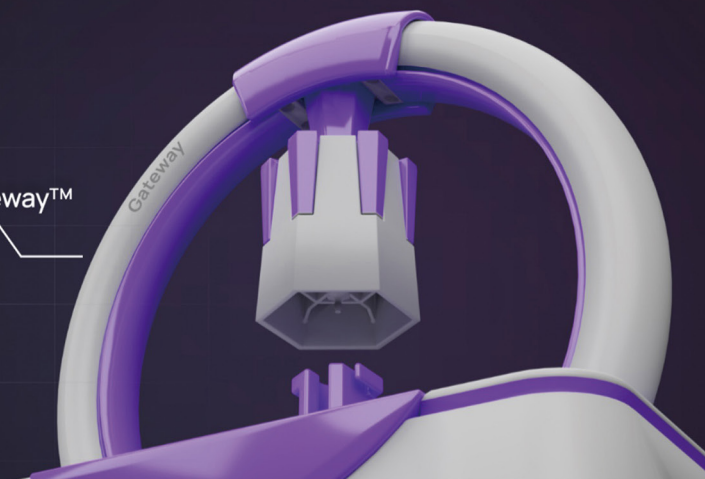# PORTAL

Don't Transfect, Just Deliver!

Multi-Cargo. High Viability. Better Delivery.

Gateway™

Gateway

Mechanical Delivery with Proprietary Portal™ Technology

Proprietary Membrane Technology

Deliver >10M cells / second

Flexible Buffer and Prep Requirements

Single Use Booster™ Consumables

Broad Compatibility

DELIVERY MATERIALS		VALIDATED CELL TYPES	
mRNA, siRNA, saRNA	Polymers	PBMCs	T cells
Proteins & Peptides	Nanoparticles	B cells	Monocytes
CRISPR RNPs	Antibodies	NK cells	HSCs
Small Molecules	Viruses	iPSCs	HeLa
Carbon Nanotubes	Labeling Molecules	RBCs	HEK

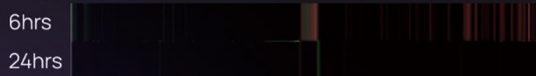
Conserve Cell Function

Cells exposed to electroporation misregulate gene expression

T cells: misregulated genes (>2-fold change, p<.05)

6hrs
24hrs

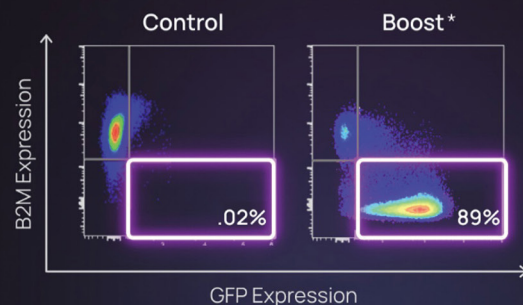Cells exposed to mechanoporation are more similar to controls

T cells: misregulated genes (>2-fold change, p<.05)

6hrs
24hrs

DiTommaso, T et al. 2018. PNAS. PMID: 30381459.

Robust Multiplex Delivery

Mechanical Delivery Enables Simultaneous Delivery of 3 Cargoes to Primary Human T Cells

T cells

$+$

CRISPR RNP, mRNA, Dextran

Control

Boost*

B2M Expression

.02%

89%

GFP Expression

*Triple positive delivery efficiency of 85%. Dextran data not shown.

PORTAL

Explore New Worlds!

Novel intracellular assays with impermeable molecules and probes.

Galaxy™

GALAXY

Mechanical Delivery with Proprietary Portal™ Technology

Proprietary Membrane Technology

Deliver >10M cells / second

**Flexible Buffer and Prep Requirements**

Compatible with Various Liquid Handlers

Broad Compatibility

DELIVERY MATERIALS

- mRNA, siRNA, saRNA
- Proteins & Peptides
- CRISPR RNPs
- Small Molecules
- Assay reagents
- Polymers
- Nanoparticles
- Antibodies
- Viruses
- Components

VALIDATED CELL TYPES

- PBMCs
- B cells
- NK cells
- iPSCs
- RBCs
- T cells
- Monocytes
- HSCs
- HeLa
- HEK

Delivering Brand P's LgBiT Reagents for Intracellular Protein Detection

Brand P

- Endogenous protein with HiBiT
- Portal LgBiT delivery for luminescence
- Degradation removes signal
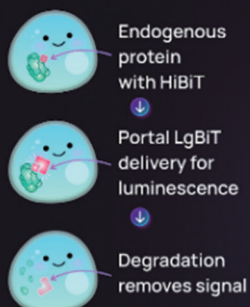
- Successful delivery of LgBiT protein demonstrating potential for intracellular measurements of protein levels
- Addition of degraders demonstrates reduction in protein signal from live cell assays
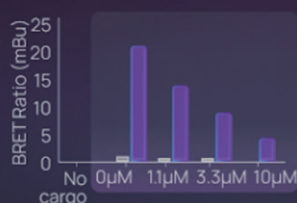
Relative Luminescence, 24h PROTAC Treatment

LC-2

Luminescence (Relative to 0 µM): 100, 80, 60, 40, 20, 0

Untreated, No Boost, No Cargo, 0 µM, 1 µM, 5 µM, 10 µM
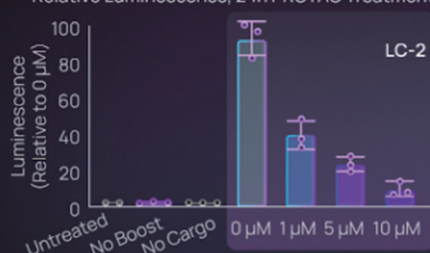
Delivering Brand P Reagents for NanoBRET Intracellular Target Engagement Assays

- HeLa cells transfected with NanoLuc-Src construct were treated with Src kinase inhibitors (Ponatinib or Bosutinib)
- Impermeable kinase tracer was mechanoporated into the cells
- Decrease in BRET ratio demonstrates reduction in intracellular kinase activity following inhibition

Ponatinib-treated NanoLuc-Src cells
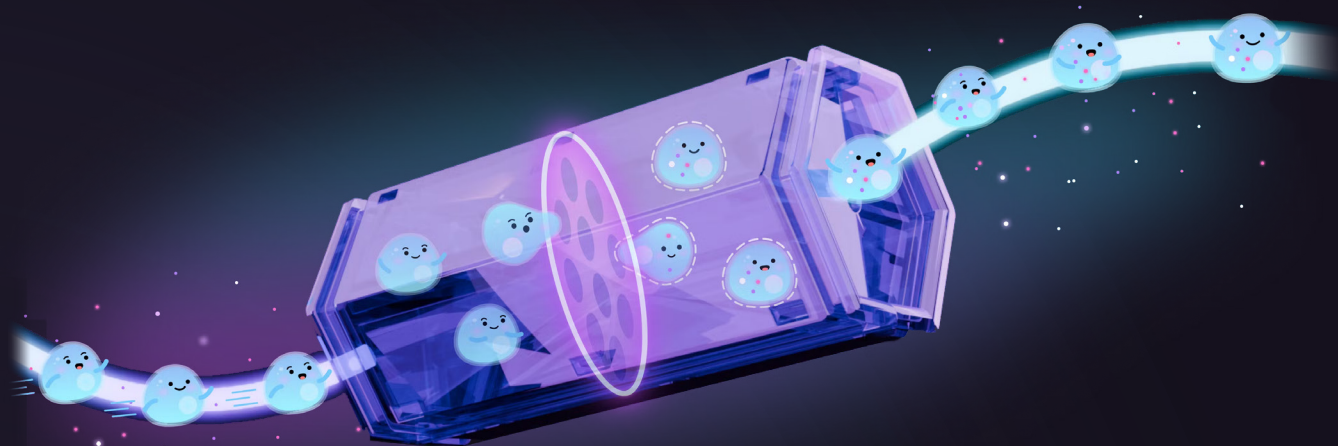
BRET Ratio (mBu): 25, 20, 15, 10, 5, 0

No cargo, 0µM, 1.1µM, 3.3µM, 10µM

Bosutinib-treated NanoLuc-Src cells

BRET Ratio (mBu): 25, 20, 15, 10, 5, 0

No cargo, 0µM, 1.1µM, 3.3µM, 10µM

• No Boost • Boost

PORTAL

Unleashing Cell Therapy's Clinical Potential

Portal's MilliBooster integrates with most manufacturing equipment

Portal's platform supports delivery with a diverse matrix of cell types and cargoes

Integrates with common GMP systems

Delivery materials

- mRNA, siRNA, saRNA
- Proteins & Peptides
- CRISPR RNPs
- Small Molecules
- Polymers
- Nanoparticles
- Antibodies
- Virus

Validated cell types

- PBMCs
- B cells
- iPSCs
- MSCs
- T cells
- NK cells
- Monocytes
- HSCs

Lovo — Brand F
Rotea — Brand T
and many more — JUST ASK!

Mixed PBMCs → Rotea + Clinical Scale MilliBooster → Dextran Expressing PBMCs

Viability of fresh PBMCs — % live cells (Control, Beginning, End)

Delivery to fresh PBMCs — % Dextran + live cells (Control, Beginning, End)

Mixed PBMCs delivered with fluorescently labeled dextran polymer using Portal's clinical scale MilliBooster integrated with Brand T's Rotea demonstrated >80% viability and >80% dextran delivery

(A) Unstimulated T Cells → RNP → Boost B2M RNPs with Gateway → via → Activate and expand Edited T Cells → Boost GFP mRNA with Lovo + Clinical Scale MilliBooster → via → Brand P → RNA expressing and Edited T Cells
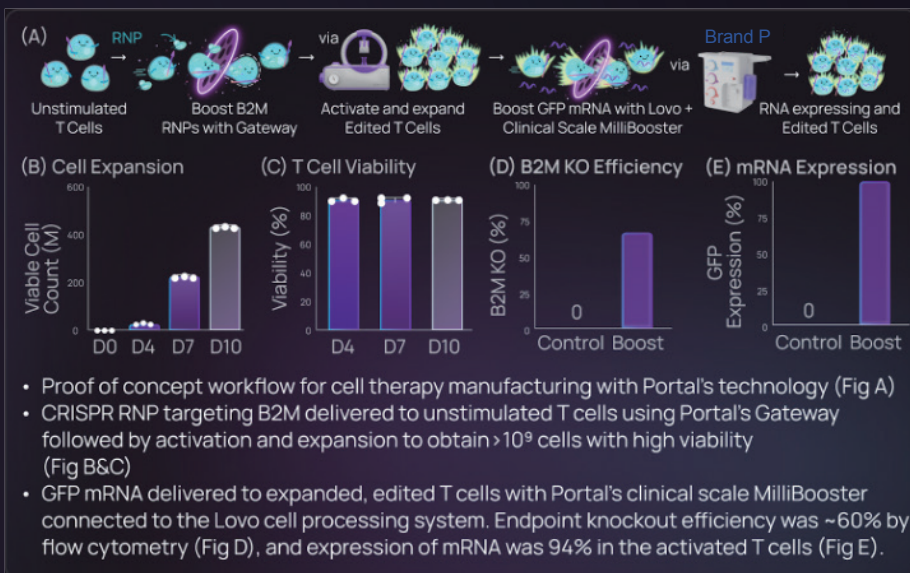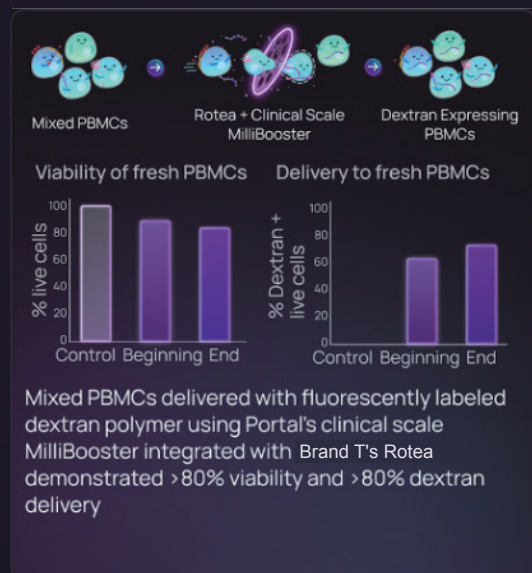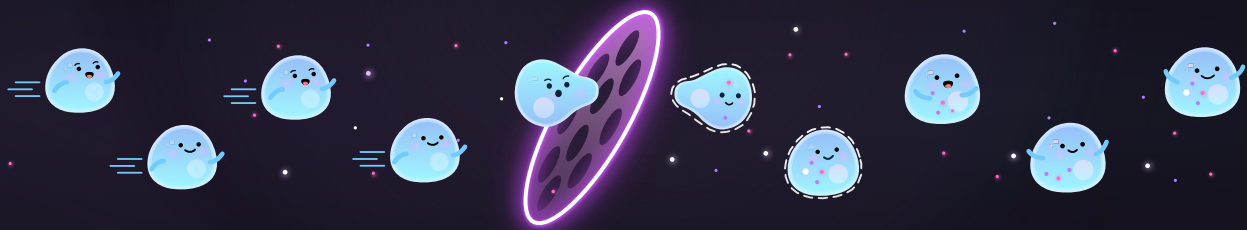
(B) Cell Expansion — Viable Cell Count (M): D0, D4, D7, D10

(C) T Cell Viability — Viability (%): D4, D7, D10

(D) B2M KO Efficiency — B2M KO (%): Control, Boost

(E) mRNA Expression — GFP Expression (%): Control, Boost

- Proof of concept workflow for cell therapy manufacturing with Portal's technology (Fig A)
- CRISPR RNP targeting B2M delivered to unstimulated T cells using Portal's Gateway followed by activation and expansion to obtain >10^9 cells with high viability (Fig B&C)
- GFP mRNA delivered to expanded, edited T cells with Portal's clinical scale MilliBooster connected to the Lovo cell processing system. Endpoint knockout efficiency was ~60% by flow cytometry (Fig D), and expression of mRNA was 94% in the activated T cells (Fig E).

PORTAL

Powered by Portal

R&D Scale

High Throughput Integrations

Clinical Scale Integrations