Sunday, February 20
3:30 PM – 5:00 PM
Esplanade, Room 157
Dynamic Biosensors

Measurement of PROTAC Ternary Complex Formation Using the switchSENSE® **Y-Structure and FRET Signals**

Proteolysis targeting chimeras (PROTACs) are essential bifunctional small molecules that engage the formation of a ternary complex consisting of an E3 ubiquitin ligase, a target protein of interest and the PROTAC itself.

Using **switch**SENSE® technology and the novel DNA Y-structure, an E3 ligase as well as a target protein can be functionalized on each separate end of two FRET pair color-coded Y-arms. The Y-structure closes upon PROTAC binding and the subsequent ternary complex formation bringing together the green donor and the red acceptor dye into a closer, FRET sensitive, distance. The change in red fluorescence signal intensity directly correlates with ternary complex formation kinetics.

Here, we show that the Y-structure is an extremely versatile tool for studying any type of protein-protein complex formations with a dissociation constant between 1nM to 10µM. With the **switch**SENSE® technology and the highly sensitive FRET read-out, it is possible to perform high-throughput PROTAC screening and to characterize their kinetics (PROTACs ranking), gaining information on binary and ternary binding at the same time.

Speaker
Jonathan Faherty, Head of Operations, Dynamic Biosensors