

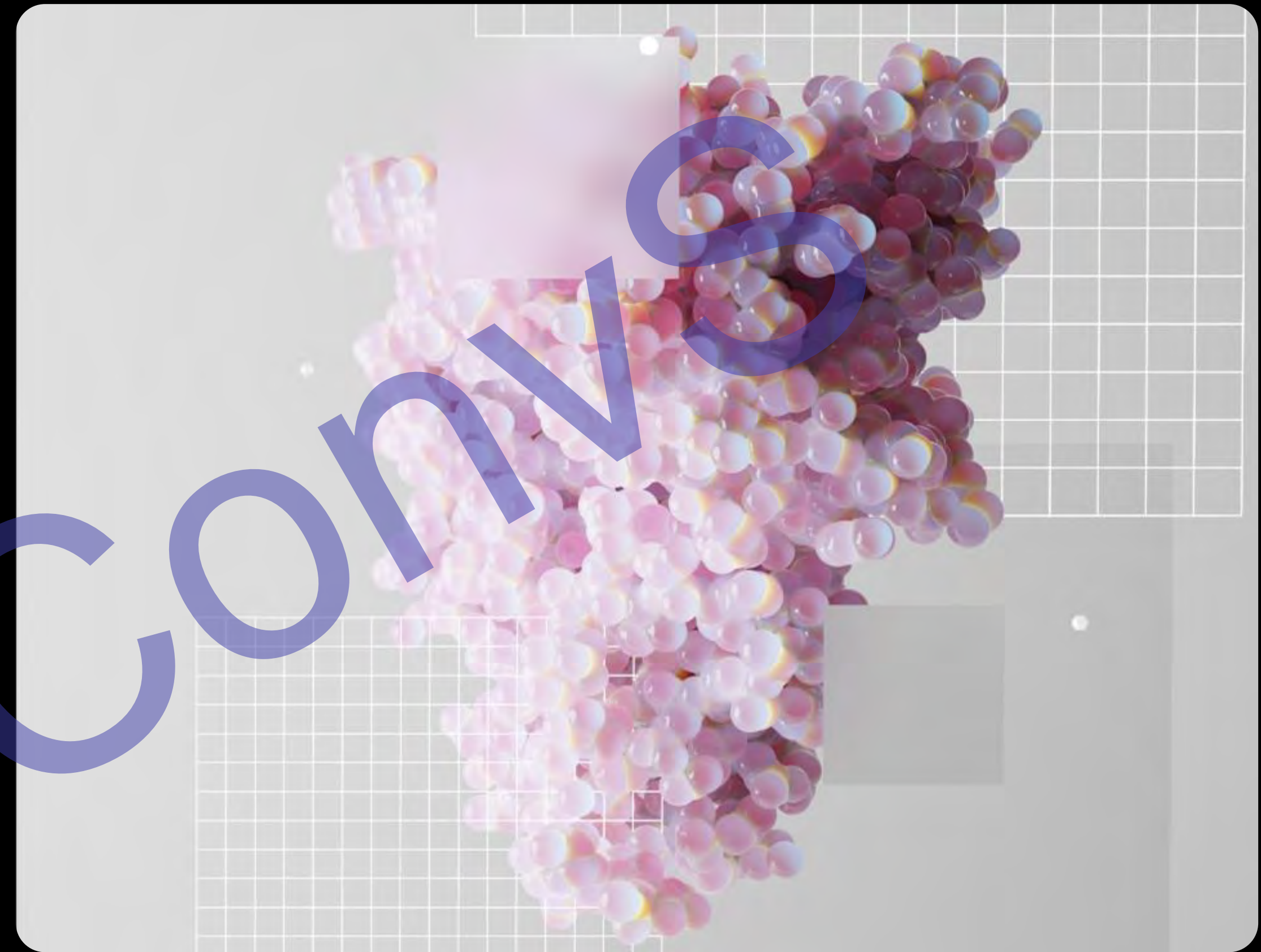
Synthetic biology in the foundry era

Jake Wintermute

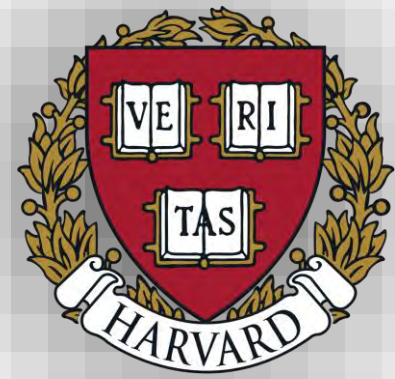
Developer Evangelist, Ginkgo Bioworks

Paris Bioconvergence

November 2023



My short biography in the US and France

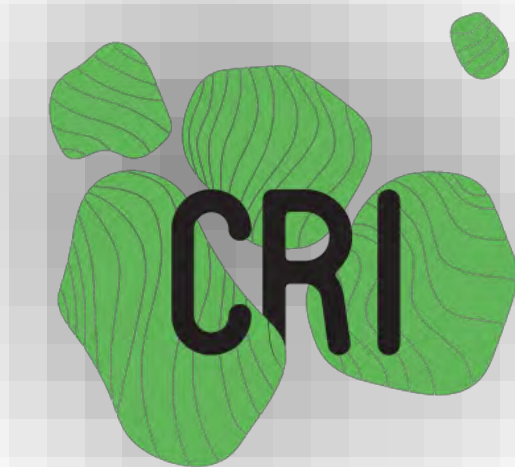


2011
Harvard Medical School



2022-2023
Ginkgo Bioworks

2011 - 2022
Centre de
Recherches
Interdisciplinaire



The world needs more biology

DIMBIOCONVS

Image created with the assistance of DALL·E 3



Biology needs more developers



The bioconvergence changes everything about how we build with biology.

DIM Biocore

How Ginkgo Bioworks works

Insights from a commercial foundry

What developers can build

Examples of foundry-powered projects

How we design R&D projects

AI makes data more valuable and reusable

Who can build with biology

The next generation of synbio startups

Where innovation happens

The case for Paris as a global synbio hub



How Ginkgo Bioworks works





A horizontal platform for cell programming and biotech R&D

Since 2008, building integrated automation, software, and biological tools

In 2021, began trading publicly (\$DNA) after raising \$1.6 billion

~1200 bioworkers including 100s of synthetic biologists, process engineers & data scientists



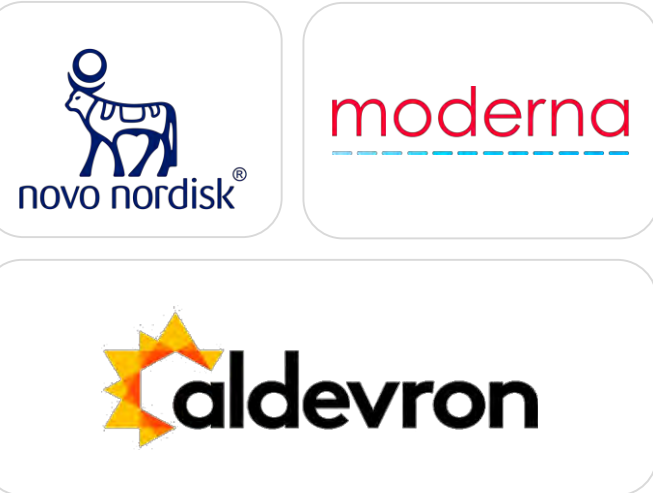
Over 100 programs across industries

Our partners select us to address challenges from discovery through manufacturing

THERAPEUTICS & VACCINES

Pharmaceutical manufacturing

Development of production hosts and processes for the production of a range of products and reagents



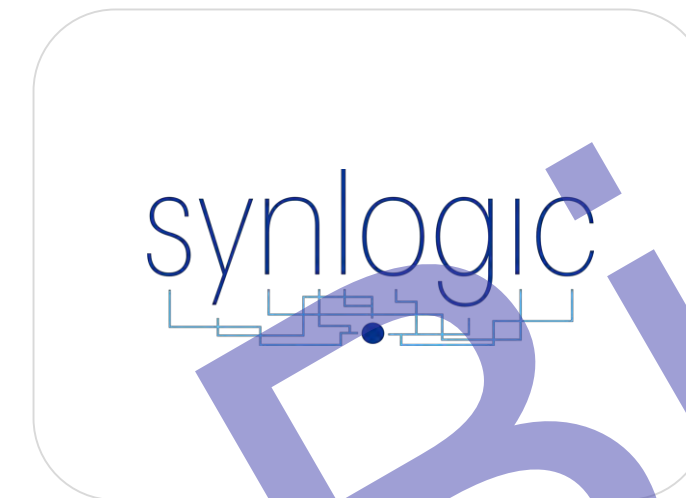
Gene Therapy Platform

Optimize recombinant adeno-associated virus (AAV)-based vectors.



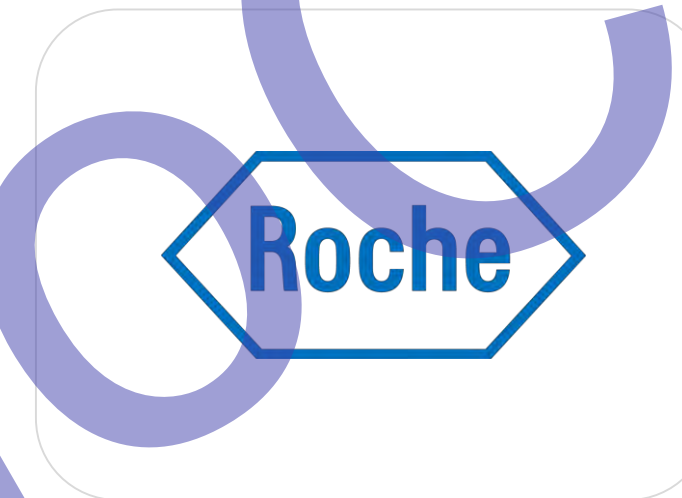
Living Therapeutics

Engineering metabolic pathways in microbes towards therapeutic candidates for metabolic disorders



Antibiotics Discovery

Genome mining for identification of novel classes of antibiotics



Enzyme Discovery

Enzyme discovery and engineering to reduce immunogenicity of therapeutics



Antibody Discovery

High-throughput screening of COVID-19 antibodies from patient RNA-Seq data



FOOD & CHEMICALS

Agriculture

Engineered crop-colonizing microbes for sustainable agriculture



Animal Products

Discovery and design to develop new sources of non-animal protein and ingredients



Plant Extracts

Engineered cells to produce cannabinoid, flavor, and fragrance ingredients



Textiles & Colors

Optimize and scale the production of fibers and colors traditionally obtained from rare sources



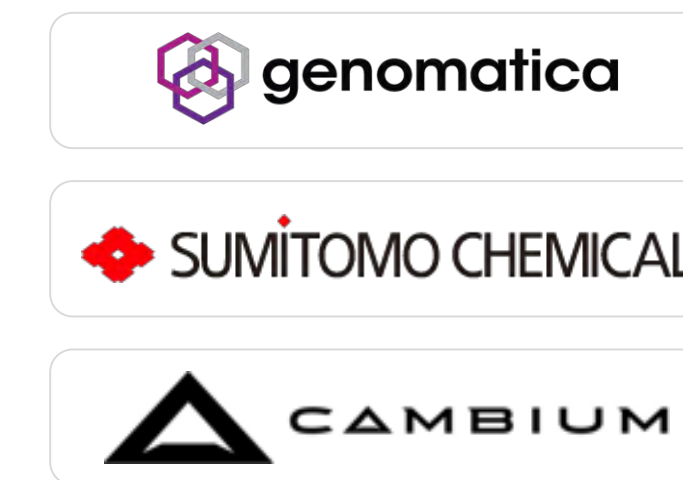
Industrial Enzymes

Create a fast and more effective way to create enzymes for the food industry



Materials

Develop sustainable bio-based chemicals in multiple industries



CCTTCAGCTAGTGGAAGATATT
GTTTAGTCGAGAGAGTTGCACA
CTTCACTGAAGTTCTGCAAATT
ATACATGAGCTGTACCCTGATT
TGCAACTTCCAGAGAAATGTTT
GGATGATAAACCTTTTGTGCCA
ACATATCAGGTGTCCAAGAAA
AGGCAAAGAGCTTGGGAATTGA
GTTTATTCCATTAGACATTAGC
CTCAAGGAAACAATTGAAAGCT
TGAAGGAAAAGAGTATCGTCAG
CTTCTGAATGAGCAACAAGGTG
GTCTGCGTCACGGGTGCCTCCG
GCTACATTGCTTCATGGCTCGT
CAAGCTCCTCCTCCAACGCGGC
TACACTGTCAAGGCCTCTGTTC
GCAACCCAAATGATCCAACAAA
GACGGAGCACTTGCTCGCACTT
GATGGAGCTAAGGAGAGACTTC
AACTTTTCAAAGCAGATCTATT
AGAAGAAGGTTCTTTTGACTCT
GCTGTTGAGGGCTGTGAGGGTG
TTTTCCACACTGCATCCACTGC

Biology is fundamentally
programmable

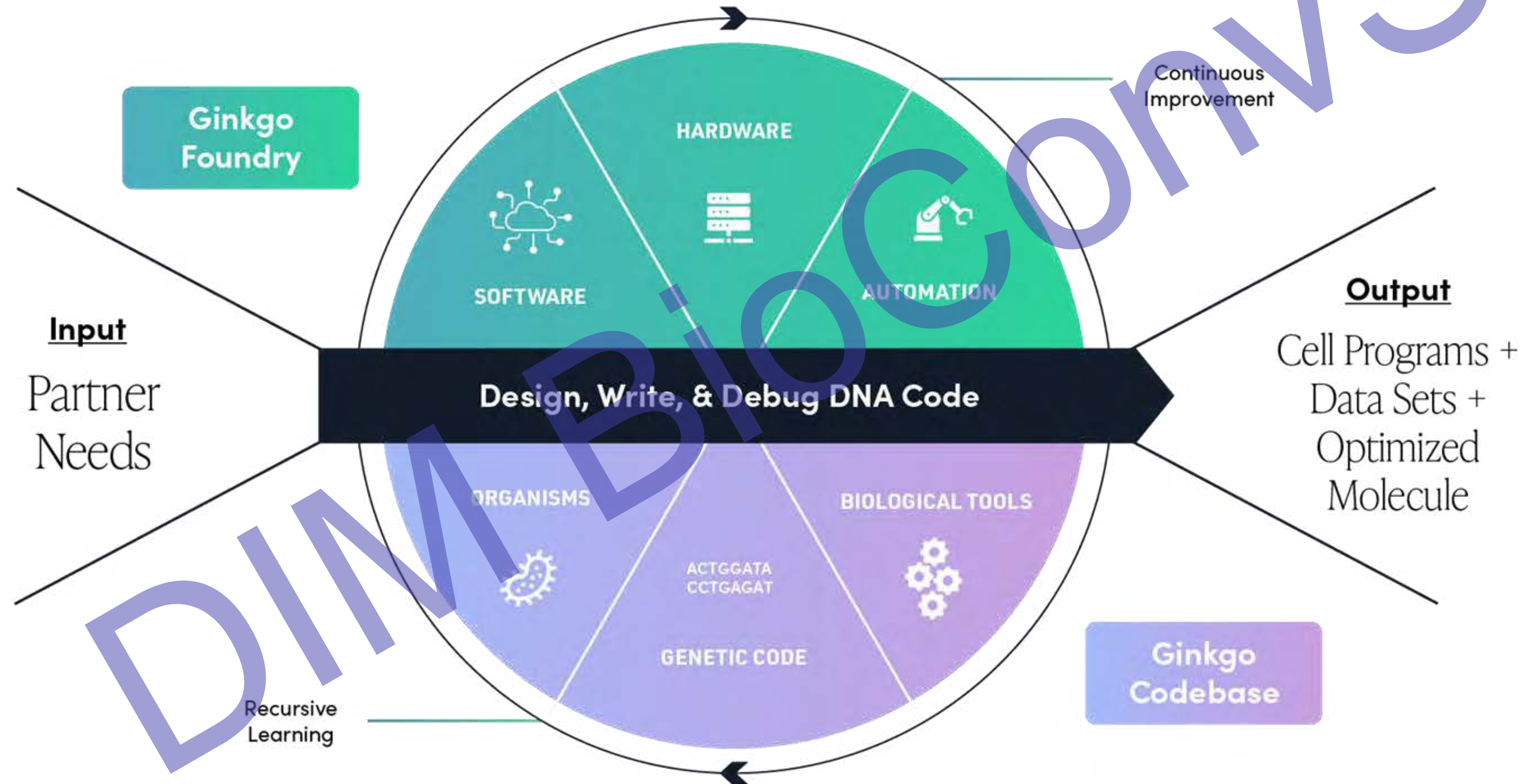


The **Foundry** is our automation infrastructure in both hardware and software

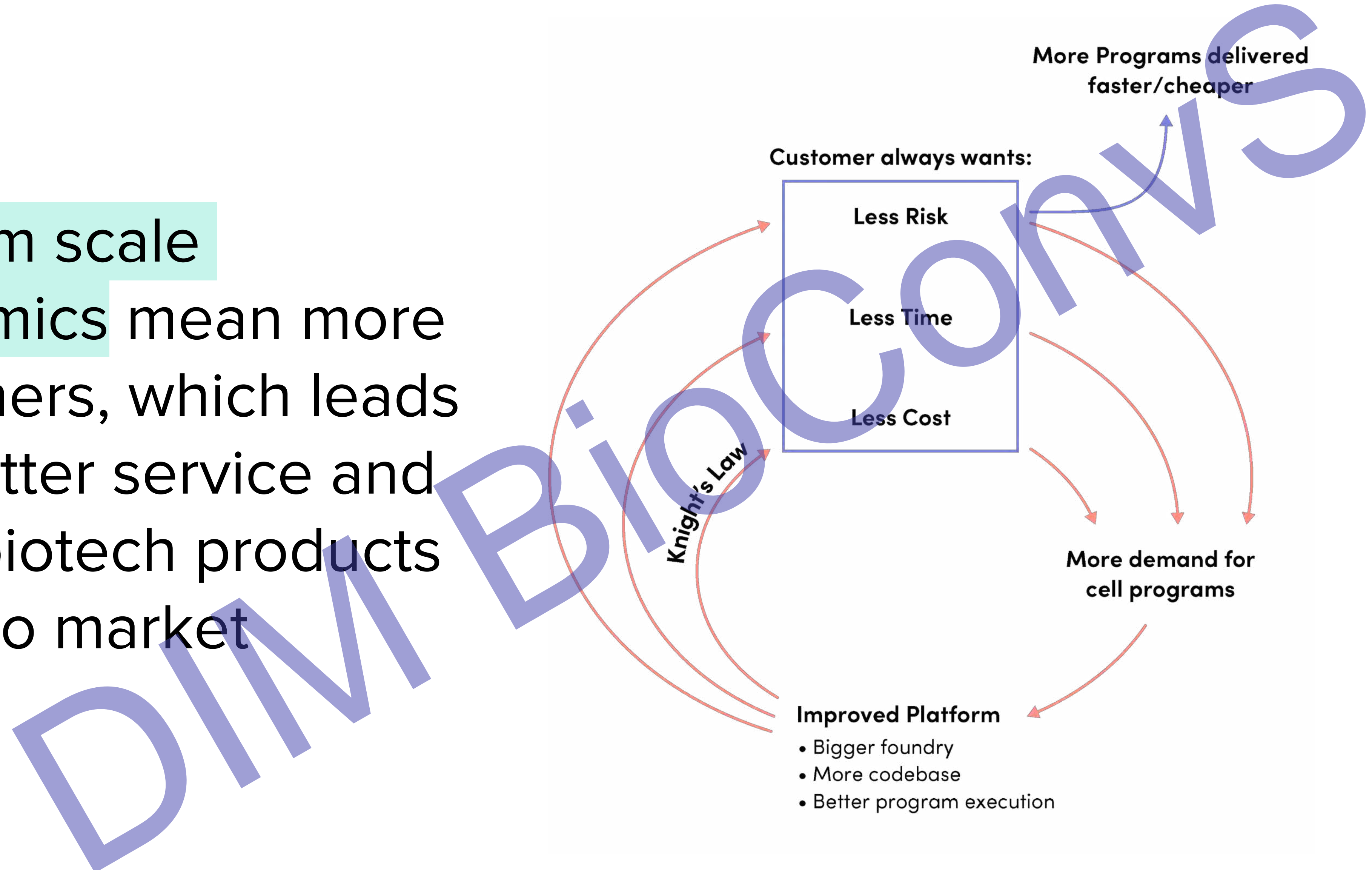
DIM BioConvs



Codebase is our reusable collection of biological tools, parts and organisms



Platform scale economics mean more customers, which leads to a better service and more biotech products going to market



WORK WITH US



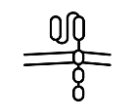
Services make it easy for developers to access our platform



Ginkgo Enzyme Services



Ginkgo Microbe Services



Ginkgo Cell Therapy Services



AAV Services for Gene Therapy



RNA Therapeutics Services



DIM Bioconvs



What developers can build



Examples of foundry-powered R&D

Many emerging therapeutic modalities are **programmable**



Cell Therapy

Emily Whitehead, first pediatric CAR-T patient. Cancer free nearly 11 years later.



AAV Therapy

Jack Hogan, one of the first patients to receive AAV gene therapy to correct progressive blindness.



CRISPR Therapy

Victoria Gray, first recipient of CRISPR-edited blood cells to correct her sickle cell disease.



Stem Cell Therapy

Brian Shelton, first recipient of insulin producing pancreatic cells generated from stem cells.

We need to increase efficacy, safety and access to these remarkable medicines
Making biology easier to engineer is the way

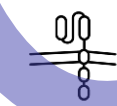


Mammalian cell engineering at Ginkgo is a platform of platforms

OUR THREE THERAPEUTIC SERVICE AREAS



RNA Therapeutics Services

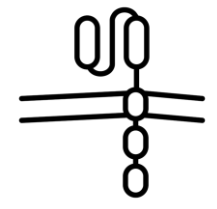


Cell Therapy Services



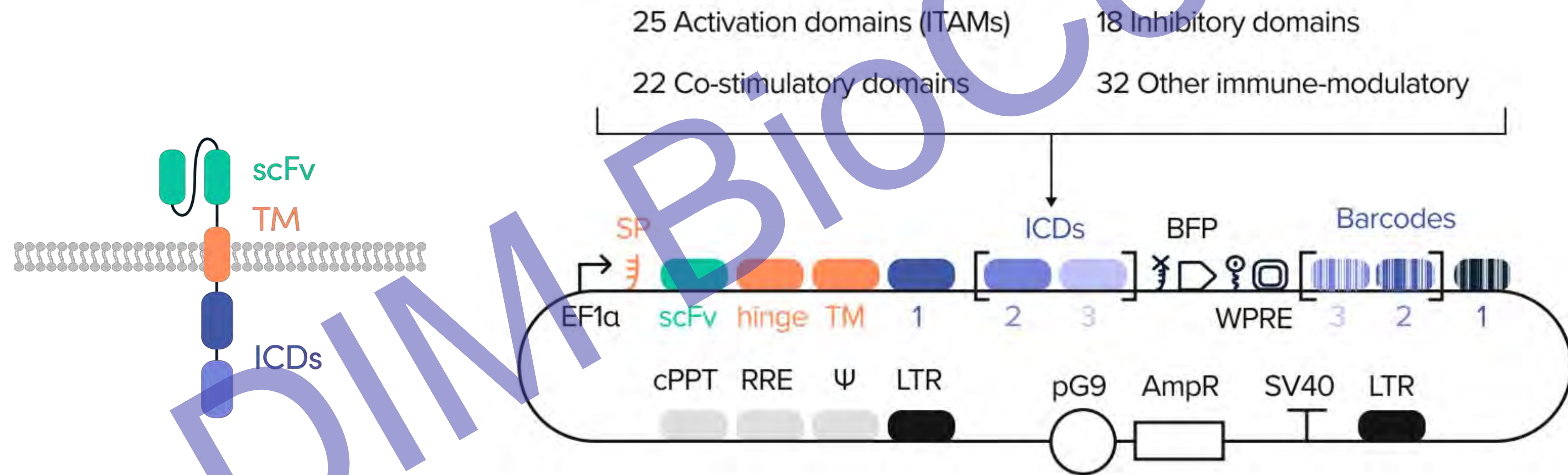
AAV Services for Gene Therapy

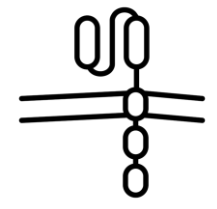




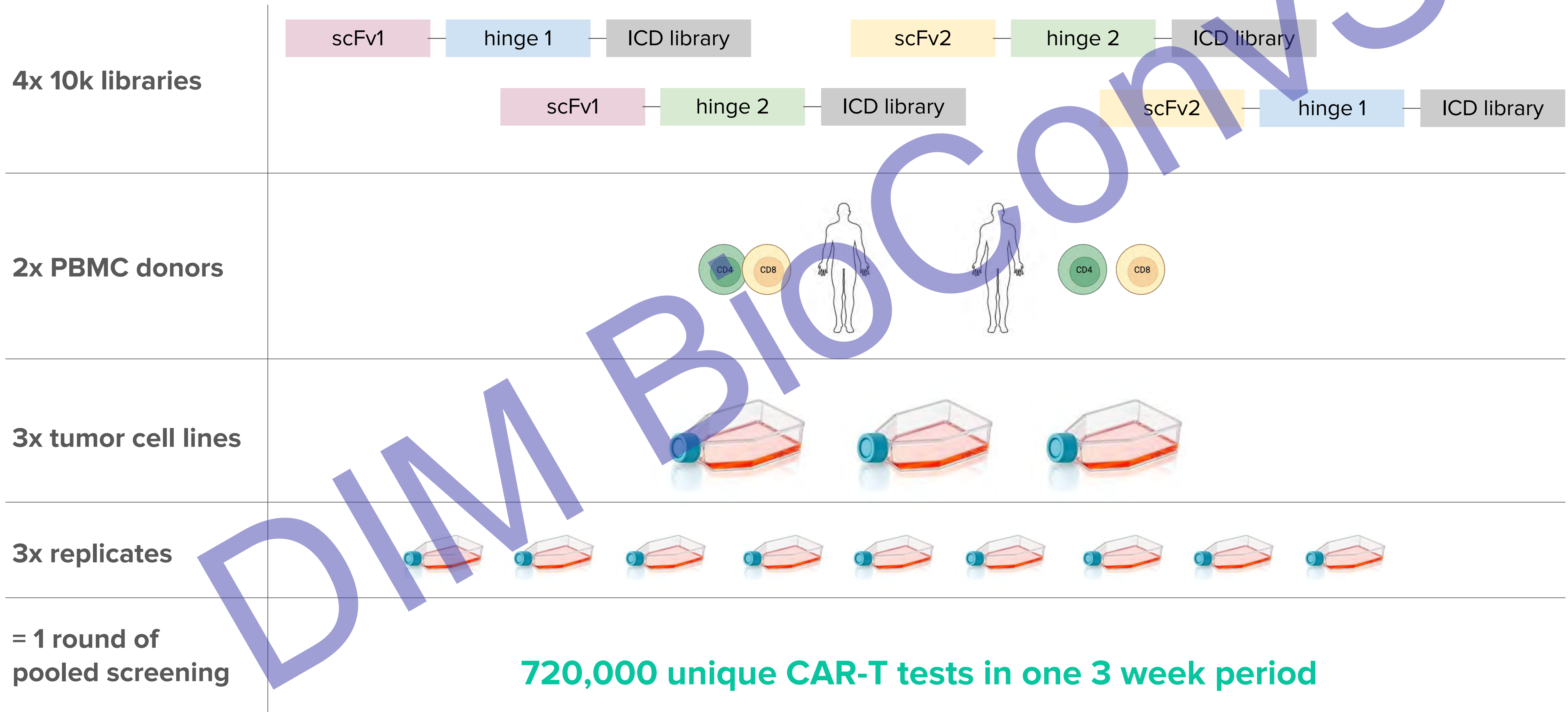
Cell Therapy Services

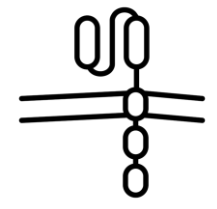
Combinatorially screening CAR libraries at foundry scale





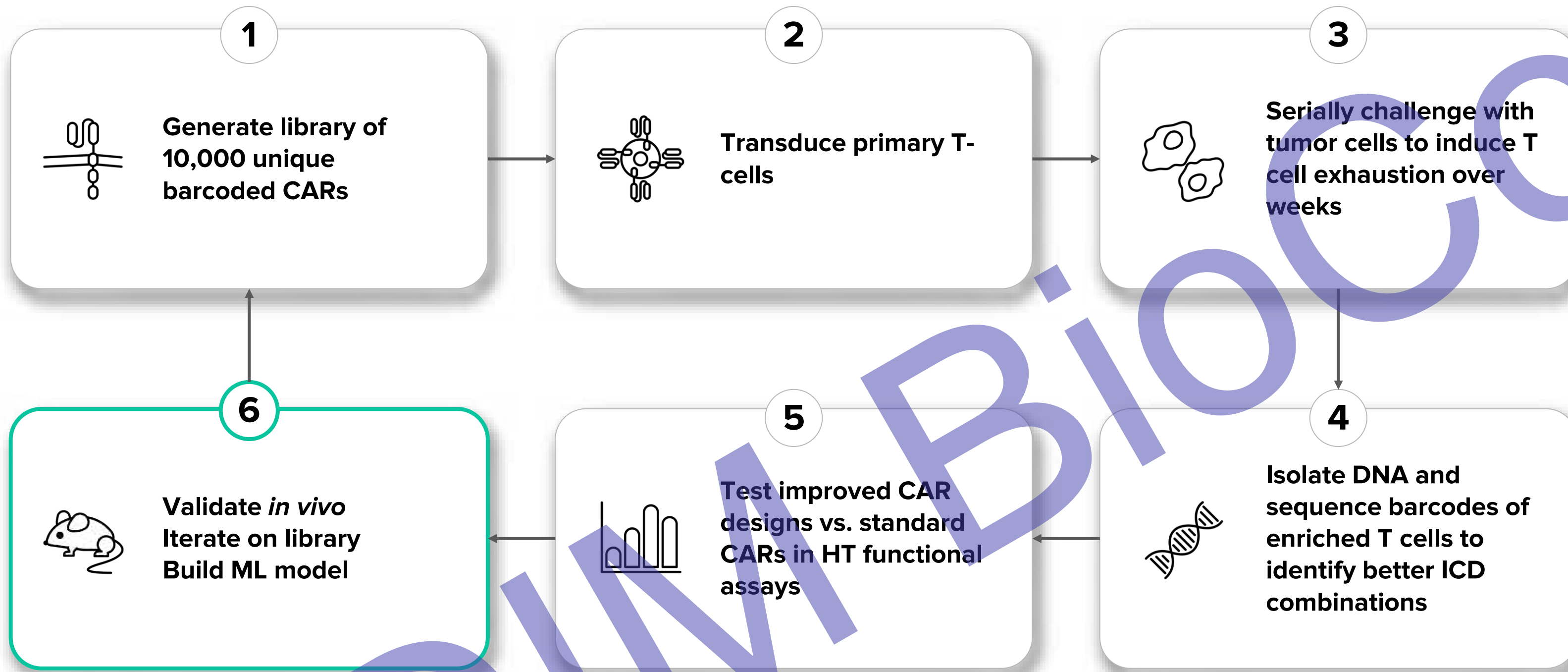
Cell Therapy Services





Cell Therapy Services

CAR-T POOLED SCREENING WORKFLOW



10K Unique CAR-T signaling combinations

>700K Functional CAR-T tests in one screening campaign

>100M T cells transduced

WAYS TO WORK TOGETHER

Pooled screening

Pooled ICD screening with your CAR binder in 6 months

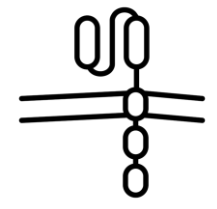
Validation testing

Testing our validated hits in your CAR format

Bespoke work

Bespoke library and assay design for your context

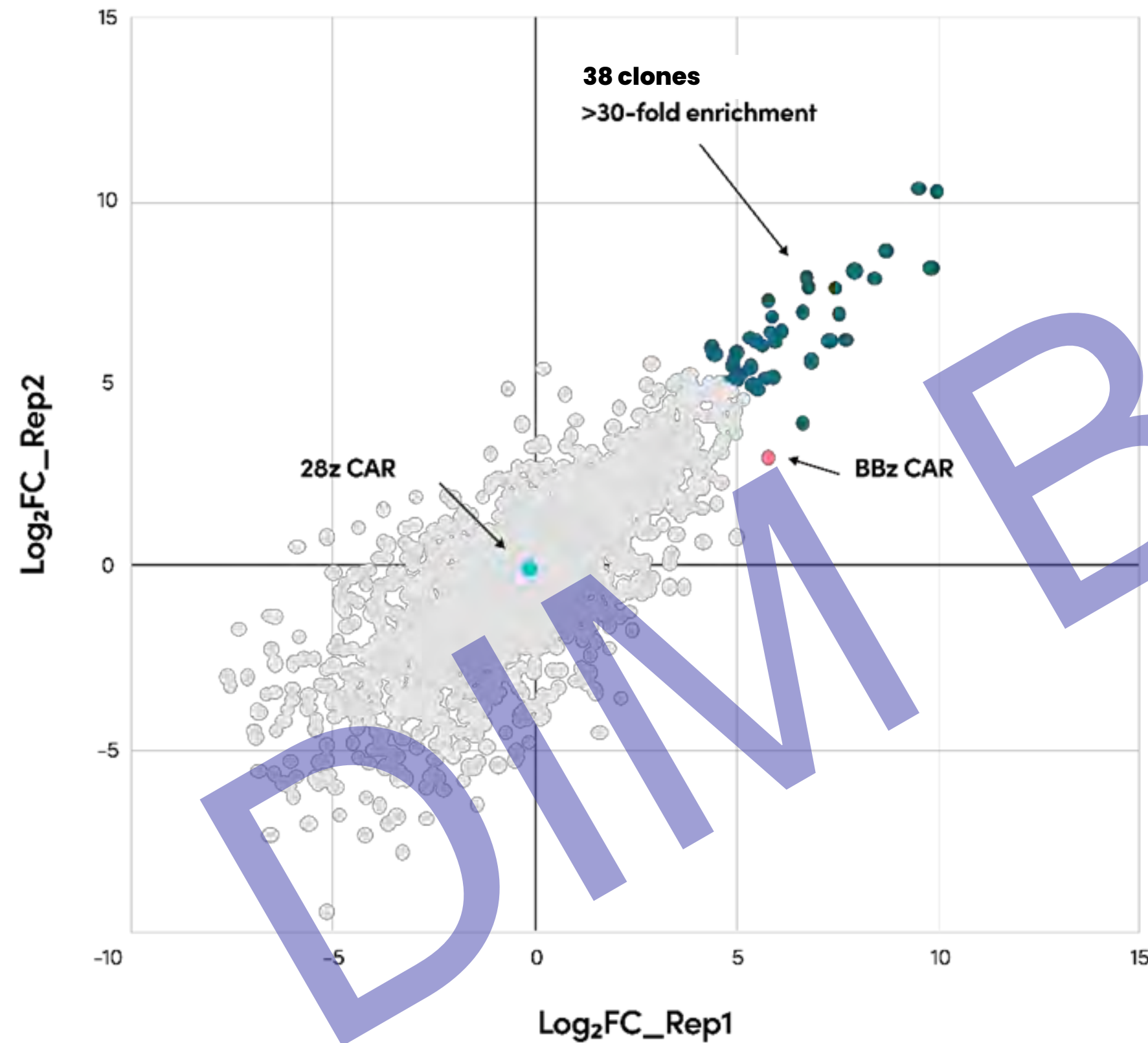




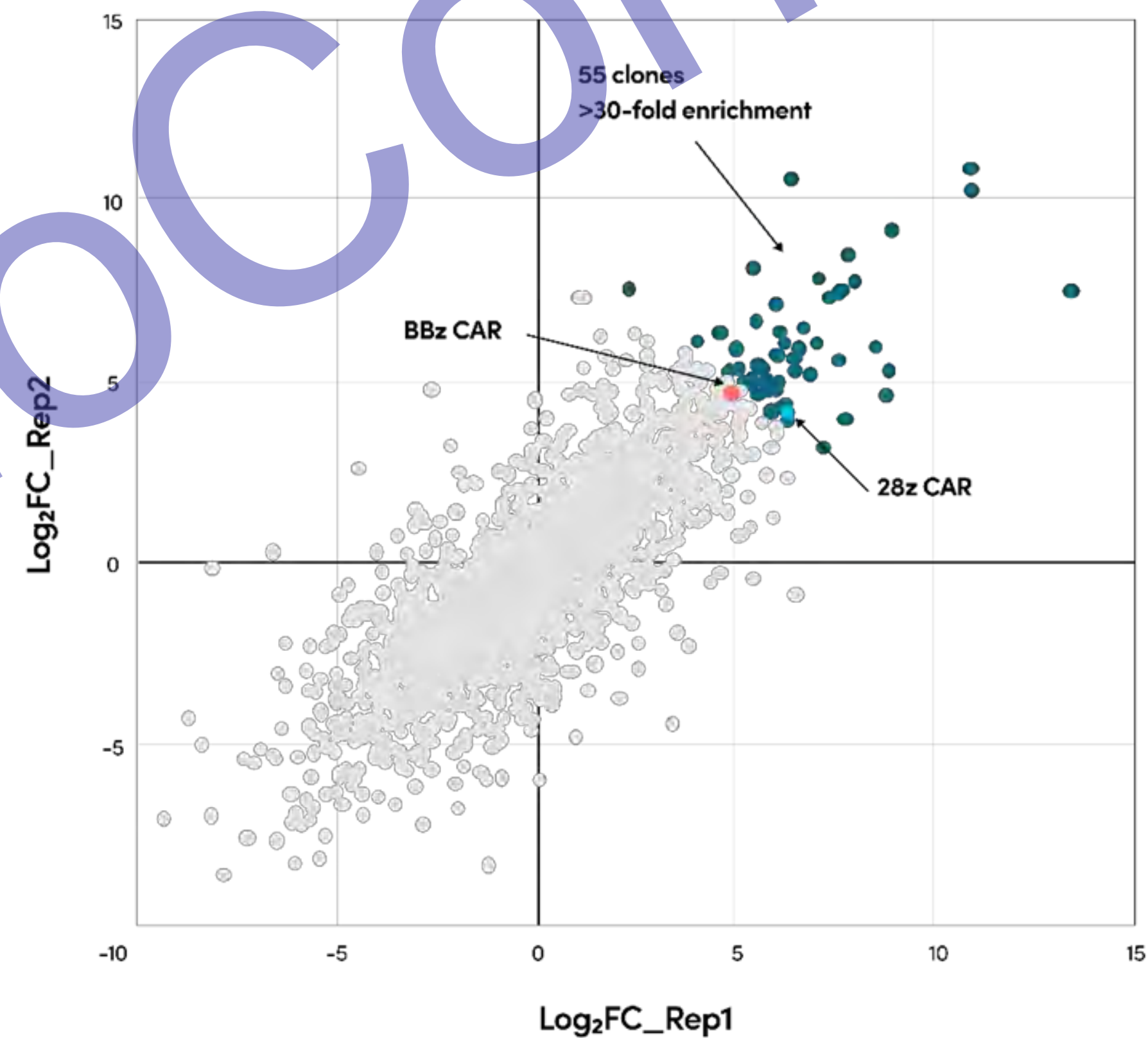
Cell Therapy Services

10,000 2-ICD library screen identifies ICDs that outperform standard 28z and BBz

Enrichment of barcodes at Day 20 of tumor stimulation



High affinity scFv to solid tumor antigen



Low affinity scFv to solid tumor antigen

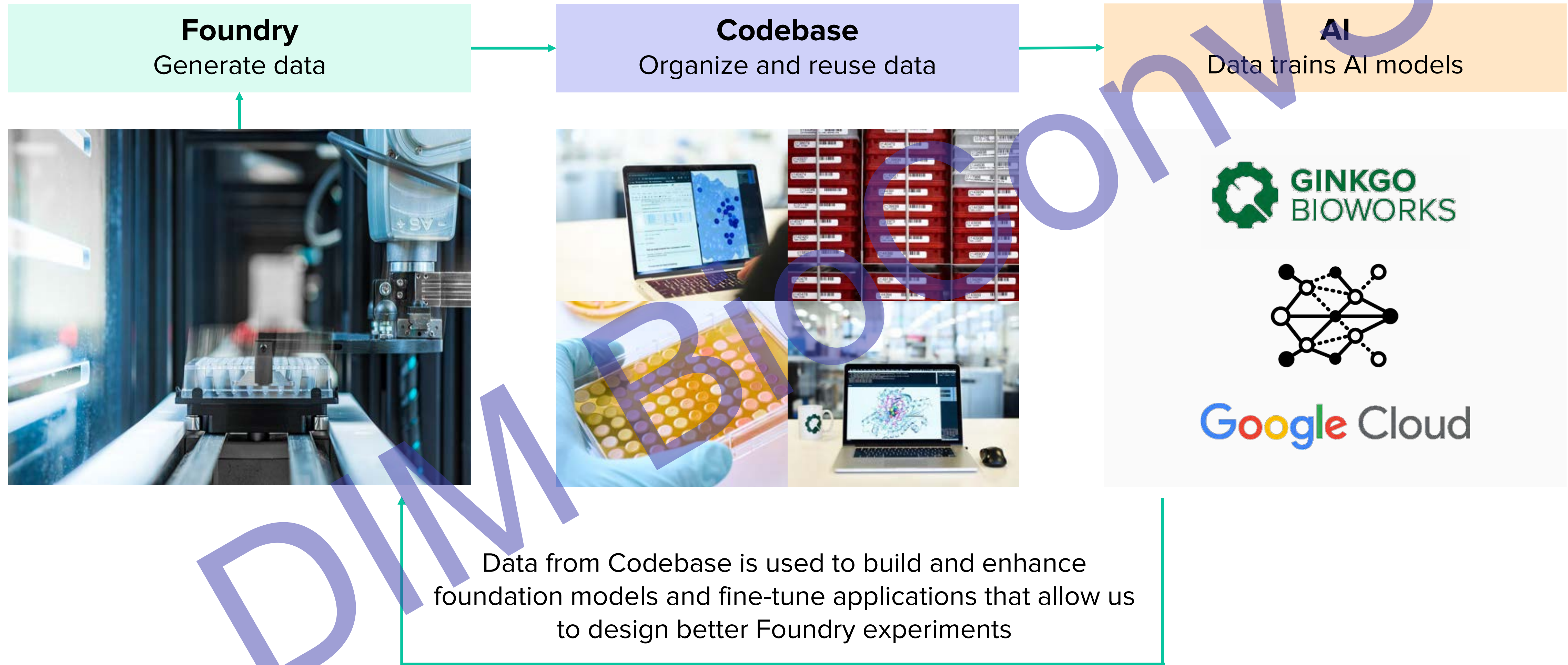


How we design R&D projects



AI makes data more valuable and reusable

AI makes data more valuable and reusable



Ginkgo invests in data resources and expansive data-generating capacity, making it available to our developers

Foundry Data generation

RACs

(Reconfigurable Automation Carts)

For rapid deployment of high throughput screening workflows

Functional assays

10,000+ Enzyme screens per week

Encapsulation & Screening

Up to **1 million** strains screened per run in nanoliter-scale bioreactors.

Mass spectrometry

10,000+ Metabolomics profiles per day

Next-Gen Sequencing (NGS)

1,000s of genomes sequenced per week

Fermentation process data

8,000+ small-scale fermentations annually

Codebase Data resources

Metagenomic Discovery

~**2 Billion** gene sequences in our proprietary DNA database.

Cell Therapy

10,000+ combinatorial library of characterized CAR designs

Gene Therapy

100,000+ AAV capsids partially or extensively characterized

RNA Therapeutics & Vaccines

Structural and regulatory elements for mRNA and circRNA

The hardest problems in biotech require multi-modal data

The Ginkgo foundry is integrated facility for producing high quality and interoperable data

Biological Data Types

70+ million strain tests annually

Metabolomic

10,000+ metabolomics profiles per day

Fermentation Data

8,000+ small-scale fermentations annually

DNA & RNAseq

Trillions of base pairs sequenced per day

Functional Screens

10,000+ enzyme screens per week

Genomic

100 Million+ multiplex genome edits performed each year

Phenotypic Screens

High-content imaging in high throughput

Cell-Based Assays

~720,000 data points generated in a single recent CAR-T experiment

Pooled *In Vivo* Screens

100s of barcoded constructs for use in biodistribution studies

Application Areas

Across biopharmaceutical & industrial biotech

Cell Therapy

Gene Therapy

RNA Therapeutics & Vaccines

Biosecurity

Diagnostics

Enzymes for API Manufacturing

Ag Biologicals

Protein Engineering

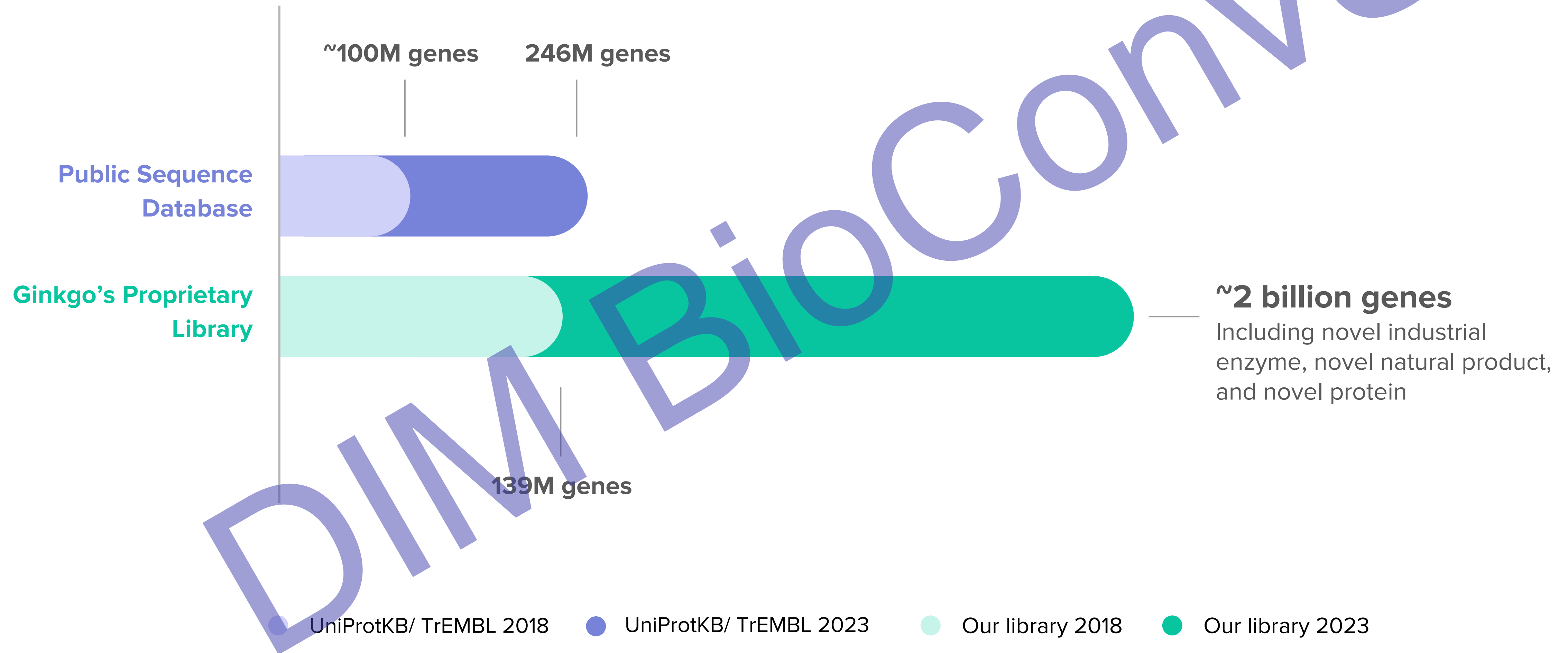
Strain Optimization

Fermentation & Scale Up



We've collected roughly 2 billion wild-type gene sequences

Available for use in metagenomic discovery projects or training sequenced-based foundation models



Our experience with enzymes is broad

We have covered a lot of functional space



Arrayed experimental sample tests, color coded by program

>200

unique customer programs
with enzyme campaigns

>5M

total arrayed experimental
assay tests

>60M

total multiplexed
experimental assay tests

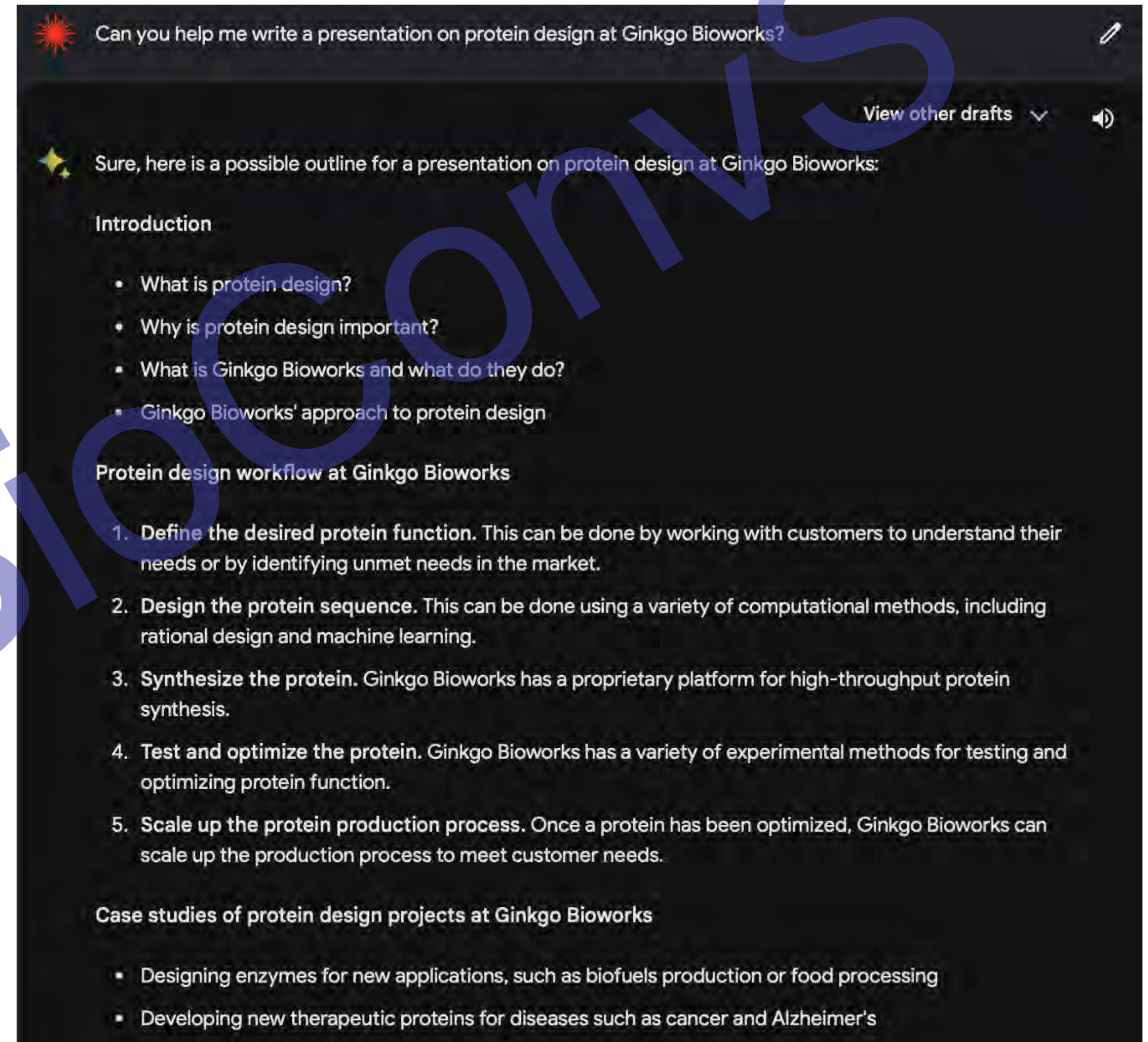
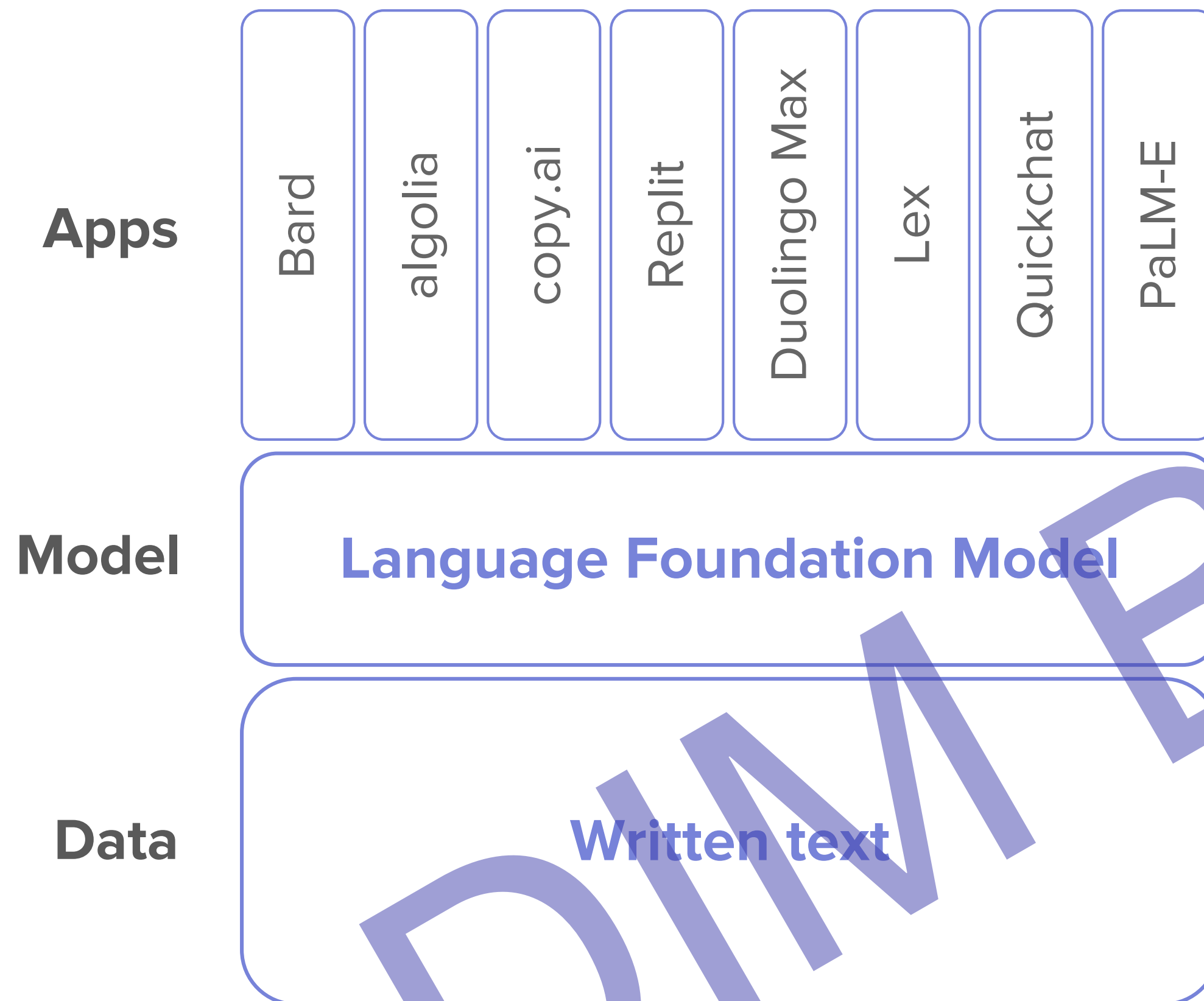
>400

unique enzyme improvement
campaigns



AI is transforming how businesses operate

As an example, chat-based apps are quickly revolutionizing day-to-day business operations



AI is revolutionizing protein science and design

Transformative machine learning research coupled with the existence of the PDB and public sequence databases have led to disruptive developments in our field

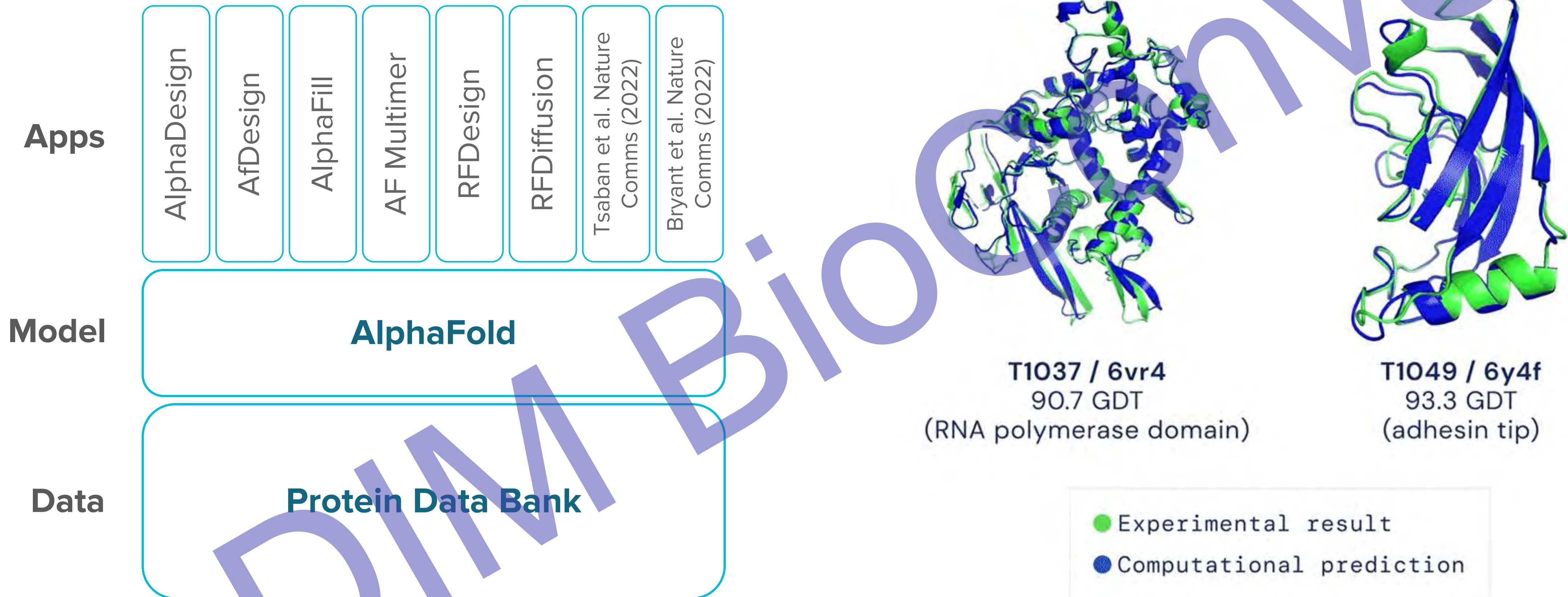
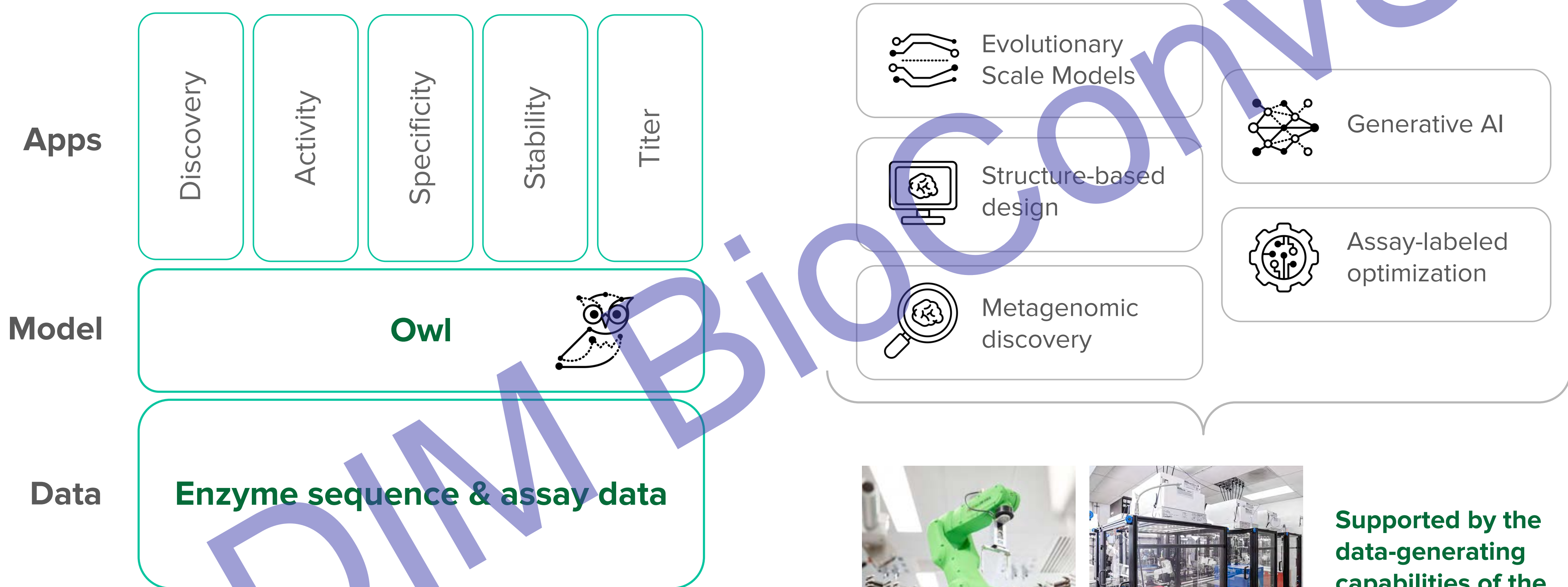


Image credit: DeepMind



Owl is Ginkgo's established AI platform for enzyme engineering

With proven performance across a range of enzyme classes



Supported by the data-generating capabilities of the Ginkgo foundry

Owl delivers better enzymes with fewer iterations

By learning from large datasets and diverse data types

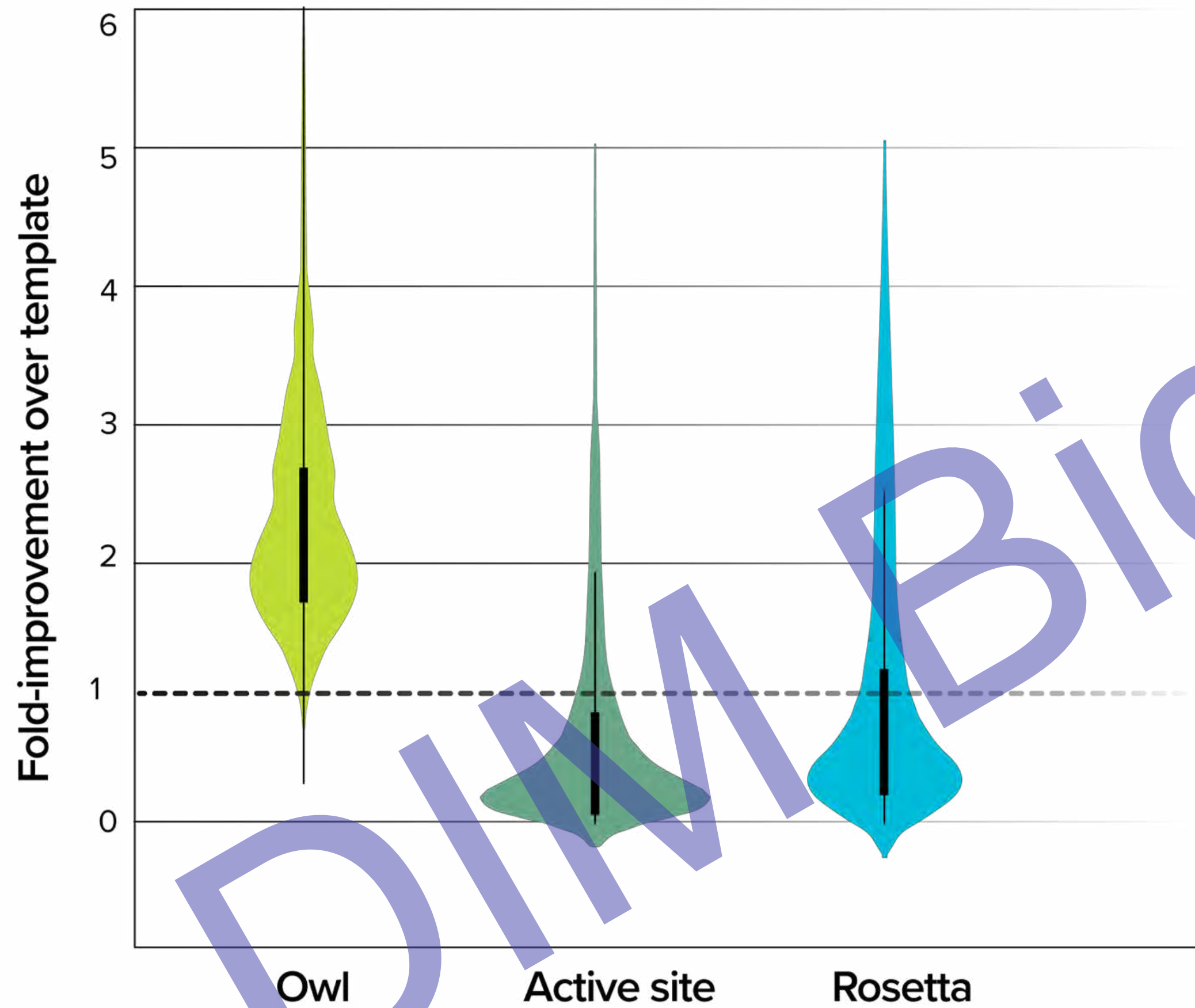


| | Gen 1 | Gen 2 | Gen 3 | Gen 4 |
|--|---|---|--|--|
| Library Size (unique enzymes) | 2,000 | 2,000 | 4,000 | 100 |
| Design Approach | <ul style="list-style-type: none"> ● Sequence-based (self-supervised) model predictions ● Active site mutagenesis ● Rosetta docking & design | <ul style="list-style-type: none"> ● Hit recombination ● Sequence-based (self-supervised) model predictions ● Rosetta docking & design | <ul style="list-style-type: none"> ● Owl ML-guided design ● Active site mutagenesis ● Molecular dynamics ● Rosetta docking & design | <ul style="list-style-type: none"> ● Owl ML-guided design |
| Experimental Screening Methods | <ul style="list-style-type: none"> ● Arrayed activity testing | <ul style="list-style-type: none"> ● Arrayed activity assay ● uHTP pooled abundance screening on comprehensive site-saturation libraries | <ul style="list-style-type: none"> ● Arrayed activity assay ● uHTP pooled abundance and activity screening on large (>10⁶) combinatorial libraries | <ul style="list-style-type: none"> ● Arrayed activity assay |
| Fold Improvement over Wild Type | 1.5X | 3.9X | 4.5X | 10X |

DIMITRIOS



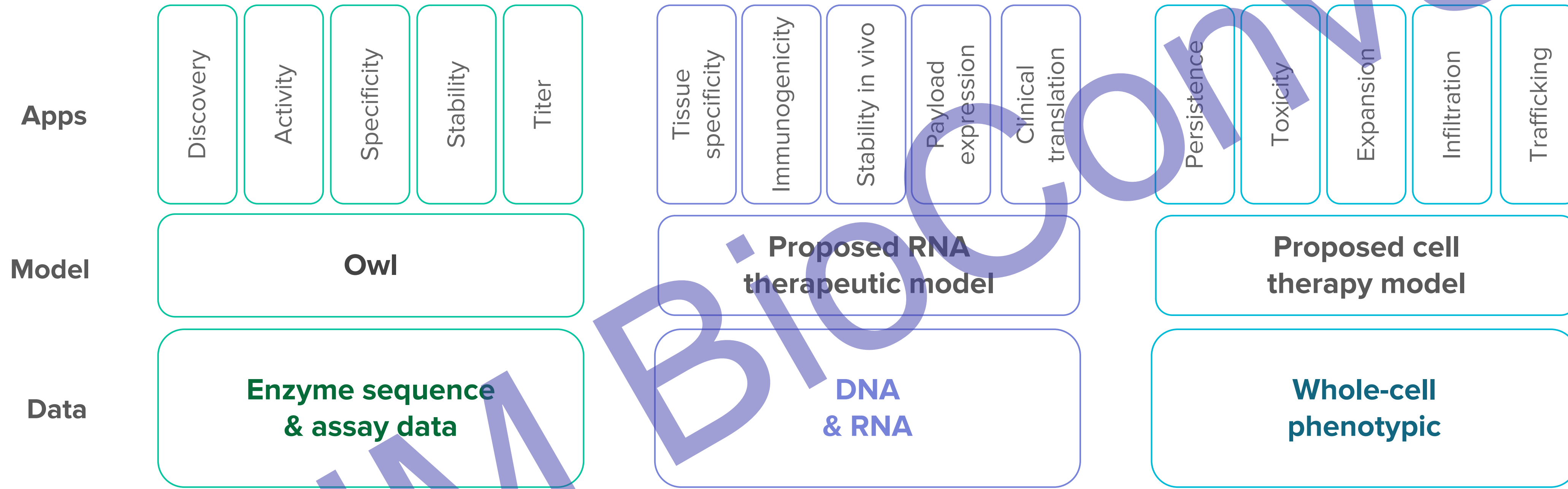
Data-guided AI with Owl produces consistently high performance



Large experimental datasets coupled with Owl ML-guided design yield more variants with improved performance as compared to traditional methods.

Google's Vertex AI enables us to build foundation models & apps across applications

To take on the hardest problems in biotech



Seeking pharma innovation partners in therapeutic modalities including:

- Cell therapy
- Gene therapy
- RNA drugs & vaccines
- Biologics & protein drugs

DRAFT

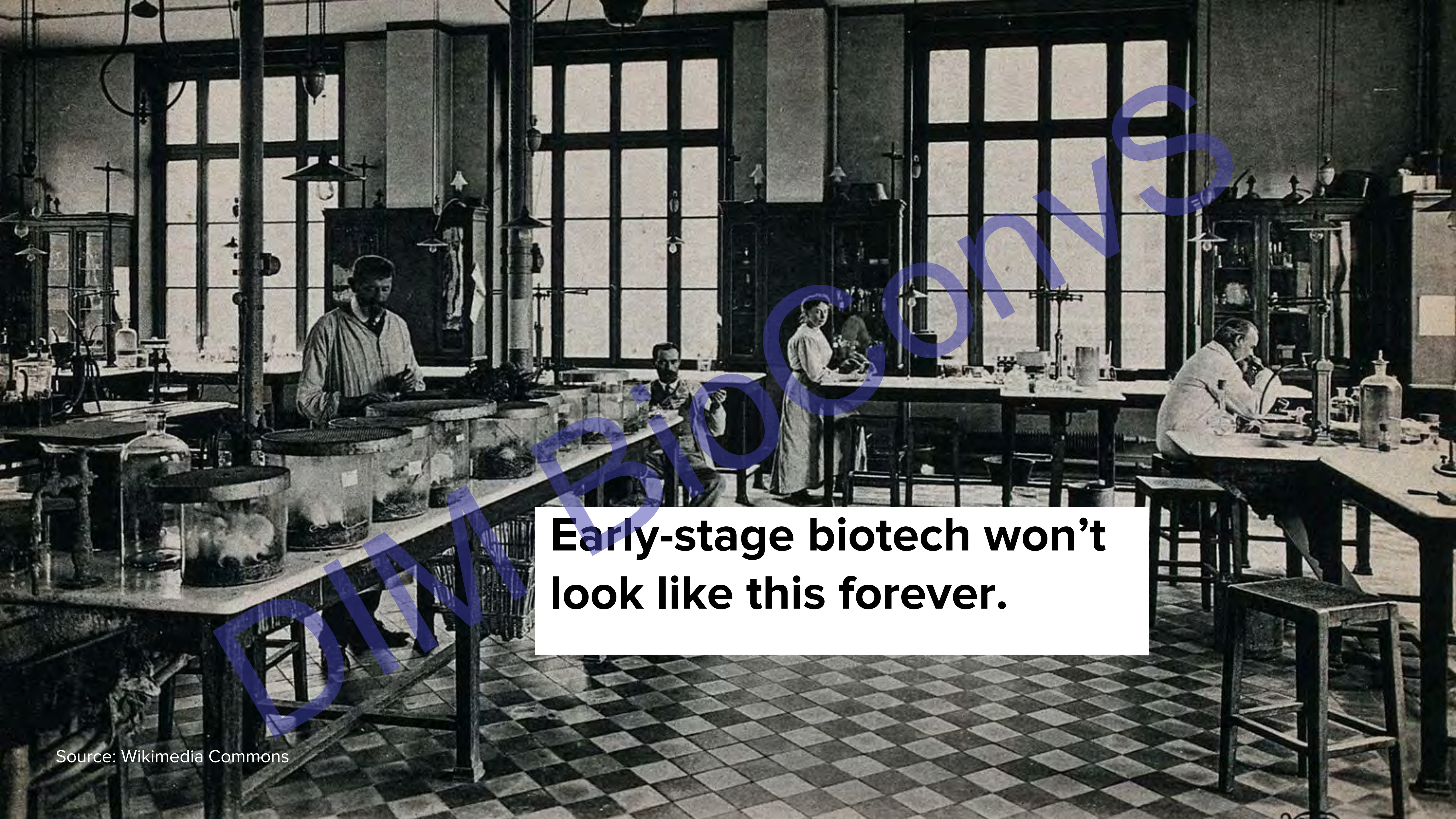


Who can build with biology

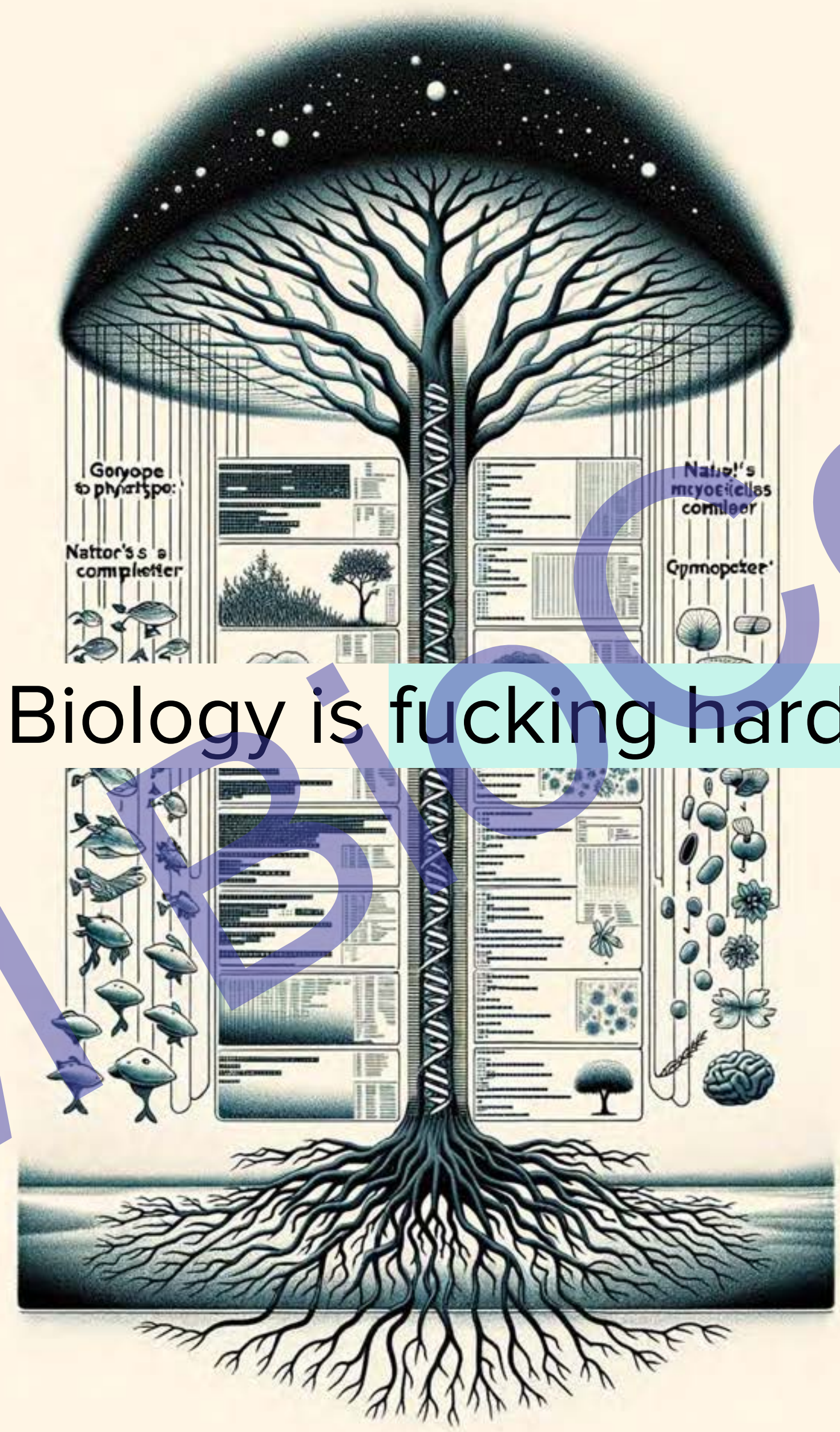


DIM BioConvs

The next generation of synbio startups

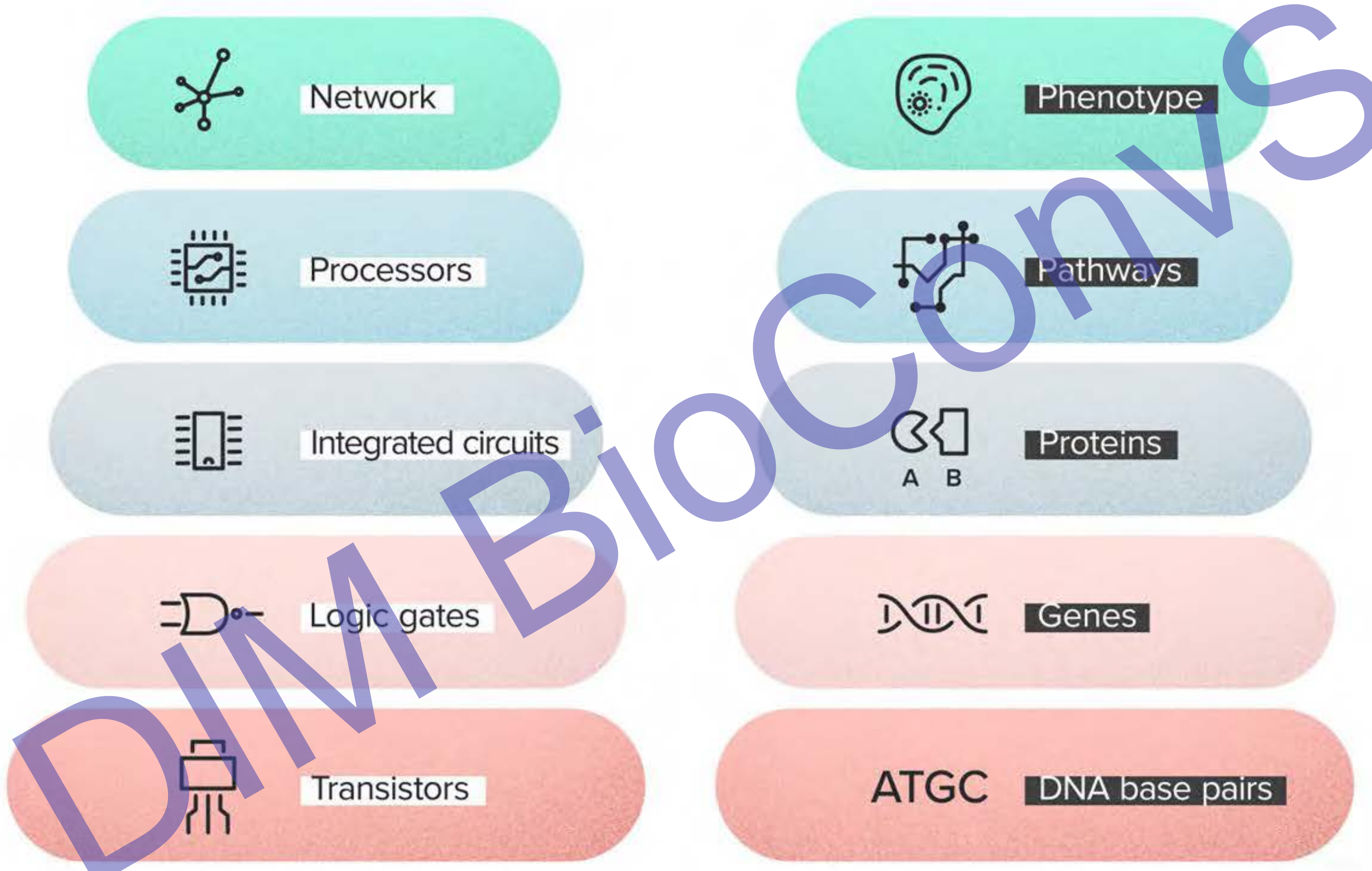


Early-stage biotech won't look like this forever.



Biology is fucking hard





Physical lab space is optional for a synthetic biology startup

Startups can avoid spending on overpriced lab space and overpriced lab equipment



Jasmina Aganovic — Arcaea
Chief Executive Officer

“Arcaea was able to **begin lab work in weeks without building out our own biotech capabilities** but more importantly, we were also able to **access high throughput automation within Ginkgo’s Foundry**. That meant our team could access an enormous amount of data that helped us move quickly and stay focused on what we do best in personal care product development. This is a driver to why **we were able to launch a compelling, differentiated product in less than two years**. Had we not worked with Ginkgo, we would never have been able to move this fast or deliver as great of a product.”

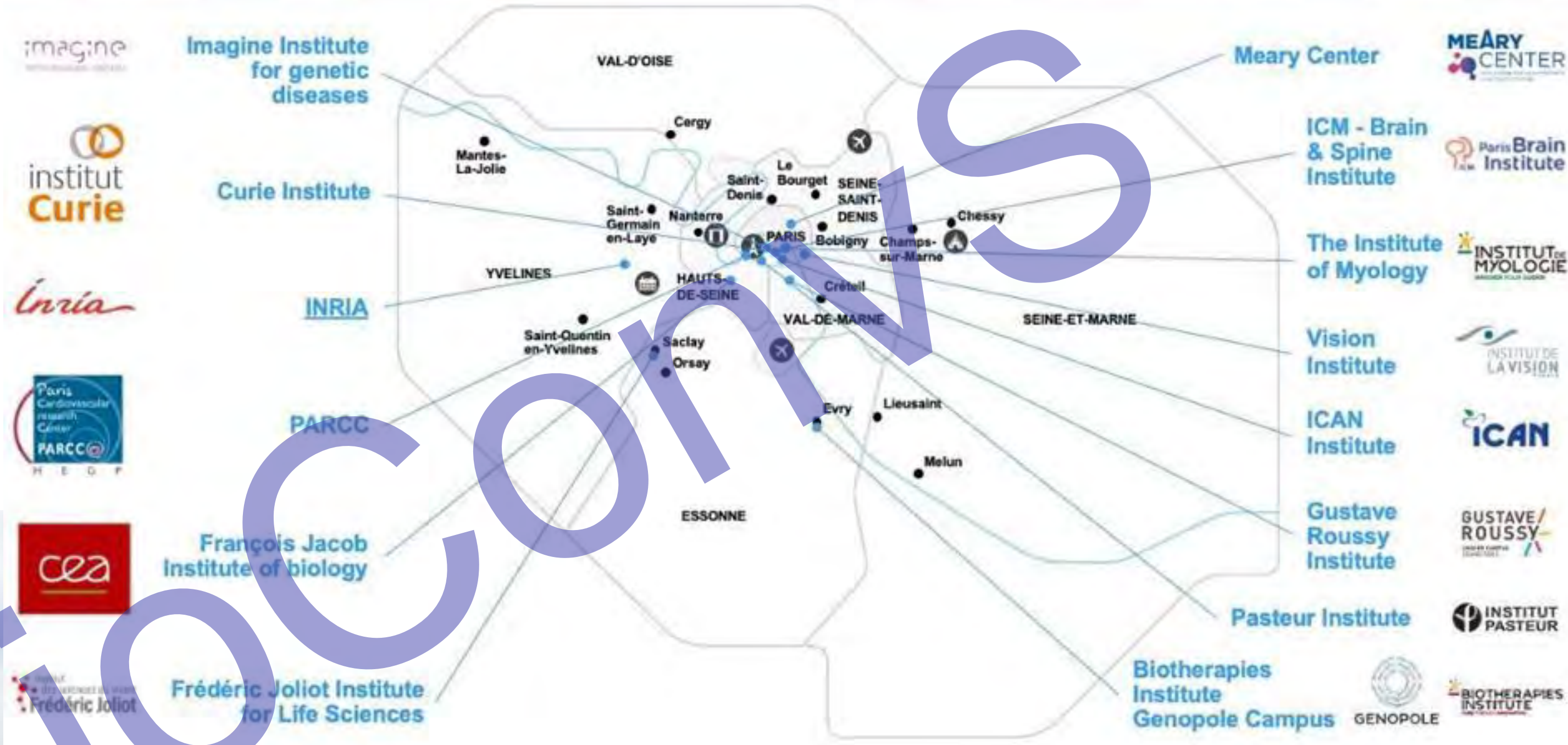
Where innovation happens



The case for Paris as a global synbio hub city

In the foundry era, talent and product matters more than infrastructure

Health Research Centers



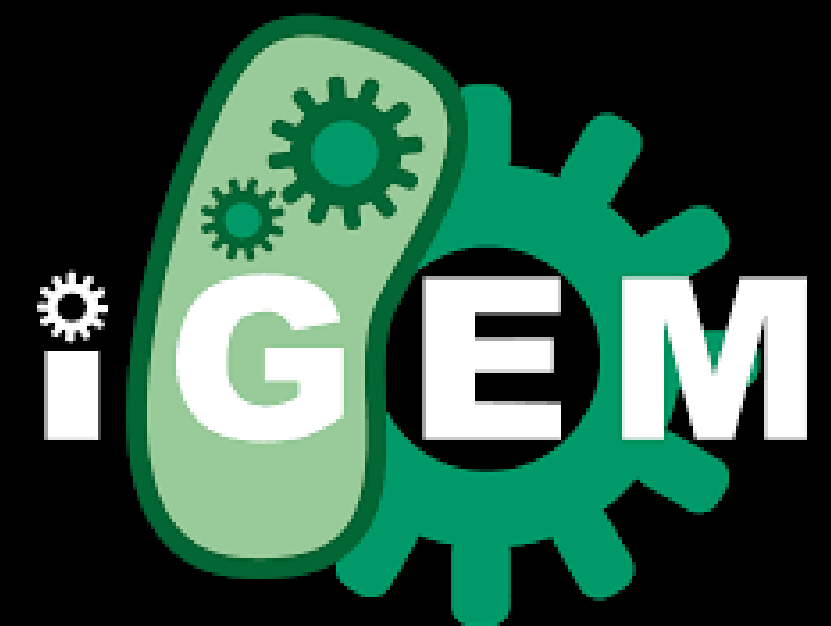
iGEM is the global heart of
synthetic biology

(and it's right here in Paris)

400 teams in 2023

66 countries

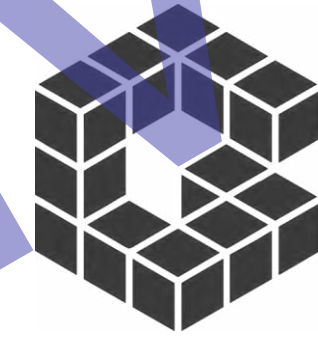
~5000 participants





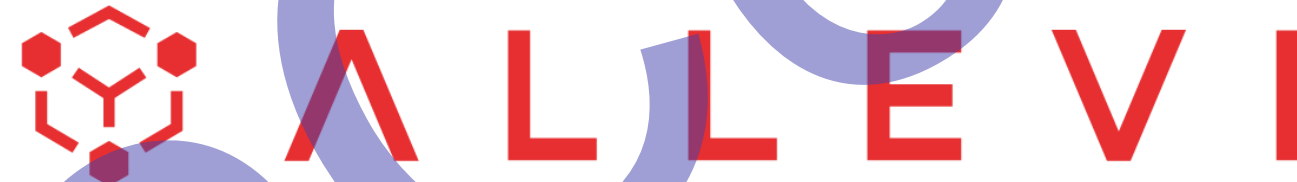


iGEM Startups (150+ and counting)



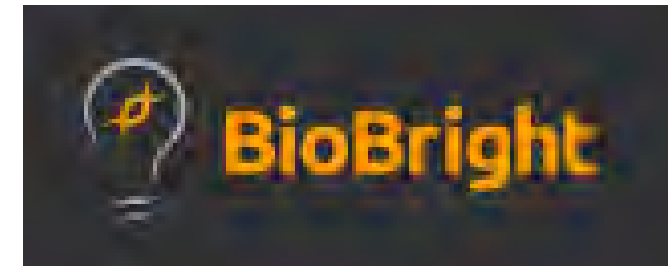
LabGenius

ASIMOV



XENON

LA PAILLASSE



BIOCONNS



France has lots of talent for **product**



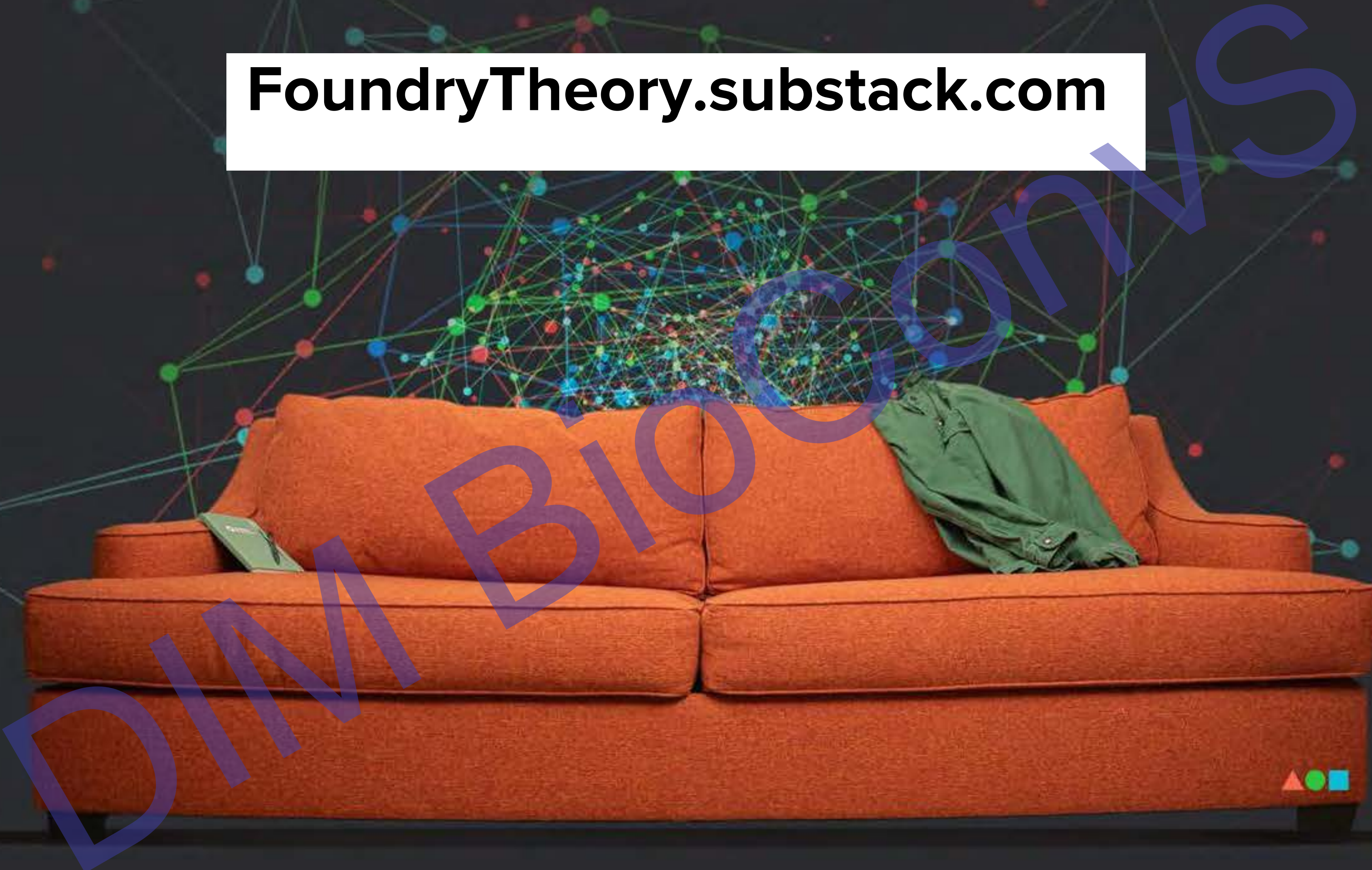
The world needs more biology

DIMBIOCONVS

Image created with the assistance of DALL·E 3



FoundryTheory.substack.com





What is a Foundry for Biology?

You can think of it as an integrated platform for all things synthetic biology. Or you can think of it as a place that is really good at moving drops of...

OCT 16 • JAKE WINTERMUTE

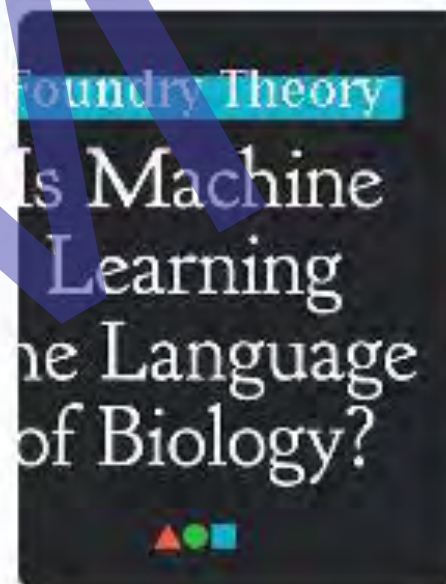
New



End to End with Circular RNA

RNA therapeutics are programmable...

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Is Machine Learning the Language of Biology?

We explore why biology is hard to grasp...

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Foundry Theory

Making Ginkgo Bioworks easier to understand

GINKGO

[Ginkgo Bioworks Homepage](#)

[Ginkgo Sociotechnical Studio](#)



Foundry Theory

Making biology
easier to understand

