# Correlation of Antibody Specificity With Clinical Safety

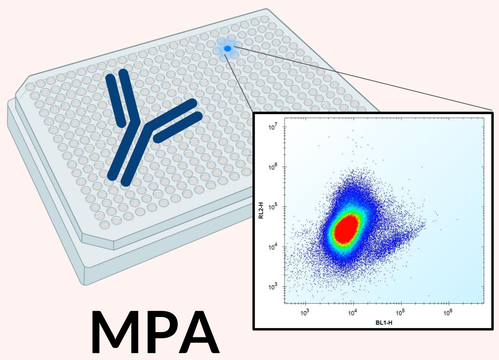
*A comparative analysis of safety data with Membrane Proteome Array and Tissue Cross-Reactivity Studies*

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## *Membrane Proteome Array (MPA)*

*Antibody binding to an unexpected protein?*

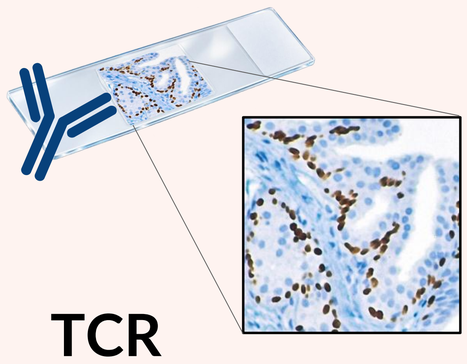



MPA

- Binding across ~6,000 proteins expressed in native cell membrane
- Interactions quantified using high-throughput flow cytometry
- Compatible with all MAb-based drugs
- Used in lead selection and/or pre-IND

## *Tissue Cross-reactivity (TCR)*

*Antibody binding to an unexpected tissue?*

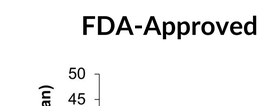


TCR

- Binding across ~37 tissues
- Interactions detected using frozen/fixed tissue immunohistochemistry
- Implemented during pre-IND

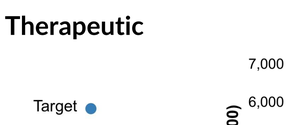
## MPA Identifies Off-Target Proteins That Bind Drugs

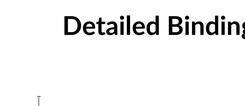
**Cell-Based Protein Array** *~6,000 native human membrane proteins* → **Assay Setup** *in unfixed cells by flow cytometry* → **Test Specificity** *across the membrane proteome* → **Validate Interactions** *using antibody titration analysis*

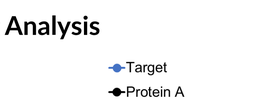


384-well plate

Includes fetal, neonatal, and placental proteins, with optional secreted and NHP libraries available



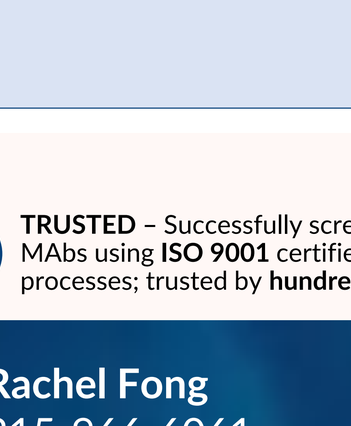

### Up to 33% of Antibody Drugs are Nonspecific

| Clinical MAbs Screened on the MPA | | | |
|---|---|---|---|
| | Approved | Phase 2/3 | Withdrawn |
| # MAbs screened | 40 | 25 | 18 |
| Off-target (rate) | 6 (15%) | 5 (20%) | 4 (22%) |

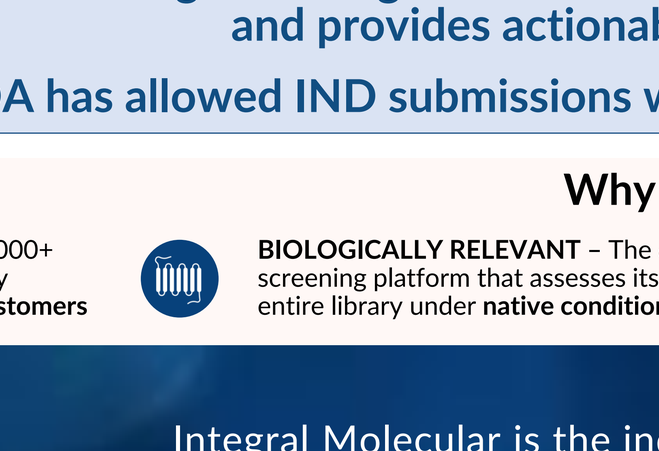
| Preclinical MAbs | |
|---|---|
| | Leads |
| # MAbs screened | 254 |
| Off-target (rate) | 83 (33%) |

Norden et al., 2024, *mAbs*

**FDA-Approved Therapeutic**




**Detailed Binding Analysis**




**The MPA identified off-target binding at all stages, underscoring the need for better specificity testing**

**MPA in final review for FDA qualification as a Drug Development Tool**

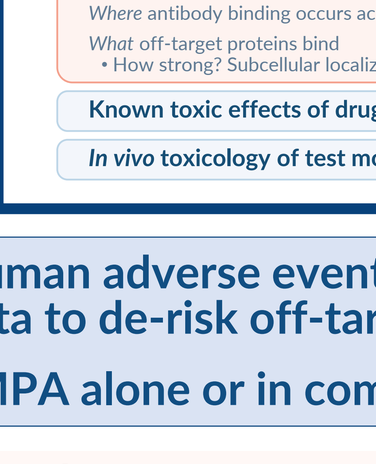



## MPA vs TCR
## Predicting Safety of Drugs in Humans

- 35 FDA-approved MAbs were tested for off-target binding on the MPA
- Results were compared to TCR summary data obtained from BLA applications

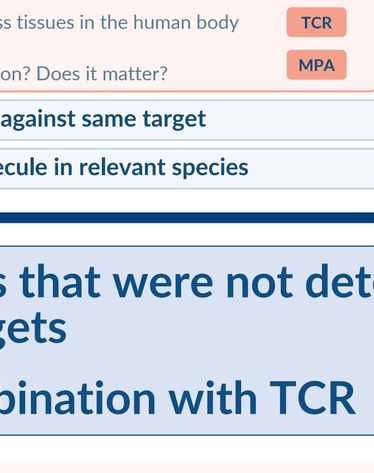
| # MAbs | MPA Result | TCR Result |
|---|---|---|
| 7 | Off-target binding | Clean |
| | 4 have FDA black box warnings<br>2 have FDA warnings of severe side-effects<br>1 shows no toxicity, but MPA off-target is in brain | |
| 3 | Clean | Unexpected cross-reactivity |
| | In all cases, no off-target toxicity was identified in NHP or human studies | |
| 17 | Clean | Clean |
| 8 | Clean | Inconclusive (additional cytoplasmic staining, technical limitations, variability, false-positive staining) |

**Drug #1**
**TCR missed off-targets**



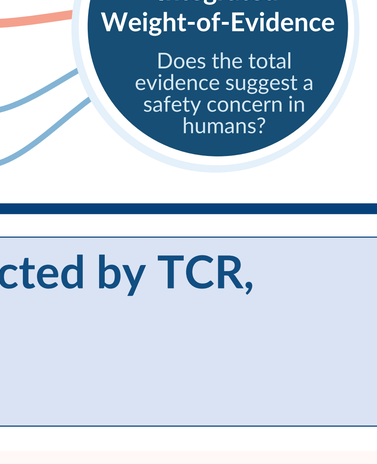

Adverse reactions

**Drug #2**
**Off-target masked in TCR**




Black box warning

**Drug #3**
**Off-target buried in TCR**




Black box warning

**MPA results identified drugs with off-targets that were missed in TCR studies and have safety issues in humans**

Norden et al., 2024, *mAbs*

### Evaluating Safety Risk in Preclinical Studies




**MPA has identified off-target binding correlated with human adverse events that were not detected by TCR, and provides actionable data to de-risk off-targets**

**FDA has allowed IND submissions with MPA alone or in combination with TCR**

## Why Choose the MPA

**TRUSTED** – Successfully screened 3,000+ MAbs using **ISO 9001** certified quality processes; trusted by **hundreds of customers**

**BIOLOGICALLY RELEVANT** – The *only* screening platform that assesses its entire library under **native conditions**

**ACCEPTED** – Data accepted by FDA, EMA, NMPA; **200+ IND submissions** filed with MPA data

**QUANTITATIVE** – **Flow cytometry** for sensitive and quantitative measurements, compatible with all modalities

v1026

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