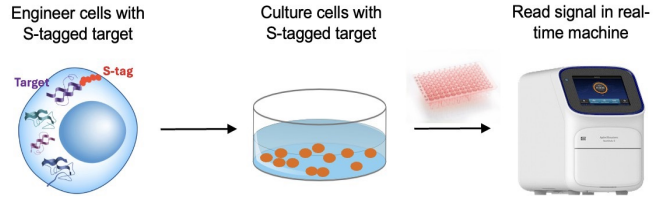
In collaboration with Foghorn Therapeutics, we applied MICRO-TAG® to ARID1B, a large chromatin-remodeling protein considered challenging to interrogate using conventional biophysical assays. MICRO-TAG® generated robust and reproducible cellular target engagement readouts for ARID1B, demonstrating its utility for studying complex drug targets. These findings highlight the potential of real-time CTE to support compound characterization, target validation, and early-stage drug discovery.

MICRO-TAG® Enzyme Complementation

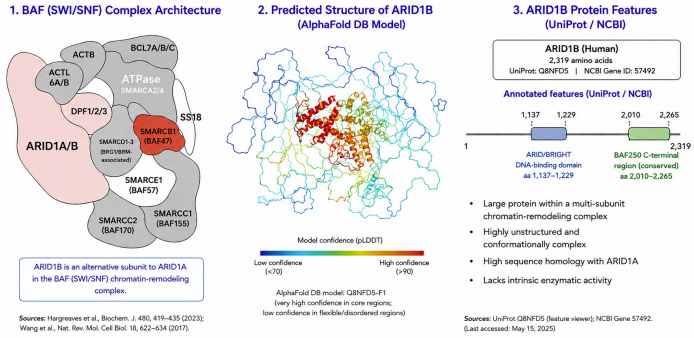
The MICRO-TAG® platform is built on a novel fluorescence-based cell target engagement system. It enables interrogation of drug targets without interfering with folding, localization and function - all within the physiological milieu of the cell.





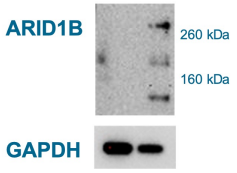


ARID1B: A Challenging Target

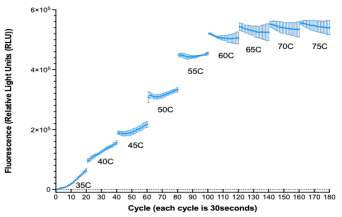


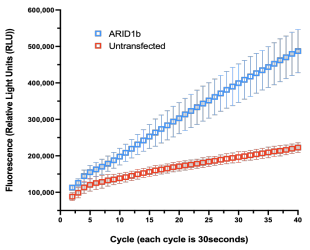
MICRO-TAG Assay for ARID1B

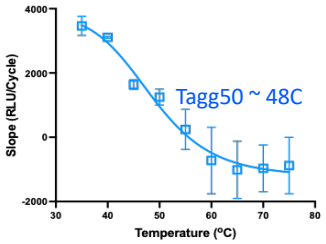
Expression & Complementation



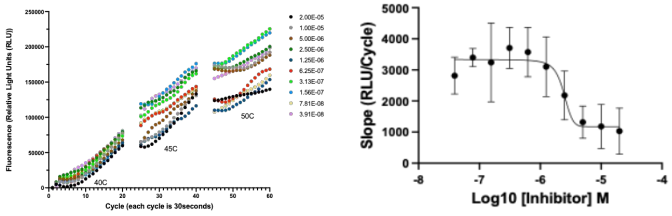
Thermal Melting Profile







Validation of Foghorn Compound 39RRW with MICRO-TAG®



Conclusions

- MICRO-TAG® enables robust cellular target-engagement measurements for challenging proteins, including ARID1B.
- MICRO-TAG® measurements show strong concordance with established internal cellular target-engagement assays (data not shown).

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Contact:
elmar@cellarisbio.com