CELL AVIDITY DRIVES THE FUNCTIONAL RESPONSES OF IMMUNOTHERAPIES WITH SUPERIOR CORRELATES TO IN VIVO PERFORMANCE

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Background While a diverse and complex array of cell-based and cell-engaging immunotherapies are currently under development, only a small subset will become approved therapies. 7 in 8 immunotherapeutic candidates fail in the clinic, suggesting that current in vitro approaches (e.g., killing assays, cytokine secretion) for evaluating efficacy, identifying toxicity, and predicting in vivo performance are insufficient and novel in vitro approaches are required.

Methods Measurement of cell avidity by acoustic force1 2 interrogates the overall strength of the interaction between an effector cell and its target to comprehensively evaluate CAR-T, CAR-NK, TCRtg, and cell engager performance.

Results Here, we review recent publications in Nature Biotechnology,3 Cancer Cell,4 and Journal of Immunotherapy of Cancer5 highlighting how the in vitro cell avidity assay can be used to:

- Generate unique mechanistic insights, where conventional in vitro assays often fail to differentiate therapeutic candidates
- De-risk on-target, off-tumor toxicities by profiling the avidity of effectors for healthy vs tumor targets
- Stratify candidates within minutes, often with more robust correlation to in vivo compared to conventional assays
- Reduce the time and expense leading up to murine studies while increasing confidence in lead selection

Conclusions Higher avidity has been significantly correlated with improved tumor control in murine models, thereby increasing confidence in candidate selection and shortening the time to IND filing.

REFERENCES

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