CASE STUDY: **TARGETING DIFFICULT PPI'S IN TROP2, CD47 AND CD3**

RECEPTOR.AI

BACKGROUND:

Trop2, CD47, and CD3 are critical targets in immuno-oncology, each playing a distinctive role in cancer cell regulation and immune response. Small molecules for these targets present a promising approach for tissue-specific cancer therapies.

METHODOLOGY:

- PPI targeting workflow of Receptor.AI
- The stock chemical space of 4.5 M compounds.
- Binding assessment as a first stage of the project
- The number of experimentally validated compounds:
  - Trop2: **31**
  - CD47: **20**
  - CD3: **31**

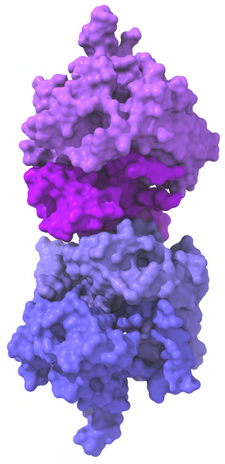
6% **hit rate for Trop2**

15% **hit rate for CD47**

10% **hit rate for CD3**

RESULTS FOR TROP2:

- **5 preliminary hits** obtained through BLI assays (Table 1).
- Hits **TP2-05** and **TP2-31** were confirmed by DSF assay.
- Internalization assay ongoing.

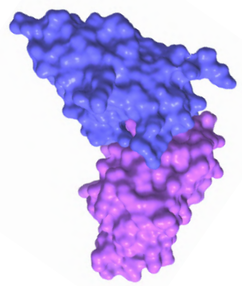


Compound	Specificity BLI	DT
TP2-05	1.56	-1
TP2-07	2.76	1.9
TP2-09	1.37	1.2
TP2-18	3.22	2.6
TP2-31	1.51	2.7

Table 1. The Trop2 hits identified via BLI assay. DT - dissociation time.

RESULTS FOR CD47

- **3 hits** obtained by BLI and confirmed by DSF assay (Table 2).
- Assessment of CD47/SIRPα complex destabilisation and *in vivo* efficiency on cell culture ongoing.

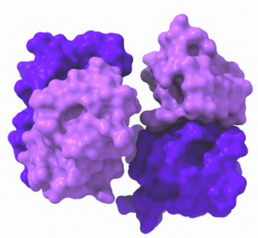


Compound	Response CD47	Specificity BLI
CD47-4	0.3575	1.92
CD47-12	0.0124	124.00
CD47-13	0.1337	1.50

Table 2. The CD47 hits identified via BLI assay

RESULTS FOR CD3

- **3 preliminary hits** obtained by BLI (Table 3).
- **CD3-7** shows specificity to CD3 εδ, **CD3-15** shows specificity to CD3 εγ, and **CD3-30** is bispecific.
- T-cell activation assay and further biophysical assays ongoing.



Compound	Response CD3 εδ	Specificity CD3 εδ	Response CD3 εγ	Specificity CD3 εγ
CD3-7	0.016	1.96	null	null
CD3-30	0.152	1.80	0.052	0.61
CD3-15	null	null	0.012	1.86

Table 3. The CD3 hits identified via BLI assay