

Of Models and Media: Advancing next generation therapies with tailored cell culture media



Caelan Anderson
Co-Founder and CEO
Tolemy Bio



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engineering cell metabolism
for next-generation therapies



MELBOURNE
SPACE PROGRAM



Caelan Anderson

Co-founder & CEO



Alex Ward, PhD

Co-founder & CSO



UNIVERSITY OF
CAMBRIDGE



University of
BRISTOL

Founding Team

Advisory



Tom Heathman, PhD

CCO, Ori Biotech

Commercial & Strategic



Michael P. Chu, MD

A/Prof Uni. Alberta

CAR-T & Clinical



Lake-Ee Quek, PhD

Fellow, Uni. Sydney

Systems & Modelling



Max Tejada, PhD

VP-level Pharma

GMP & QC



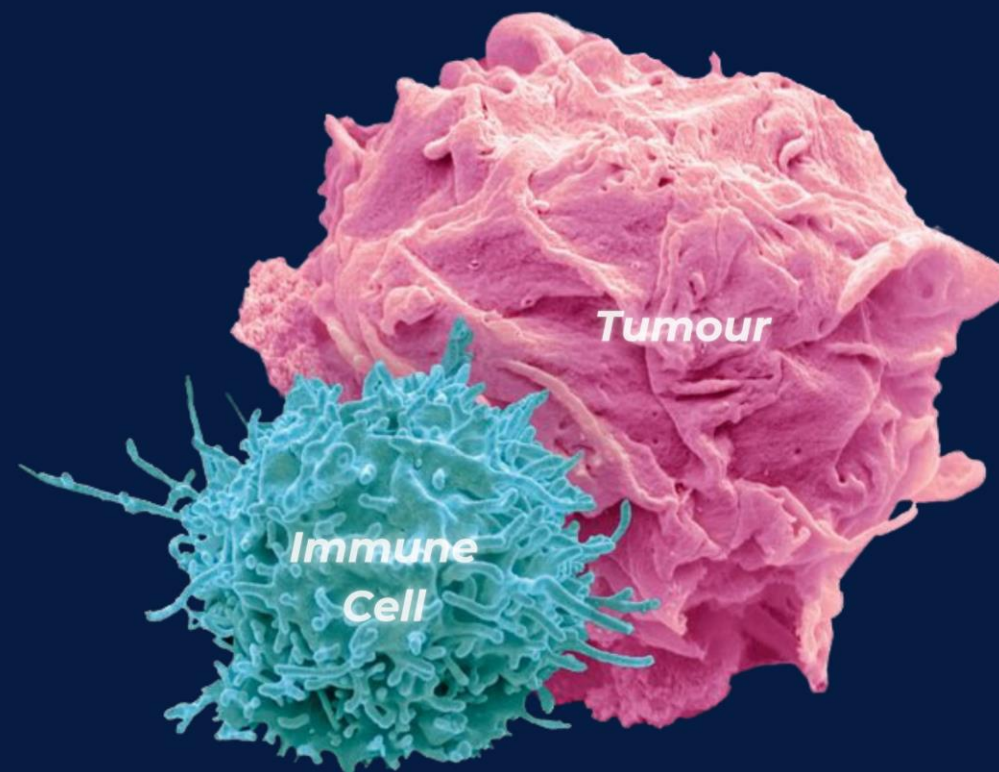


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10 years ago, Emily Whitehead was the first cancer patient cured by CAR-T cell therapy

Treating previously incurable blood cancers and unlocking a new wave of medicine...

These therapies are now being expanded to treat hundreds more diseases

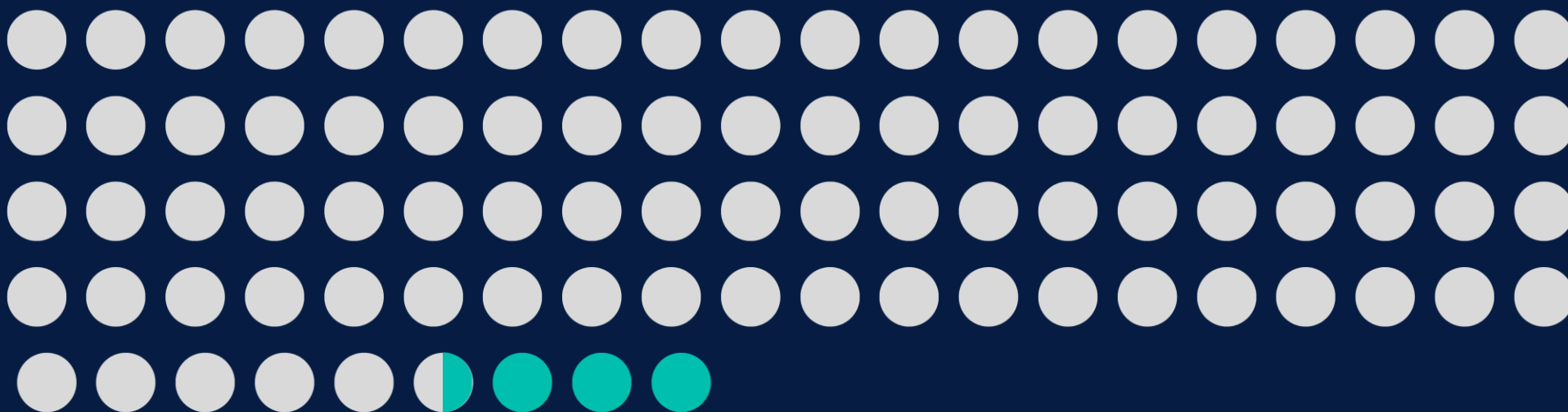




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Today, less than ~3% of treatable patients
receive life-saving **CAR-T cell therapy**

950k Available Patients Globally *



~35k Patients Treated

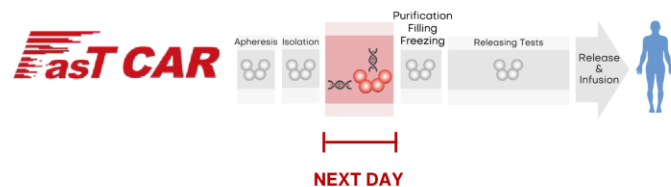
* Five blood cancer types



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Due largely to critical failures and complexities in manufacturing **leading to insufficient supply**

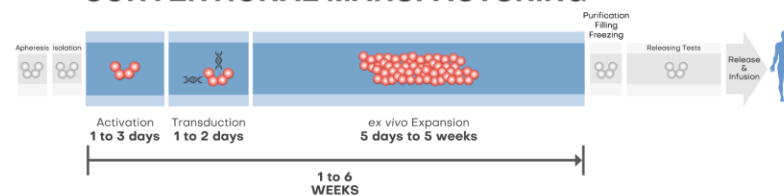
First Generation CAR-T Cell Therapy



+
Stem/Naive
No wait-time
Lower cost

-
Higher CRS
Poor control

CONVENTIONAL MANUFACTURING



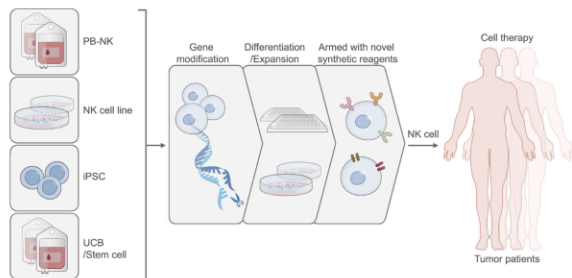
+
Higher Dose
Controlled

-
Exhaustion
Higher cost
Long wait time

Image courtesy of Gracell

Allogeneic Cell Therapies

CAR-NK cell therapy



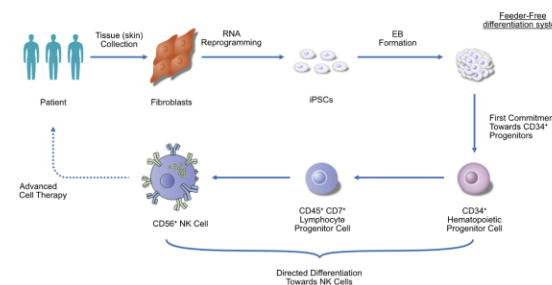
Complex Cell Sources

Very Slow Expansion

Novel Cell-line
Engineering

Fang et al., 2022, Cell. & Mol. Immunol.

iPSC-based cell therapy



Complex Starting
Material

Poorly Understood
Differentiation

Image courtesy of Reprocell



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Our solution aims to address these challenges through the customisation and optimisation of cell culture media



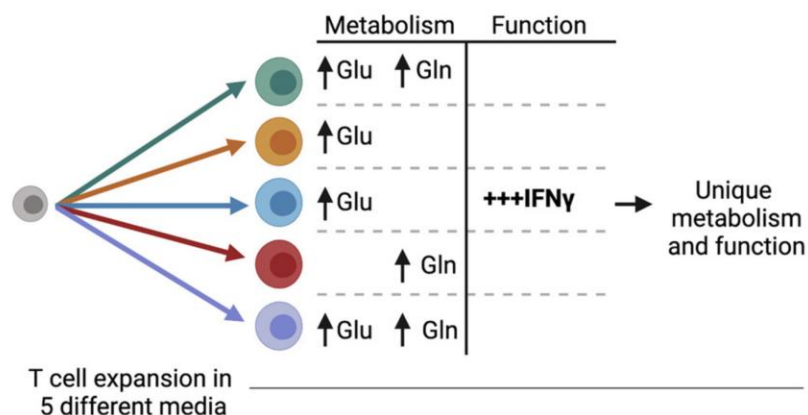
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Media has a profound impact on **quality and yield** during cell therapy manufacturing

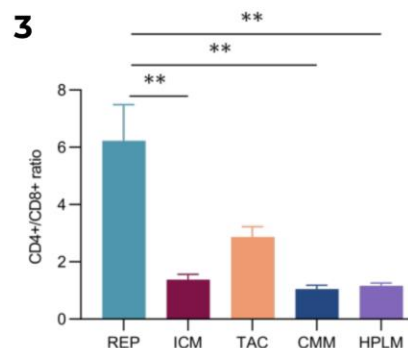
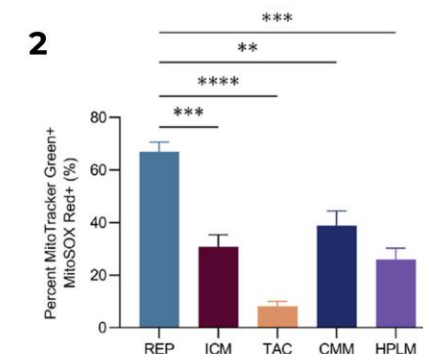
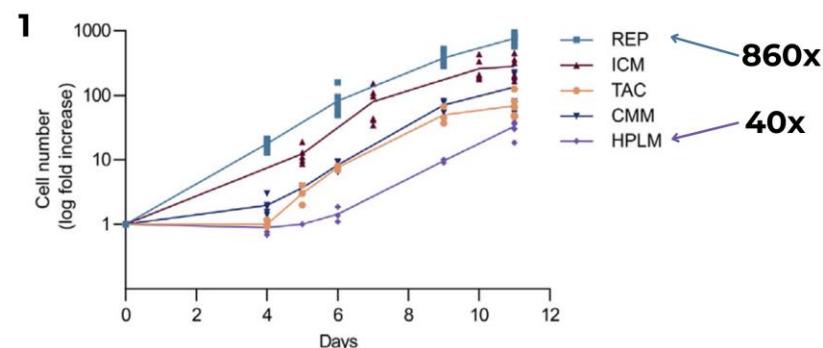
Molecular Therapy
Methods & Clinical Development
Original Article

Clinically relevant T cell expansion
media activate distinct metabolic
programs uncoupled from cellular function

Sarah MacPherson,¹ Sarah Keyes,¹ Marisa K. Kilgour,^{1,2} Julian Smazynski,^{1,2} Vanessa Chan,^{1,2} Jessica Sudderth,³ Tim Turcotte,⁴ Adria Devlieger,⁴ Jessie Yu,⁵ Kimberly S. Huggler,^{6,7} Jason R. Cantor,^{6,7,8,9} Ralph J. DeBerardinis,^{3,10} Christopher Siatskas,⁵ and Julian J. Lum^{1,2}



Identical T-cell-line + Identical Process + **Different Media**



Different Media can:

1. have 20x difference in growth
2. change cell metabolism
3. alter T-cell phenotype



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Media is hard to optimise because the search space is so large and complex

DIFFERENTIATION TRAJECTORIES

CELL TYPES - T, NK, M, IPSC

CONCENTRATION LEVELS

INGREDIENT COMBINATIONS

10²⁰⁰ combinations to try

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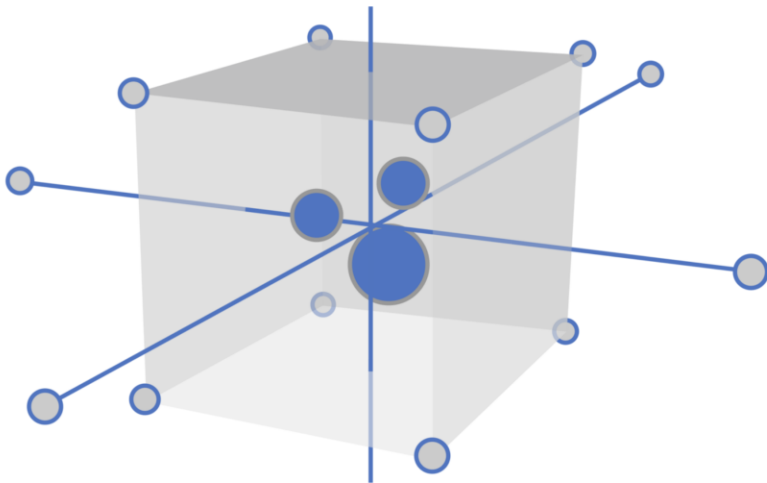


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Design of Experiments (DoE) is the current approach but it is **not sufficient**

DoE



Limitations

Brute force search

5-10 parameters at a time

Knowledge-based

*10¹⁸⁰ years to search
media space fully*

Result

Only a **small number** of **acceptable** media formulations are found



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This leaves the industry with a small number of **non-specific** and “**off-the-shelf**” formulations

But generic media cannot work for personalised medicine (autologous cell therapies)...

...Or the increasing number of allogeneic applications



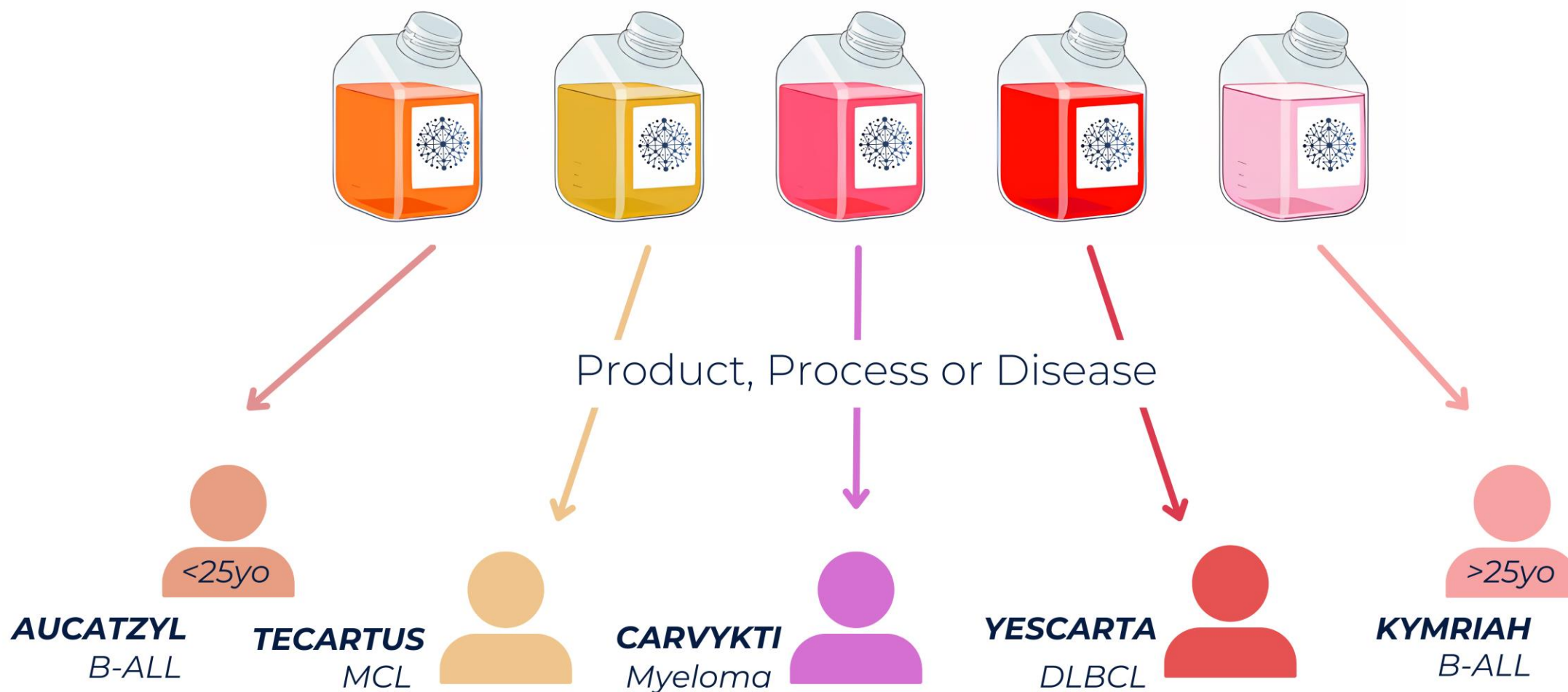
Product, Process or Disease





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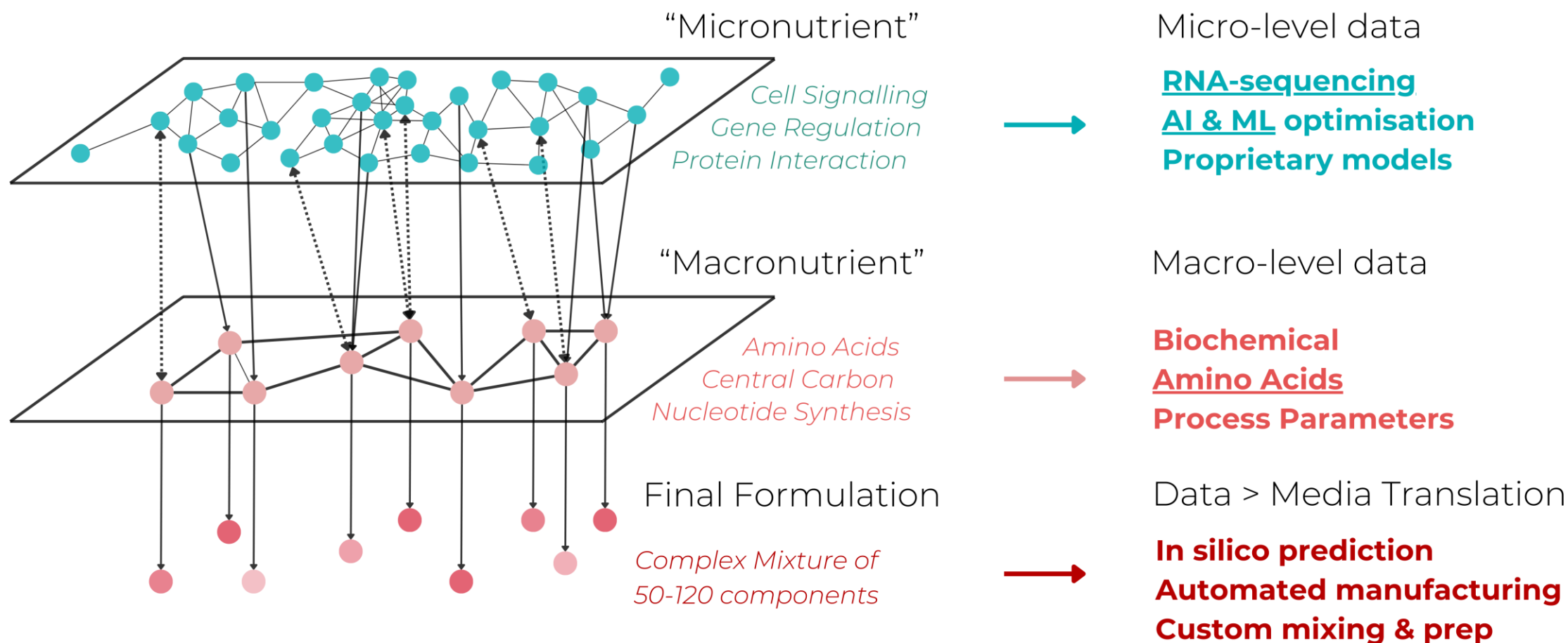
We provide manufacturers with media that is uniquely tailored to the product or process





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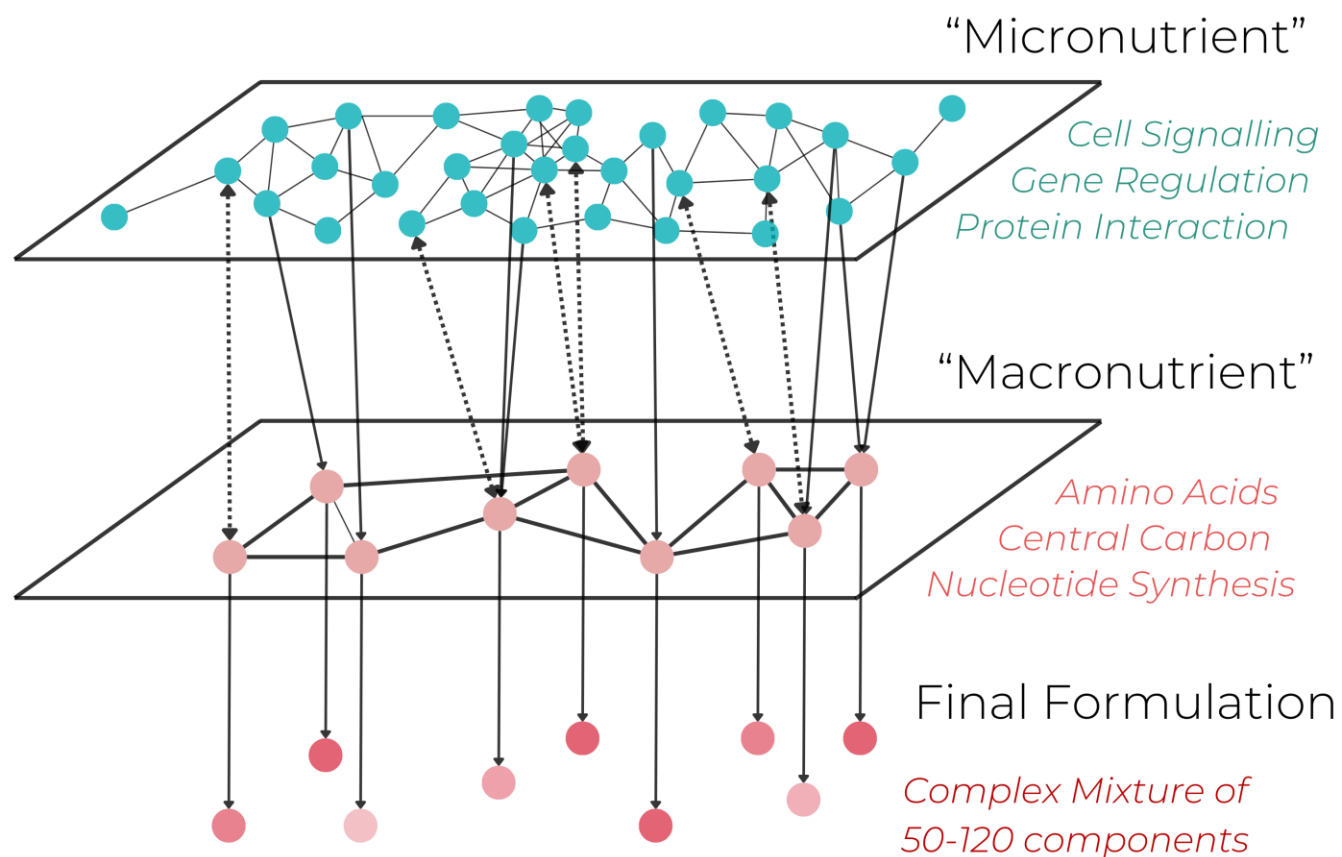
Our solution uses **relevant data**, integrated using **AI and ML** to tackle this size and complexity





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Allowing us to simultaneously optimise multiple functional layers



Micro-level function

**T-CELL
EXHAUSTION &
TUMOUR-KILLING**

Macro-level function

**T-CELL
EXPANSION &
VIABILITY**

Data > Media Translation

**MACRO-/MICRO-
NUTRIENT DELIVERY**

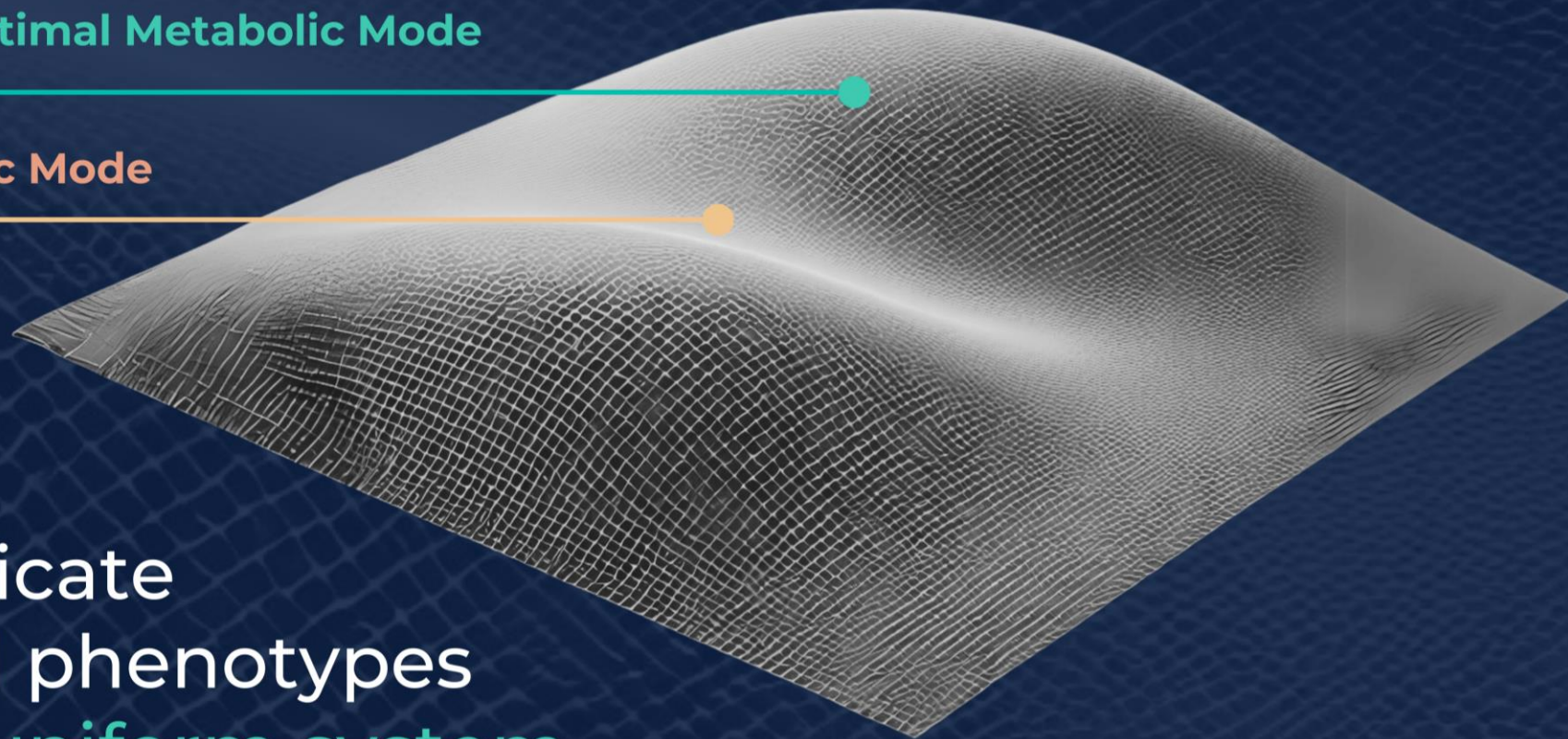


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Current media optimization methods **oversimplify metabolism**

Apparent Optimal Metabolic Mode

Apparent Suboptimal Metabolic Mode



Treating the intricate
landscape of cell phenotypes
as a mostly **flat, uniform system**

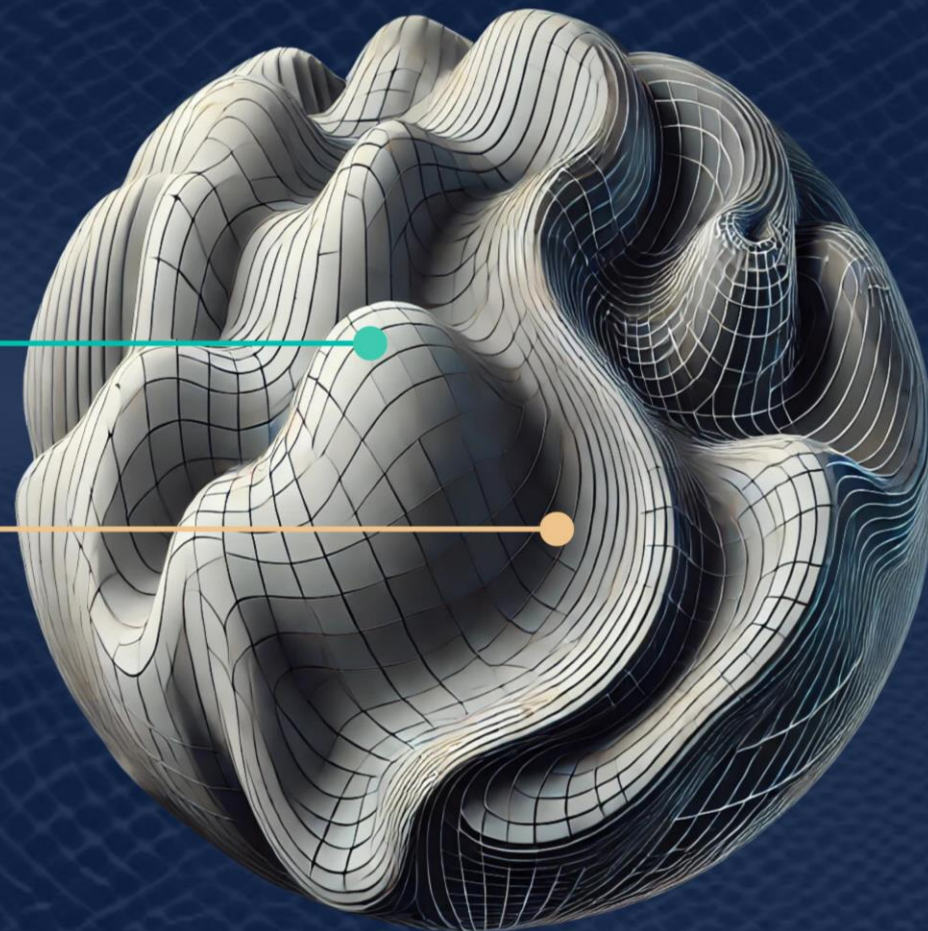


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Our metabolic models provide a **true map of the media landscape**

True Optimal Metabolic Mode

True Suboptimal Metabolic Mode



**Eliminating the need
for biologically implausible
guesses or exhaustive trial-
and-error searches**



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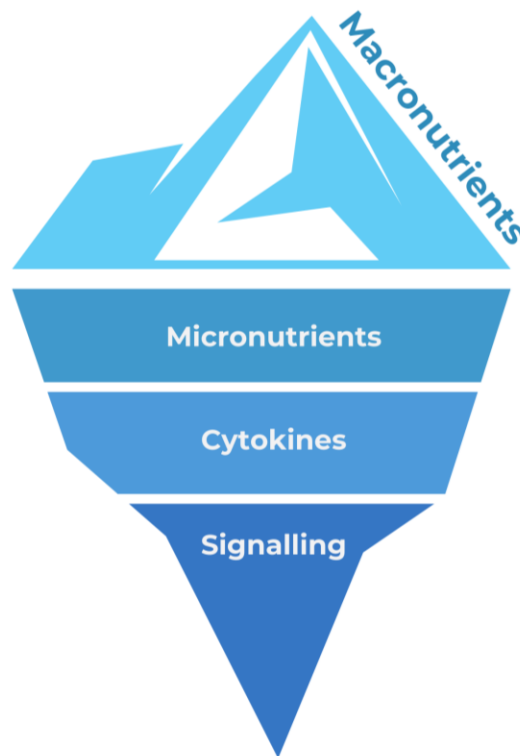
We optimise **multiple objectives**, at a **deeper level**, rapidly

Speed

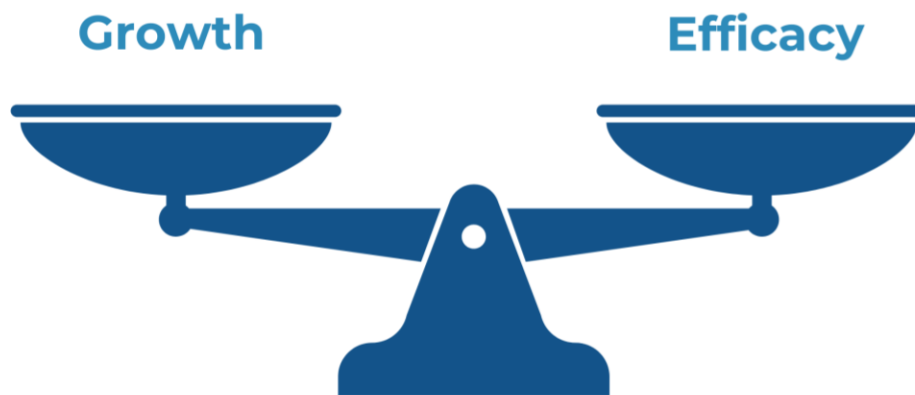
> 12 months

We deliver in weeks

Depth



Multiple Attributes





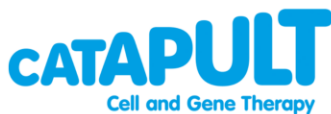
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In 4-6mo, we've demonstrated this can work for HEK293s, now we are **extending and refining**

What we've done HEK293 & CHO



For HEK293 & CHO, we're working with:



What's coming next

CAR-Ts & TILs

Early Access Program



UNSW
SYDNEY



CAR-NKs & iPSCs

**DATA
COMING SOON**





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Let's work together to make your
technology **accessible to the
patients who need it**



Email

alex@tolomy.bio

caelan@tolomy.bio



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We've already produced media that **enhance** **HEK293 cell growth by >50%** (with our own cash)

Process

Public Data
Scraping



Supplement
Prediction



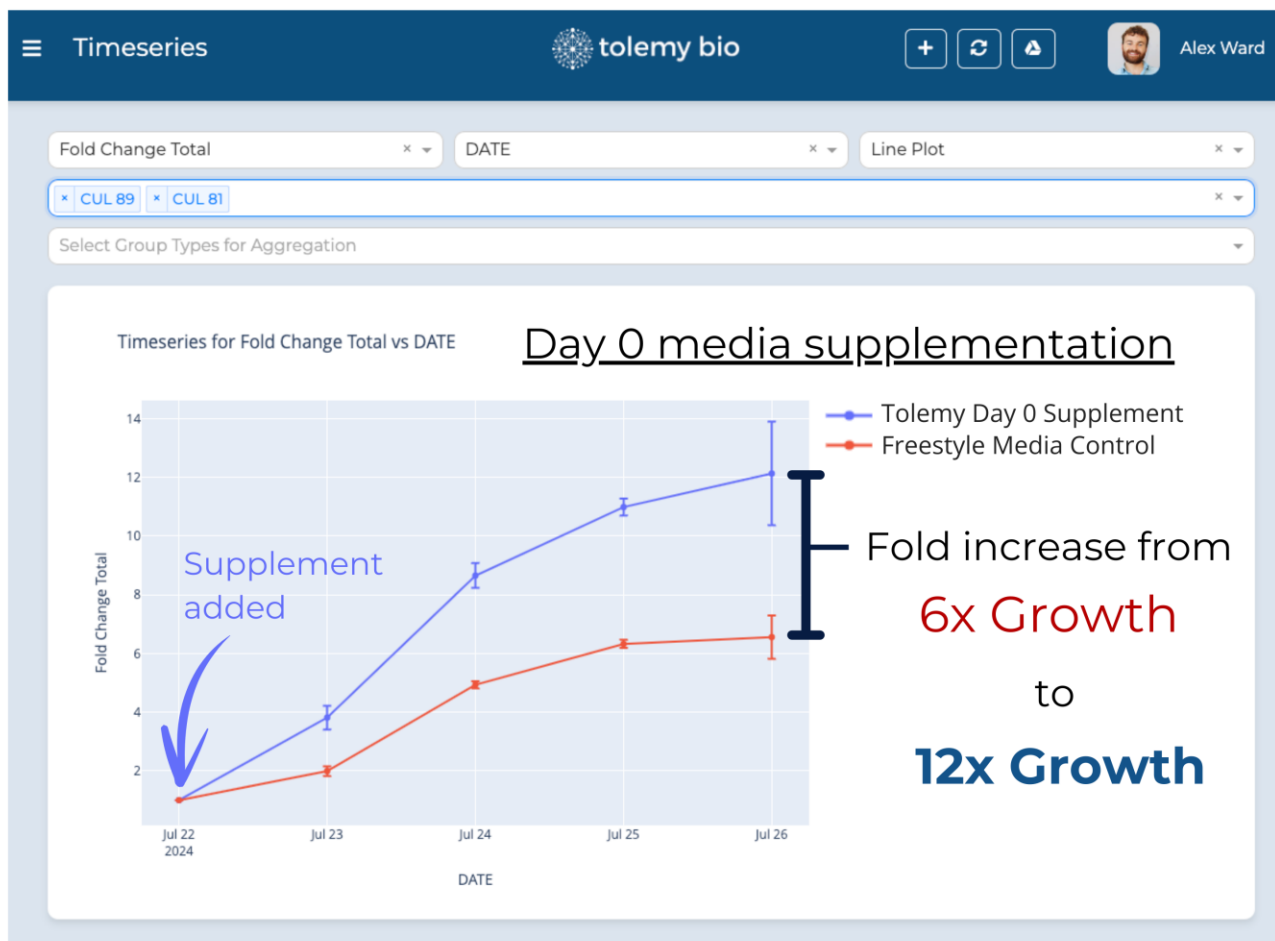
Supplement
Production



Supplement
Testing



Our Platform



Outcomes

- Our Money was well spent
- Early Tech de-risking
- Early Access Products to sell
- Early IP assets
- Working in-house SaaS product