# Cell Avidity

## Revolutionize binding for the future of cell & antibody therapeutics

True binding, measured in a cellular context

lumicks.com/**cell-avidity**

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**Technology brochure**

# See more.
# **Know more.**

LUMICKS is pioneering real-time single-molecule and single-cell analysis, empowering researchers worldwide to transform how advanced immunotherapies are discovered and developed.

**Our mission**

## Empowering academic & pharmaceutical communities

We empower the academic and pharmaceutical communities with cutting-edge technologies to deeply understand the mechanisms of life and disease, driving the discovery and development of life-saving therapies.

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**Achievements**

# Follow our journey

We are an international team exceeding 150 people with more than 30 nationalities. We are proud of our great sense of ownership with the mentality of being open-minded in teamwork. We embrace challenges and maximize opportunity and experience.

**16**

Average impact factor of publications including Cell Avidity measurements

**>60**

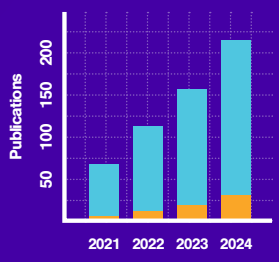
Research institutes and biotech/pharma companies working with LUMICKS Cell Avidity technology

**>220**

Instruments installed by LUMICKS across the globe

**>230**

Publications include LUMICKS technology measurements



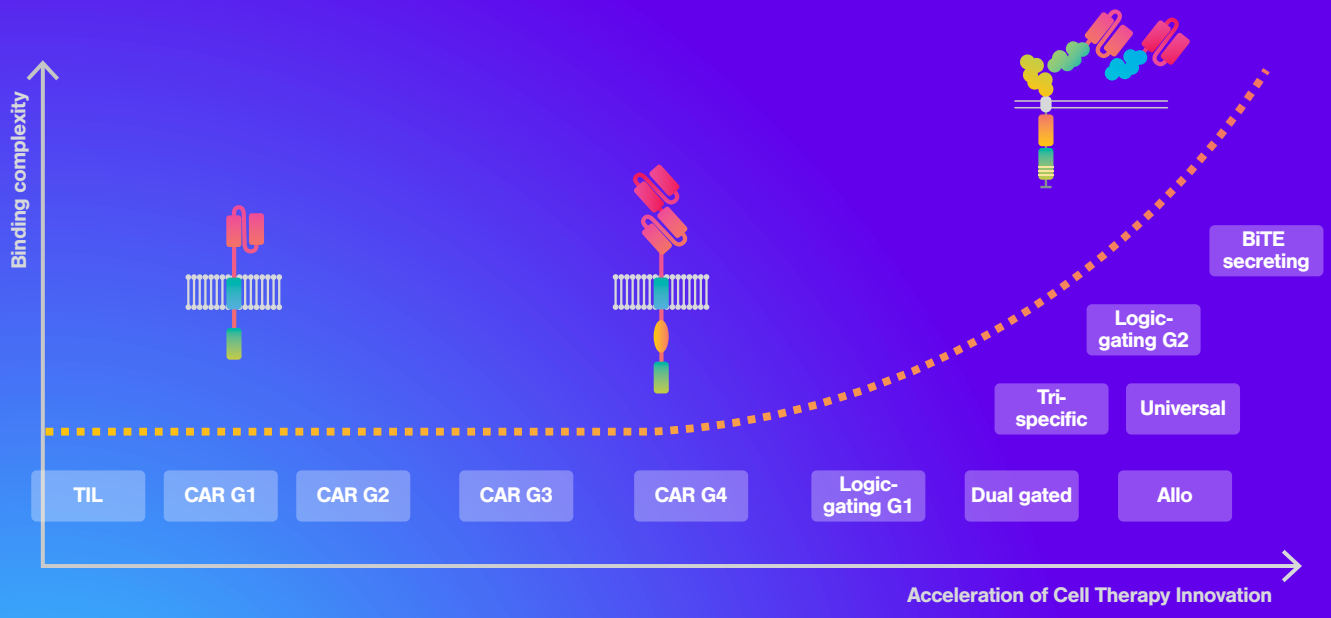
# Why Cell Avidity?

## Immunotherapeutic designs are getting more complex

### There are no simple answers to immuno-oncology's greatest challenges

Despite decades of progressive technical breakthroughs in cell and antibody therapy, immuno-oncology is still an intricate puzzle. From battling the immuno-suppressive tumor microenvironment, avoiding antigen escape, ensuring T-cell persistence or preventing high OTOT toxicity, improving engage plasma half-life; the complexities of these challenges often lead to disappointing *in vivo* results and failed clinical trials.

These challenges force us to push the boundaries of immunotherapy design. State-of-the-art therapeutic candidates now integrate complex signaling mechanisms or engage multiple targets in parallel. Logic-gated CAR T cells, trispecific cell engagers and biparatopic antibodies are just a few examples of this trend towards more and more complicated therapeutics. The increased complexity in therapy design is matched by a growing sophistication of binding mechanisms in these novel therapeutics.




Many immunotherapies adapt to solve the field's most pressing issues (an intricate balance between persistence, potency, and safety) by integrating multiple signaling mechanisms and engaging with more than one target in parallel. With that trend, the binding mechanisms between binder and target also complexify.

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# Shouldn’t your binding assay capture that complexity?

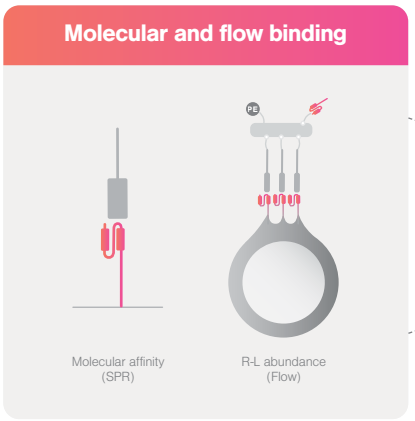
## Measure true binding, in the cellular context

With each step forward, binding mechanisms of immunotherapies have become more intricate. Yet, most binding assays haven’t kept up.

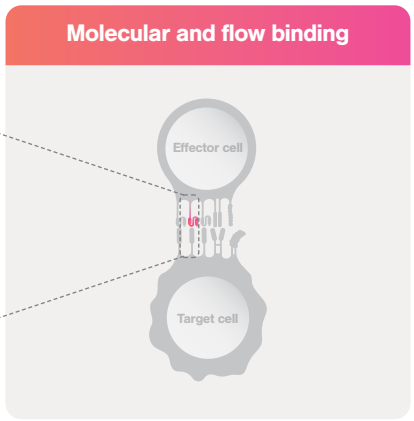
- Molecular assays like tetramer binding and surface plasmon resonance (SPR) offer simplified snapshots. Focusing on isolated ligand-receptor interactions or abundance, they can miss cellular context and don’t correlate well with outcomes.

- Functional assays such as cytotoxicity and activation assays generally measure the outcome of binding yet may fail to provide direct mechanistic insights.

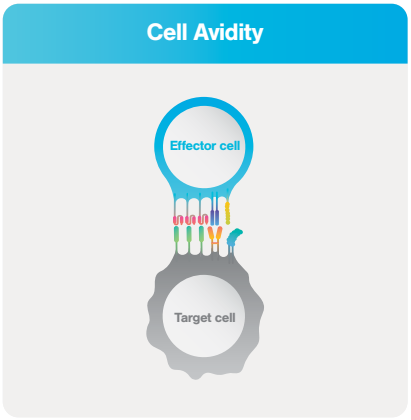
This creates a gap between what we can measure and what we need to understand to advance next-generation immunotherapies.




Molecular binding assays measure preconditions for binding...




... providing limited insights into actual cell binding.




While Cell Avidity captures the full complexity of cell binding.

# Cell Avidity, the missing link

Cell Avidity bridges that gap. By measuring the combined strength of cell-cell / cell-protein binding with controlled forces, Cell Avidity generates direct, physiologically relevant measurements of binding in its full, dynamic complexity (see p. 6).

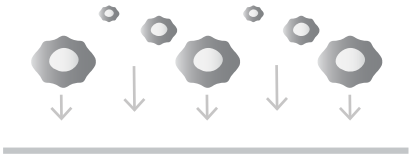
Applied to cell or antibody binding research, in experiments on functional modifications or microenvironment modulators, Cell Avidity is shown to reveal the mechanisms of action, facilitating rational design choices, selecting the right candidates fast and early, and ultimately improving therapeutic outcomes (see p. 7-9).

**To support progress in immunotherapy, we need to measure binding the way it happens—in real life, in real cells. This is Cell Avidity.**

# The Cell Avidity workflow

Cell Avidity: Assays that measure the overall strength of interaction between cells, or between proteins and cells.

## 1

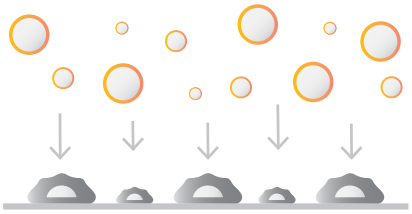


### Target cell seeding

Target cells (adherent or non-adherent) are generally of two types:

- Tumor cells to assess potency or antigen sensitivity
- Healthy cells to assess on-target off-tumor toxicity

## 2

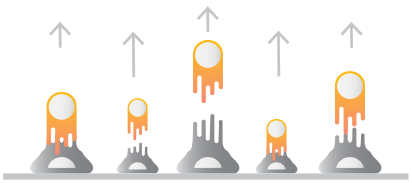


### Effector cell / molecule introduction

Introduction of labeled binders to the uniform monolayer. These can include:

- Therapeutic effector cell products like CAR T, TCR T, NK.
- Effector cells with compound drugs such as cell engagers, small molecule inhibitors or modified environmental factors.
- Fluorescent beads coated with antibodies or other proteins.

## 3

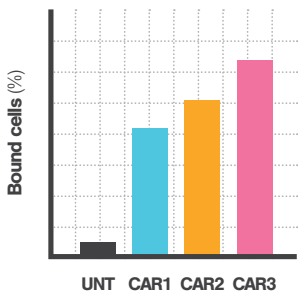


### Controlled force application & fluorescent imaging

Controlled force applied to the bound cells probes the strength of interactions between labeled and target populations.

Fluorescence microscopy captures the number of bound cells before and after force application. The percentage of bound cells after force application indicates the population's Cell Avidity.

## 4




### Instant data acquisition

Cell Avidity quantifies cell binding with hundreds of cells per measurement.

- Percentage (%) of cells bound
- Percentage (%) of antibody-coated beads bound.

# A wide variety of applications

The Swiss army knife for next generation binding

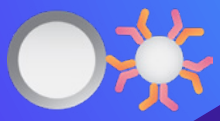
## Cell-cell binding

### Cell Therapy

CAR-T, TCR T, NK, etc.

### Cell Engagers

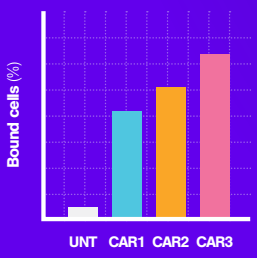
Bispecific, trispecific, etc.



## Protein-cell binding

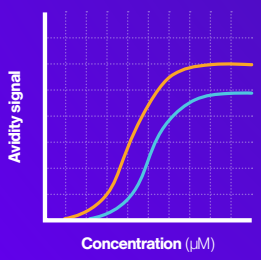
### Antibody Therapy

Mono/multi-specific, nanobodies, etc.



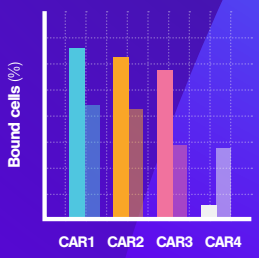

### Binding potency

Avidity ranking & cell characterization




### Binding sensitivity

Titration assay for CE / Peptide / Ab



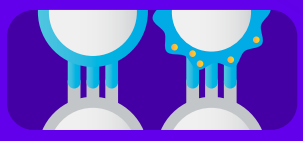

### Binding specificity

Monolayer safety screening

### Binder screening and optimization

Optimize binding to overcome exhaustion, improve potency, minimize OTOT and refine sensitivity to overcome immune escape.

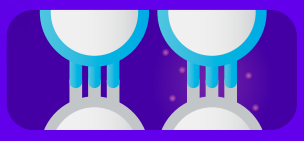
Understand the impact of different antibody formats and fine tune avidity to select candidates based on multi-domain binding measured in a single assay.



### Effector functional modification

Measure how functional modifications in effector cells impact binding. Intracellularly driven differences in Cell Avidity can inform on potency and persistence.

Reveal the mechanism of action in therapy designs that, e.g., change signaling sensitivity, activate cytokine or chemokine receptors, or reduce checkpoint receptors.



### Tumor microenvironment response

Measure the tumor microenvironment's impact on binding by measuring Cell Avidity in the presence of tumor or TME modifying compounds.

Get insights into immune trafficking, effects of environment-modulating compounds, hypoxia effects and more.

### Donor selection and quality control

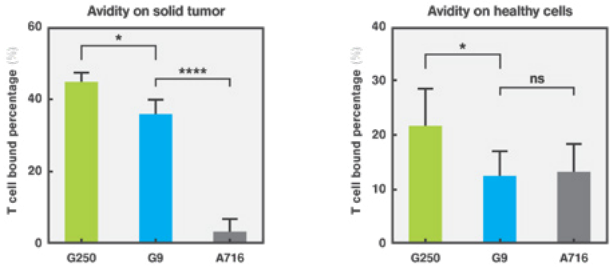
Measure the combined effect of donor/host interactome or assess the combined effect of cell fitness, receptor expression, and population purity.

Quantify the degree of (Mis) matching between donor and host or assess product quality across multiple key product attributes.

# A selection of success stories

Learn how immuno-oncology pioneers apply Cell Avidity to break through some of immunotherapy's biggest challenges like exhaustion, low potency and antigen escape.

## Cell Avidity tackles OTOT mechanism in CAR T therapy for solid tumor




**Cell Therapy (CAR T)** **Binder screening & optimization**

**Safety OTOT**

**Yufei Wang, PhD,** Dana-Farber Cancer Institute

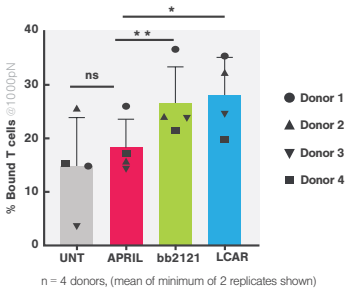
On-target off-tumor toxicity (OTOT) remains a challenge for CAR T-cell therapies, especially in solid tumors such as clear-cell renal cell carcinoma. This has led to the exploration of innovative CAR-T treatments targeting CAIX, an antigen highly expressed in the cancer while present in lower concentrations on healthy cells.

Wang *et al.* (2023) studied and optimized the G250, anti-CAIX, CAR which shows OTOT activity in the clinic, but the mechanism of toxicity is poorly understood and difficult to demonstrate with conventional assays.

By measuring Cell Avidity, the G250 anti-CAIX clinical CAR was shown to have off-tumor on-target binding to healthy cells, while alternative G9 CARs obtained low avidity against low-density CAIX healthy cells, indicating improved safety while maintaining sufficient avidity against high-density CAIX on tumor cells.

**Wang, Y. *et al.*** 2024 Mol. Cancer doi.org/10.1186/s12943-024-01952-w

## When insights into Cell Avidity would have prevented clinical trial failure




**Cell Therapy (CAR T)** **Binder screening & optimization**

**Persistence**

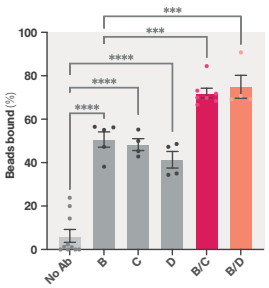
**Lydia Lee, PhD,** University College London

A retrospective study, conducted by Lee *et al.* (2023), interrogates the cause of phase-I clinical trial failure with the then-promising ligand-based APRIL CAR therapeutic.

Whereas functional assays characterized the APRIL CAR as well-performing, measuring Cell Avidity revealed insufficient Cell Avidity, due to decreased CAR surface expression, as the mechanistic cause of poor persistence. The results suggest that incorporating Cell Avidity into the pre-clinical assay matrix, would have allowed for better informed decision-making, potentially leading to the selection of a different lead candidate or further optimizing the APRIL CAR before moving to clinical trial.

**Lee, L. *et al.*** 2023 JITC doi.org/10.1136/jitc-2023-006699

## Cell Avidity measures true binding of biparatopic antibodies, inaccessible with affinity assays




**Antibody Therapy** **Binder screening & optimization** **Potency**

**William Sellers, MD, PhD,** Broad Institute and Dana-Farber Cancer Institute

FGFR2 is a promising target for metastatic, non-small cell lung cancers with FGFR2 fusion proteins, but is prone to the emergence of resistance mutations. Biparatopic antibodies that target two epitopes on the FGFR2 extracellular domain may confer a solution. Chaturantabut *et al.* (2025) subjected 15 novel candidates for a binder screening.

Affinity-based assays alone could not confirm the improved avidity of the biparatopic antibodies. To increase confidence, the team directly measured binding in the cellular context with Cell Avidity, confirming two superior binders (B/C and B/D). Functional assays validated these two candidates, which went on to inhibit *in vivo* xenograft tumor growth.

**Chaturantabut, S. *et al.*** 2025 J. Clin. Invest. doi.org/10.1172/JCI182417

### Format-tuning of bispecific T cell engagers using Cell Avidity enhances potency and plasma half-life

**Cell Engagers**

**Binder screening & optimization**

**Potency**

**David B. Weiner, PhD**

**O'Connell, R.P. *et al.*** 2024 JITC doi.org/10.1136/jitc-2023-008733

### Novel checkpoint inhibitor impairing T-cell potency in the tumor microenvironment assessed with Cell Avidity

**Cell Therapy (NK)**

**Effector functional modification**

**Exhaustion**

**Marco Ruella, MD**

**Guruprasad, P. *et al.*** 2024 Nat. Immunol. doi.org/10.1038/s41590-024-01847-4

### Cell Avidity reveals mechanism of dual-targeting, logic-gated, BiTE-secreting CAR T cells

**Cell Therapy (CAR T)**

**Tumor microenvironment response**

**Immune cell trafficking**

**Marcela Maus, MD, PhD**

**Wehrli, M. *et al.*** 2024 Clin. Cancer Res. doi.org/10.1158/1078-0432.CCR-23-3841

## Improved understanding of immunomodulator Venetoclax mechanism of action by Cell Avidity

**Cell Therapy (NK)** **Effector functional modification** **Potency**

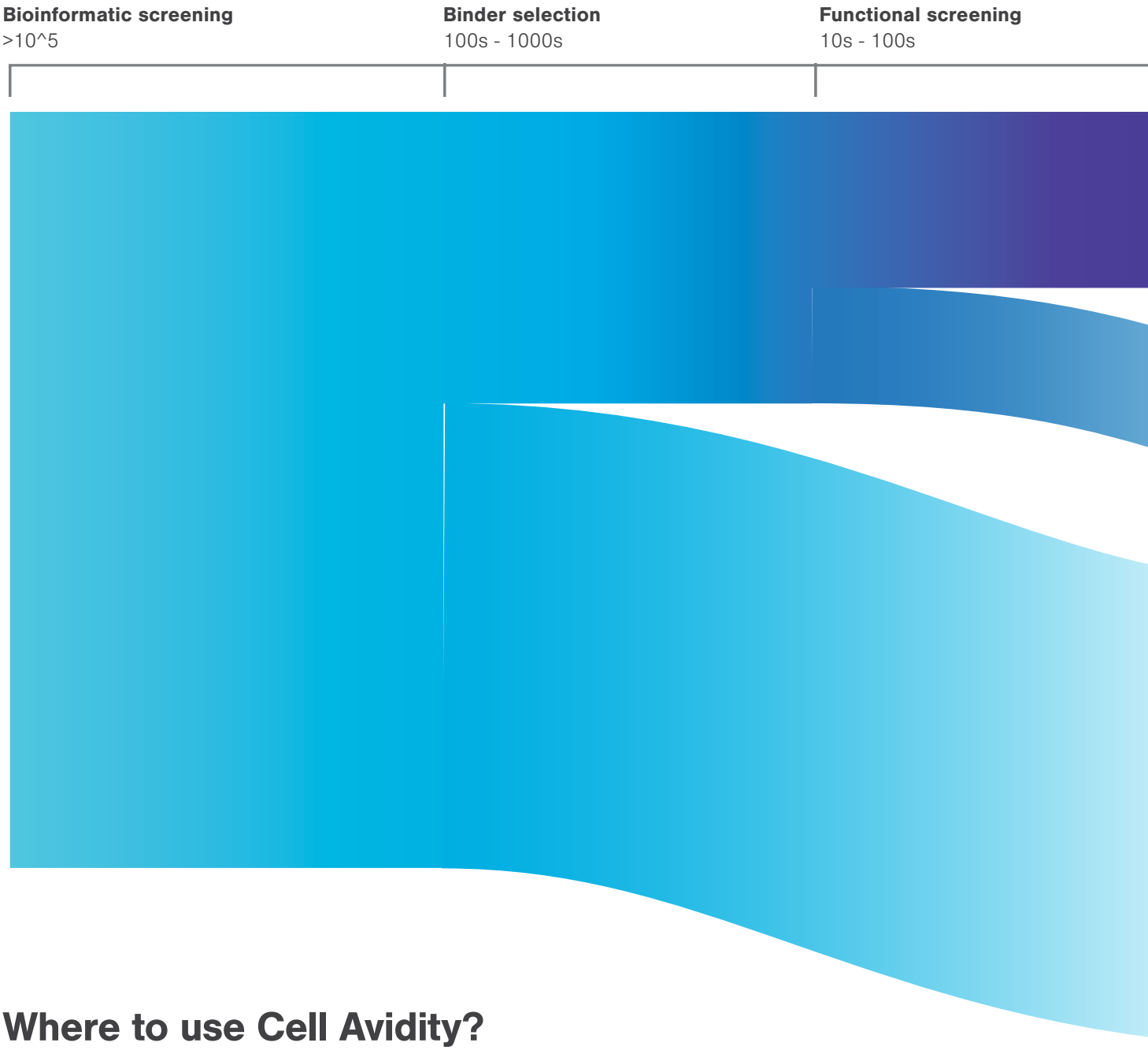
**Prof. Fang Ni, PhD,** University of Science and Technology of China

NK-based immunotherapy still faces significant challenges particularly in enhancing NK cell function and *in vivo* persistence. The FDA-approved drug for enhancing NK cell-mediated killing of AML cells, is Venetoclax; however the mechanism leading to the improved response, had initially, remained unclear. Here, Cell Avidity was used to reveal that Venetoclax enhances NK cell–target cell binding, boosting NK cell function by immunomodulation. The Cell Avidity experiments revealed a previously unclear mechanism, opening avenues for new therapies that leverage similar mechanisms to enhance efficacy.

**Wang, Y. *et al.*** 2024 Cell. Rep. Med. https://doi.org/10.1016/j.xcrm.2024.101580

# Unlock faster R&D cycles

Integrating Cell Avidity in the drug development workflow leads to faster identification of the most potent, safe and sensitive drug candidate by reducing the required number of design iterations or eliminating candidates from *in vivo* preclinical studies which ultimately bind ineffectively in a cellular context.




# Where to use Cell Avidity?

### Early in the pipeline - Select the right candidates fast

Quickly rank hundreds to thousands of therapeutic candidates to get insights into sensitivity and safety. Incorporate Cell Avidity early in the discovery workflow helps ensure that only candidates with the most promising binding characteristics progress.

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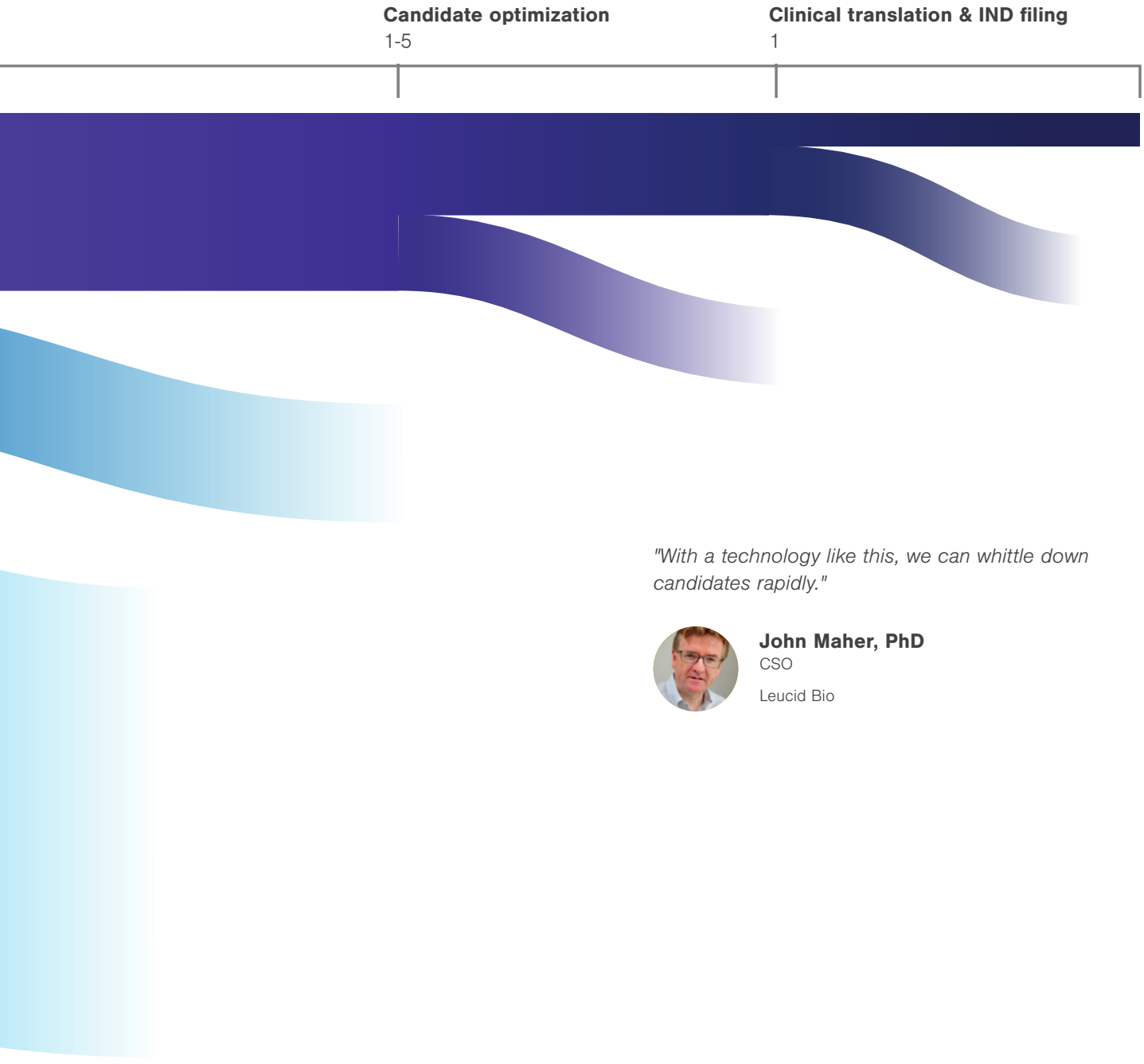


*"With a technology like this, we can whittle down candidates rapidly."*



**John Maher, PhD**
CSO
Leucid Bio

## Late-stage - Deep candidate characterization to drive clinical selection

Carry out deep functional characterization of select final candidates. Reveal differences in binding dynamics and target engagement to confidently select the optimal therapeutics for clinical development.

Solutions

# Avidion

## The next generation Cell Avidity platform

Ideal for cell therapy candidate screening and large characterization studies. Run up to 4 disposable 48-well cartridges a day for a total of 192 measurements with <80 min. hands-on time.

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**High throughput measurements with 96-well plate compatibility**

**Minimal hands-on time through automated handling and deep-learning analysis**

**Multiplexed insights through 4-color fluorescence readouts**

## Avidigo

### White glove Cell Avidity services

Full-service contract research from experimental design to data report based on Cell Avidity measurements at high throughput.

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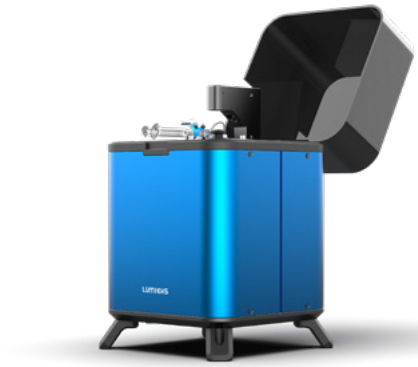
## A solution to scale

Avidion launches with full support of cell-cell avidity measurements, applicable to a broad range of cell therapy research such as CAR-T therapy development. Later upgrades give customers direct access to Cell Avidity for cell engager and antibody therapy research.



# z-Movi

### For small sized Cell Avidity studies

A fast and simple solution for single-sample Cell Avidity experiments. Run up to 20 measurements per day.

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# Cell Avidity enables pioneers working at the cutting edge of immunotherapy

Join >60 leading research institutes and biotech/pharma companies worldwide who leverage Cell Avidity measurements for their research.

**“Up to now we characterized T cells by killing, proliferation and cytokine production. Now we also add Avidity to every project because Cell Avidity helps us understanding an additional characteristic of the T cell we could not have measured otherwise. Without Cell Avidity we would not have been able to dissect the differences between h1218 and FMC63 T cells and understand the mechanism behind the phenomena that we observed.”**



**Marco Ruella, MD,** University of Pennsylvania

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**“Cell Avidity gives us insights into the blind spot we currently have between molecular binding and functional outcome. It helps us integrate different parameters that contribute to CAR function. It could give us more information than affinity alone and help us narrow down the functional relevance of a few variables in the matrix of many of these variables in the CAR world.”**

**Markus Barden, PhD,** Leibniz Institute for Immunotherapy

**“Cell Avidity measurements provide key information that can accelerate immunotherapy development by accurately predicting *in vivo* and clinical efficacy.”**

**Mark Lowdell, PhD**
University College London & INmune Bio

**“Using Cell Avidity, we can identify the results that we were able to see *in vivo*, which cannot be predicted with other strategies *in vitro*.”**

**Carlos Fernandez, MD, PhD,** Hospital Clinic de Barcelona

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