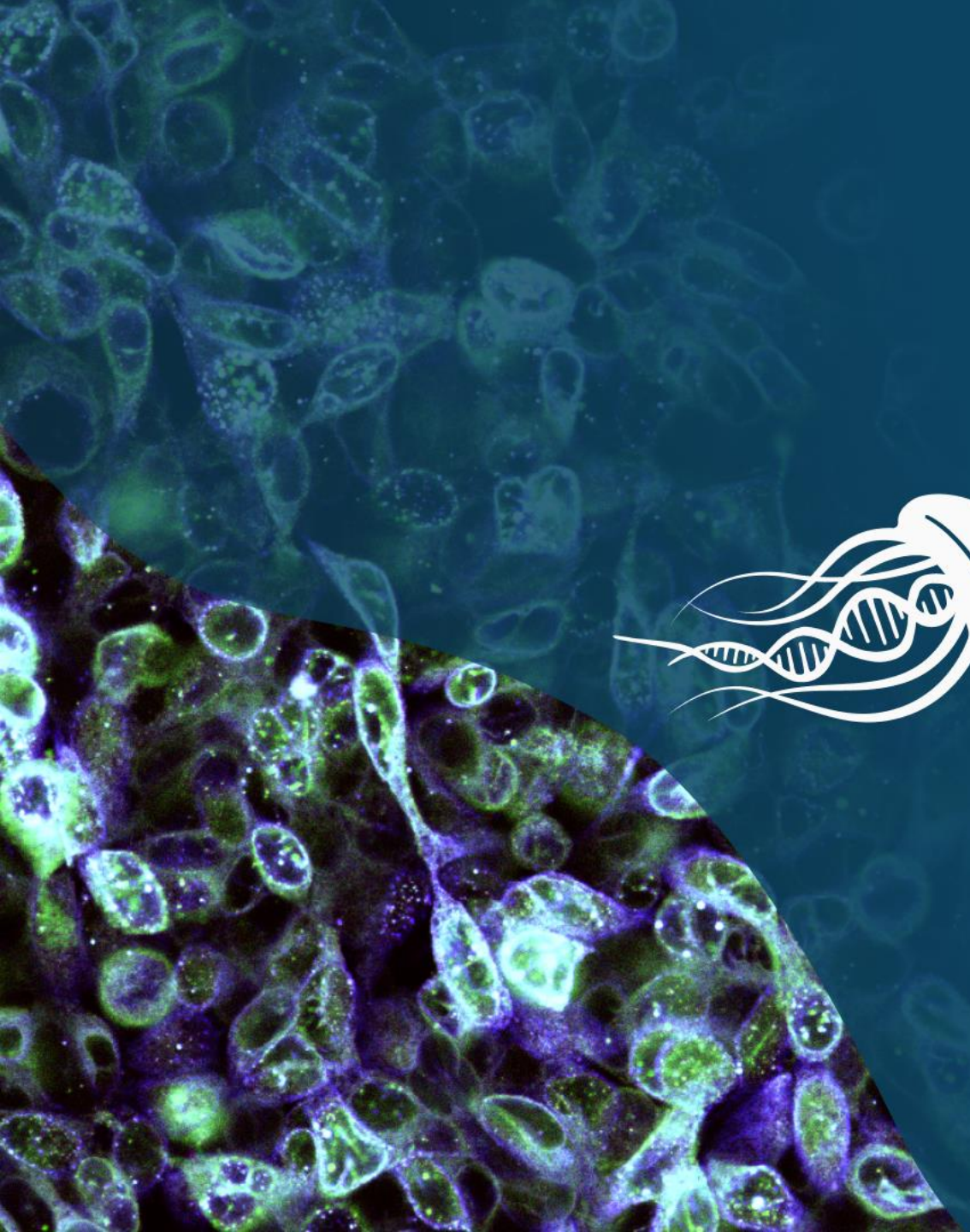
# Protein Evolution in a Microscope To Advance KAND Therapies



BioLoomics

Doug Chapnick, PhD
Founder & CEO
DougChapnick@BioLoomics.com

# Our Project Plan For Finding Candidate Treatments for KIF1a

## *PHASE I*

**Build a HTS Assay in 2 Months**

**Success Enables:**
- Screening Small Molecules
- Screening For Targets

**Find a Novel Target in 4 Months**

**Success Enables:**
- Mechanistic Understanding
- Building More Assays
- Building a Gene Therapy

**Candidate Therapy in 6-12 Months**

**Success Enables:**
- Mouse Studies
- Clinical Testing

# Our Startup Has Been Building A New Pharma Tech For 2 Years

Douglas Chapnick, PhD
**Founder, CEO**
Former Senior Researcher
DARPA RTA Program
University of Colorado

Jeremy Jacobsen, M.S.
**Dir. of Bioinformatics & Automation**
Former Bioinformatics Analyst & Mechanical Engineer
DARPA RTA Program
University of Colorado

Ted Kee
**Dir. of R&D**
Former Process Engineer at Genentech (Roche), KBI, AMGEN

Karen Foster
**Dir. of Operations**
Entrepreneur and Former Operations Management in Climate Research, Construction Industry

Michael Stowell, PhD
**Scientific Advisory Board**
Entrepreneur
Protein Pharma Veteran
Current CSO AmideBio
Current University of Colorado Professor

Michael Minson, PhD
**Synthetic Biology Scientist**
Former Scientist at ArcherDX/Invitae and Sartorius

## Inventing Our Evolution in a Microscope Technology

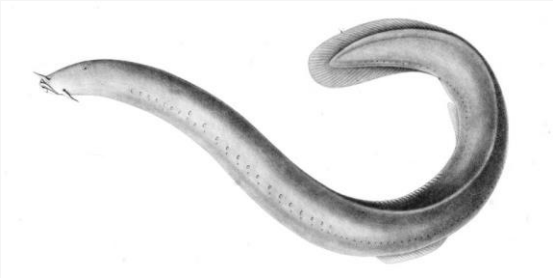
**2019**

- **Pre-Seed Financing**
- **Grant**
- **Seed Financing**

# Our Company's Mission is To Harness The Power of Evolution To Save Lives

## *It Took 300M Years For Nature To Develop Todays Insulin*

### Ancestral Insulin
(From Hagfish)
Little to No Therapeutic Value



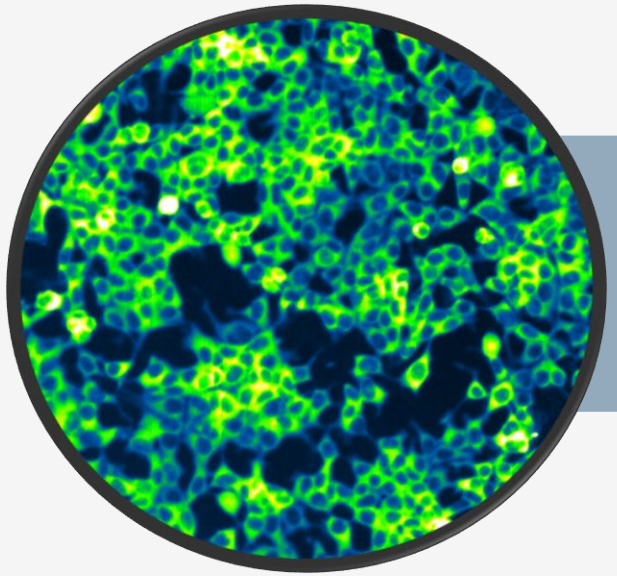
**Evolution**
20 Amino Acid Mutations (3)

### Human Insulin
Therapeutic for 463M Diabetics in the World (1)
Drives a $60B Industry (2)

(1) IDF Diabetes Atlas 9th edition 2019 (Diabetesatlas.org)
(2) Insulin Market Report 2020 (Research & Markets)
(3) Shu Jin Chan, Donald F. Steiner, Insulin Through the Ages: Phylogeny of a Growth Promoting and Metabolic Regulatory Hormone, *American Zoologist*, Volume 40, Issue 2, April 2000, Pages 213–222

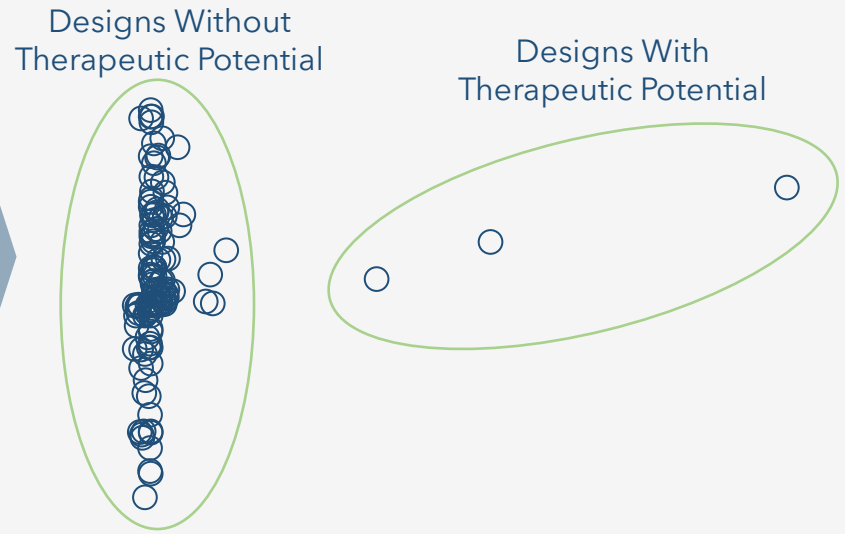
# Our Evolution in a Microscope Tech Shrinks Millions of Years of Evolution to Weeks

Arrays of Biosensor Cells Each Expressing a Unique Protein Design



***Testing Millions of Variant Protein Activities in Hours***

Searching For Rare Designs

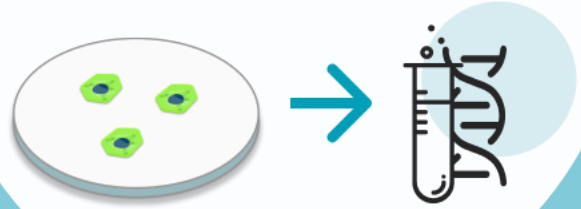


# Evolution in a Microscope Has 3 Steps

**Encode Each Design into Biosensing Human Cells**

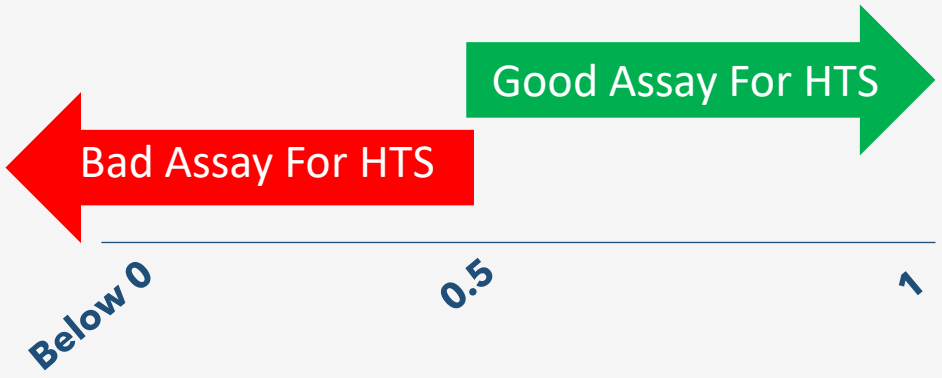
**Measure The Activity of Each Design in Each Cell**

**Isolate and Sequence Winning Designs**



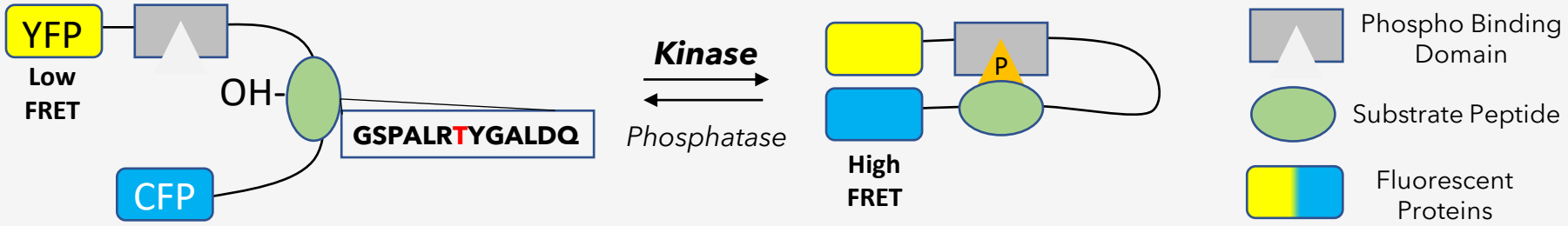
# We Evolve Drug Discovery Assays Because Most Existing Assays Are Not High Throughput Screening (HTS) Suitable

$$Z' = 1 - \frac{3(\theta_p + \theta_n)}{|\mu_p - \mu_n|}$$



# Example Using Evolution in a Microscope to Build An ERK Kinase Biosensor

## *Our Prototype FRET Biosensor For Kinases*




## *The Advantages of FRET Biosensors*

- Ratiometric (Less Artifacts)
- Non-Destructive (Smaller Sample Size and More Data)
- Genetically Encoded (Less Sample Prep)

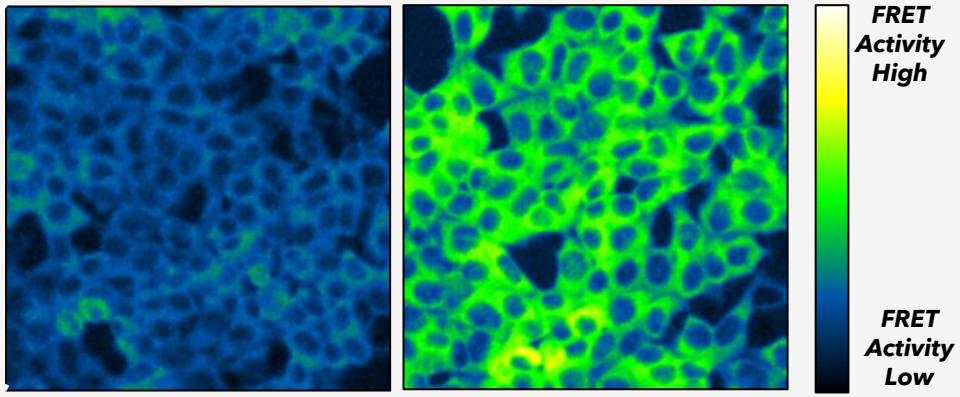
Capra et al. Cancer Research. 2006

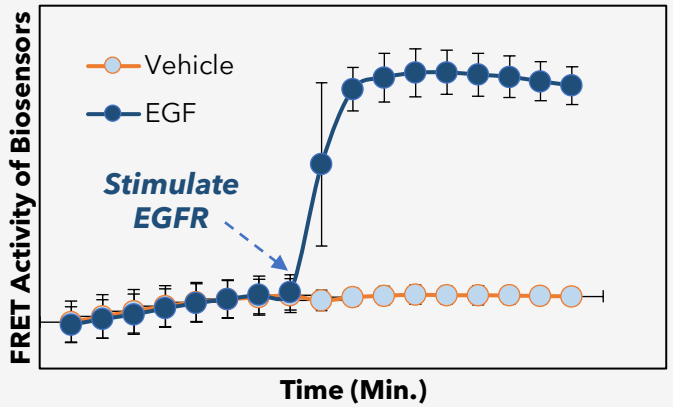
# With A Good FRET Biosensor....
# We Can Screen up to 100,000 Drugs a Day

***1,536 Tests/10 min***

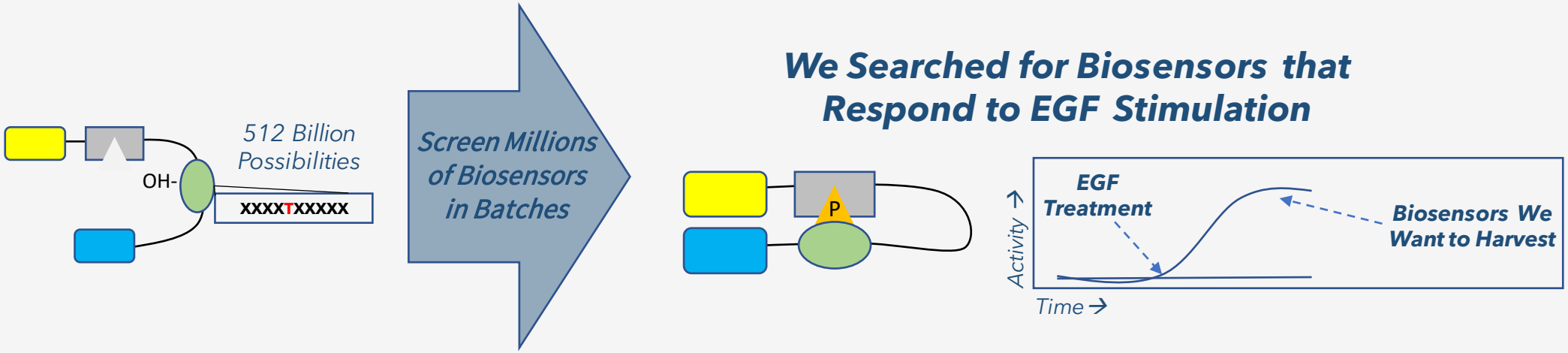
***Cells Without Stimulation***

***Cells With EGFR Stimulation***



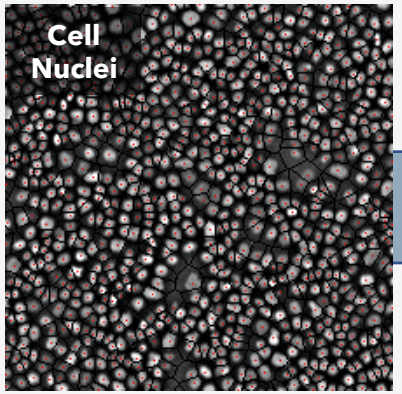



# Our Synthetic Biology Approach to Evolve a FRET Biosensor For ERK (Oncology Drug Screening Tool)

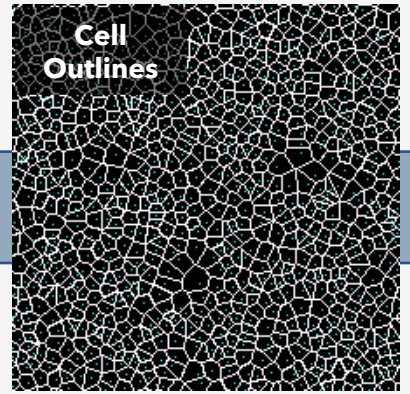


# *Measuring Biosensor Activity in Each Cell Simultaneously*

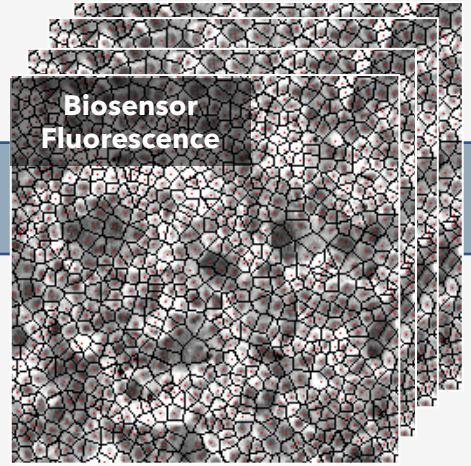
**ML To Find & Track Every Cell**



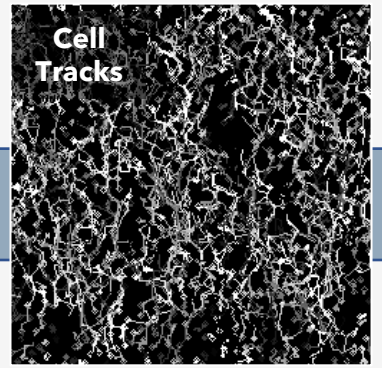

**ML + Heuristics To Outline Every Cell**




**Segment Cells to Measure Biosensor Activity at Each Time**

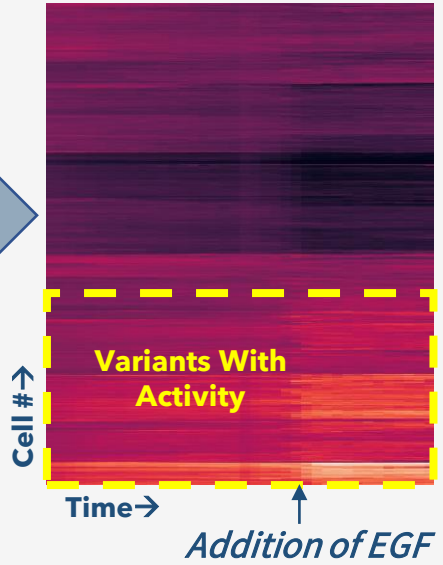



**Track Cells in Time**



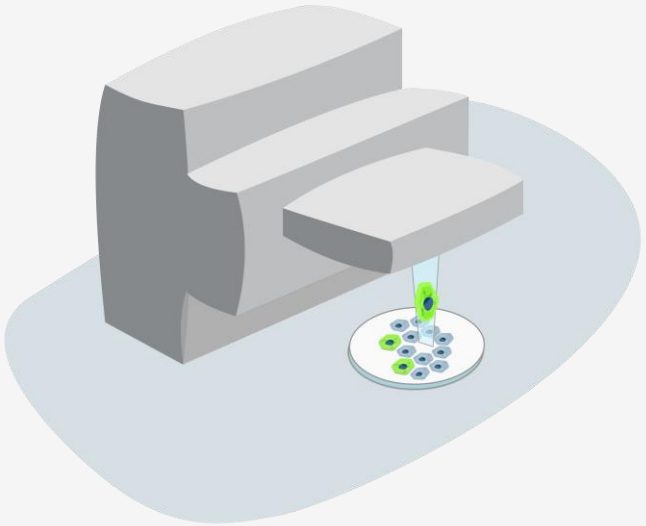

*Output*

**ML to Find Rare Variants Via Behavior**

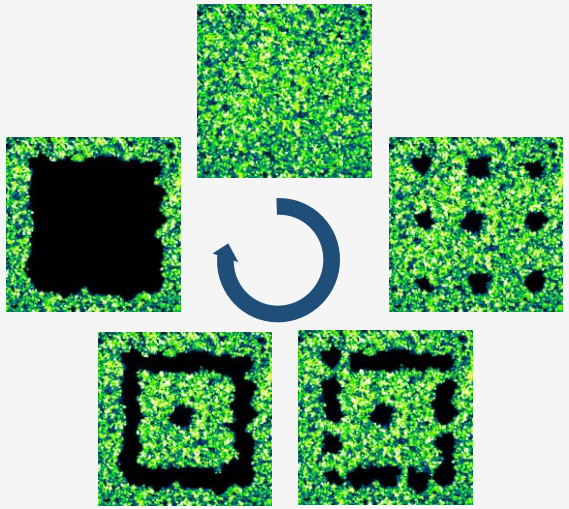


# Our Unique Hardware Plucks Rare Live Cells, Enabling Us to Go Beyond The Limitations of Multi-well Formats

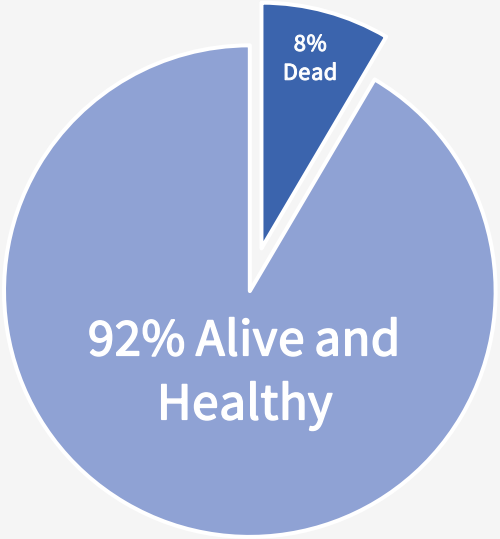
## Our Proprietary Cell Picking Hardware



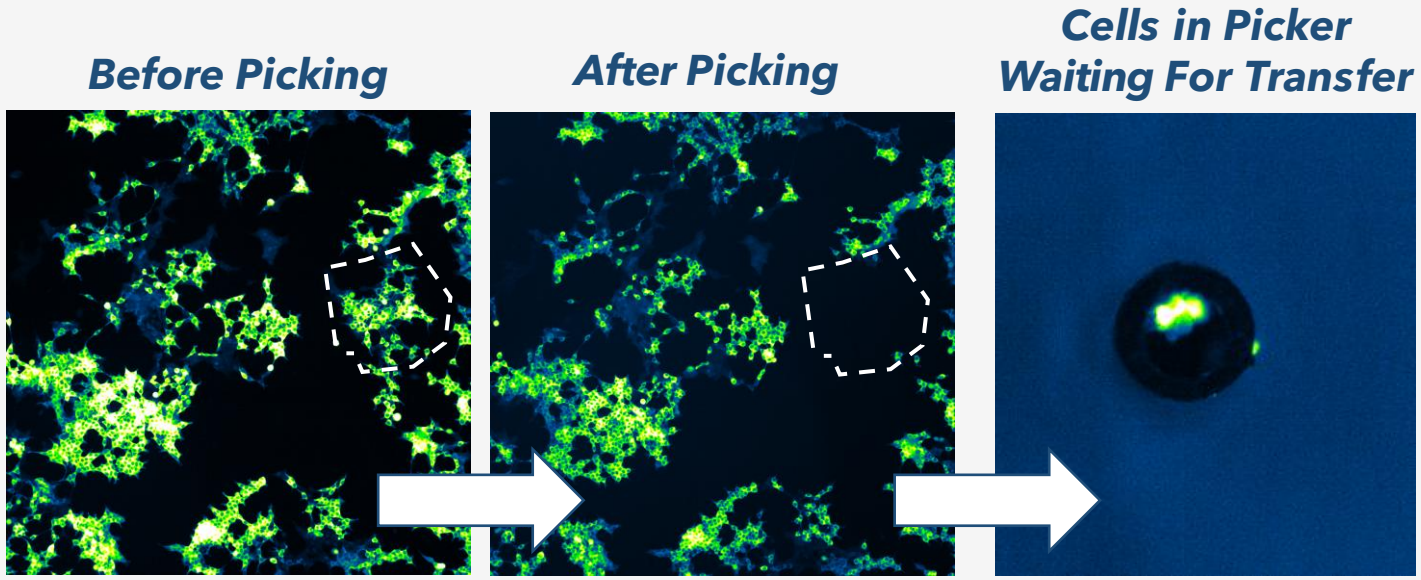
## Enables Precise Control of Target Cell Removal



## Without Killing Cells

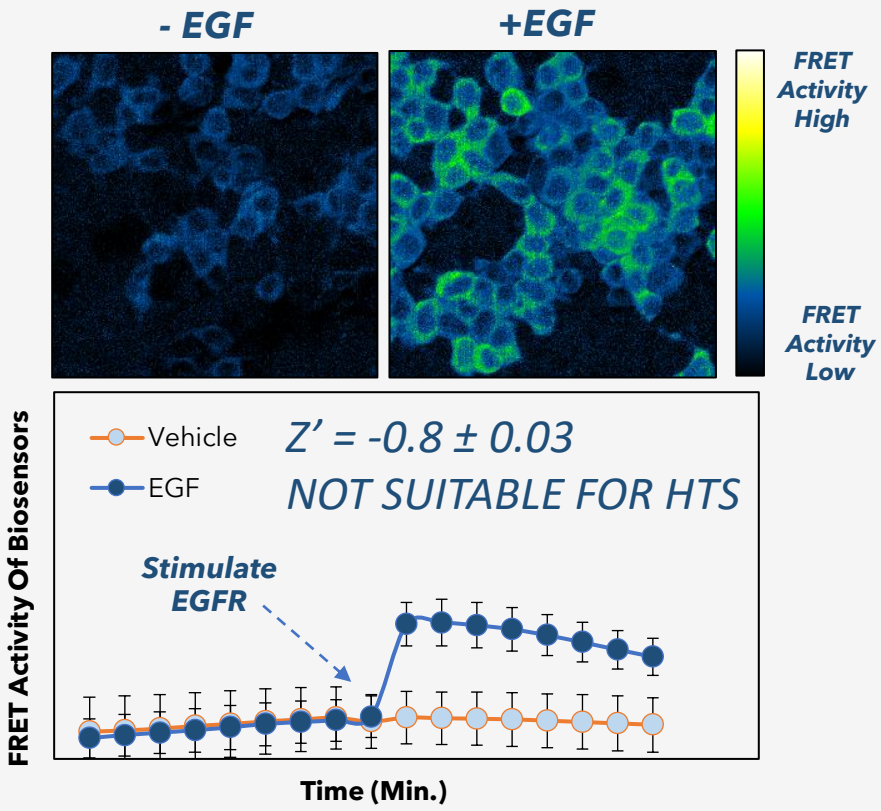


# Picking Mimics Natural Selection

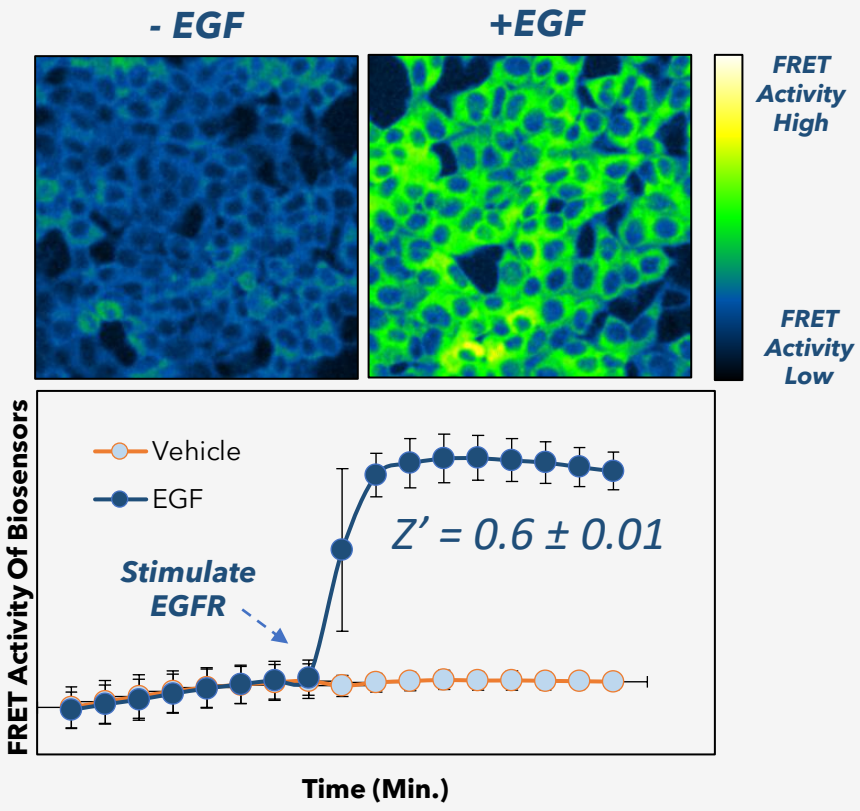


# The Assays That We Evolve Are Superior High Throughput Screening Tools With Z'>0.5

## State of The Art ERK Biosensor (1)

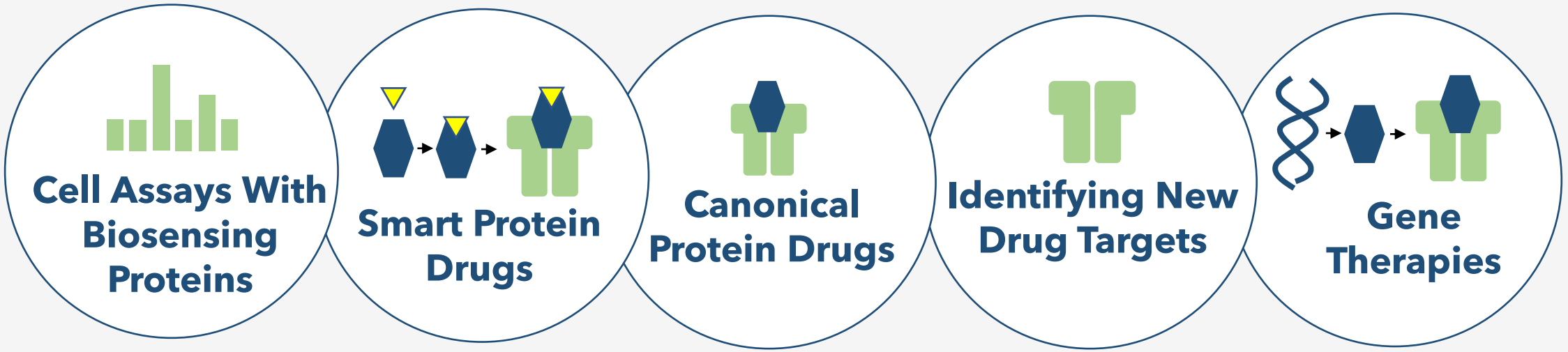



## Our Evolved ERK Biosensor




(1) Aoki K, Kondo Y, Naoki H, Hiratsuka T, Itoh RE, Matsuda M. Propagating Wave of ERK Activation Orients Collective Cell Migration. Dev Cell. 2017

# Evolution in a Microscope Can Be Applied to Many Steps of Pharma Developmental



# Our Tech Is Well Equipped to Make an Impact For KAND Therapy

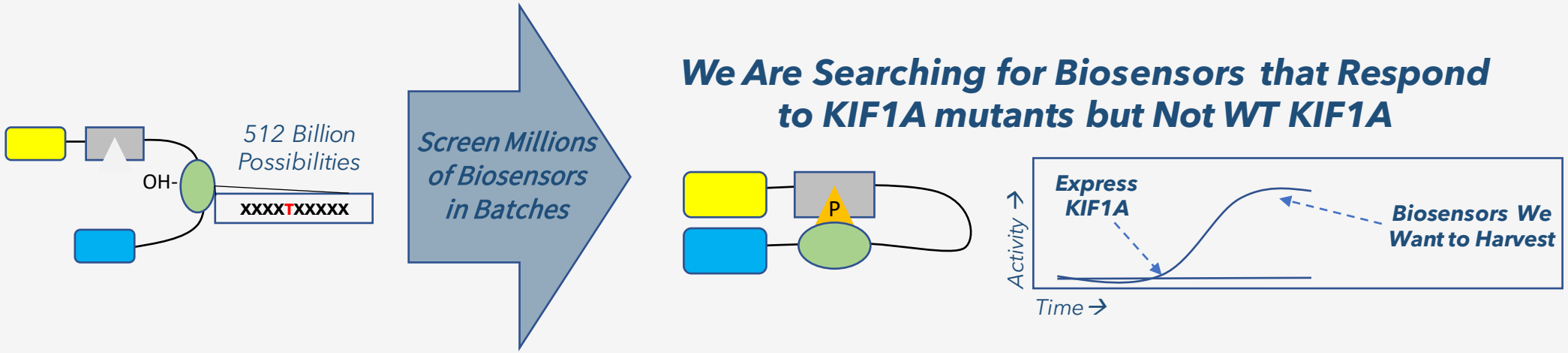
***KAND***

- No High Throughput Assays
- Limited Mechanistic Understanding
- No Drug Targets Beyond KIF1A

***Our Tech***

- Builds High Throughput Assays Quickly
- Does Not Require Substantial Mechanistic Understanding
- Has the Potential to Identify Drug Targets

# Our Synthetic Biology Approach to Evolve a mutKIF1a Biosensor



# Current Status

***Biosensor Cell Library Constructed in Both HEK293T and SKNBE2 Cell Lines***
***100% Complete***

***Introduce Inducible KIF1A to Biosensor Cell Libraries***
***30% Complete***

***Isolated & Sequence KIF1A effector Biosensors***

***Filter Biosensor Candidates to Those That Do Not Respond to WT KIF1A Expression***

# How You Can Help This Project

**Donate** to KIF1A.ORG to Enable Us to Grow the Team For The Project

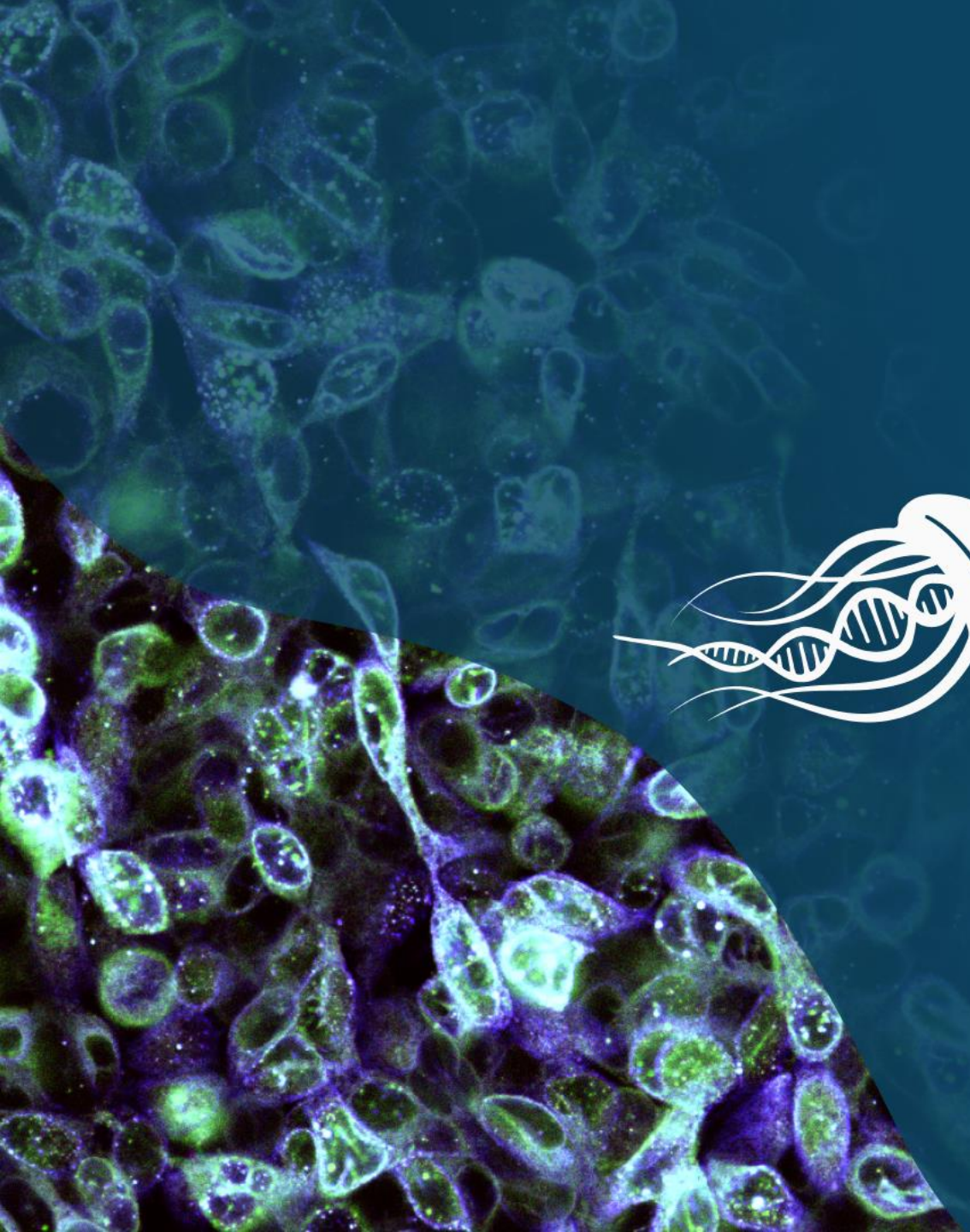
**Partner With Us to Screen Small Molecules**
Contact Dougchapnick@BioLoomics.Com

**Partner With Us If You Are Interested In Confirming Our Assay** With Your Drugs/Assays/Mouse Models

**Follow Us & Spread the Word** By Sharing Our Mission Via Social Media LinkedIn, FB, Instagram @BioLoomics,Inc. ,

*Special Thanks To The Organizers of The KAND Conference!!!*

# Protein Evolution in a Microscope To Advance KAND Therapies



BioLoomics

Doug Chapnick, PhD
Founder & CEO
DougChapnick@BioLoomics.com