Montana Molecular

Fluorescent Biosensors for Live Cell Discovery

Elevate Your Research with the highest in data quality

- **Kinetic Readouts**
- **Multiplex Measurements**
- **Easy Handling**
- **Efficient, Consistent Viral Delivery**
- **Genetic Targeting**

- CELL STRESS & TOXICITY
- GPCR BIOLOGY
- DRUG DISCOVERY & SCREENING
- PDE BIOLOGY
- CELL SIGNALING ASSAYS
- CUSTOM PACKAGING IN VIRAL VECTORS

"The best thing about Montana Molecular's biosensors has been the ease of use."

Vladlen Z Slepak, PhD
University of Miami School of Medicine

"We've been very happy with the downward cADDis cAMP indicator from Montana Molecular, which we've used in a variety of airway cell lines as well as primary human macrophages and exocrine gland acinar cells. The transfection efficiency of the BacMam is excellent in hard-to-transfect cell lines ... "

Robert J. Lee

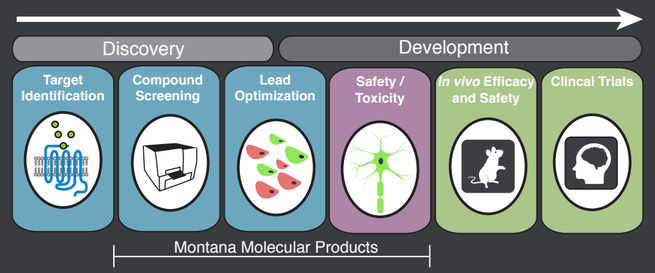
Assistant Professor of Otorhinolaryngology and Physiology, University of Pennsylvania Perelman School of Medicine

Our Technology

Fluorescent Biosensors for Live Cell Discovery

Montana Molecular's genetically-encoded fluorescent biosensor technologies produce direct, real time measurements of signaling activity in living cells. Our products are used in academic research and pharmaceutical development to monitor biological activity in primary cultures, iPSC-derived cells and standard cell lines. Each biosensor is optimized for high signal-to-noise with a single bright fluorescent protein that produces large changes in fluorescence intensity. Single fluorescent protein sensors are easy to detect on automated fluorescent plate readers or imaging systems and can be multiplexed too.

Live Cell Assays in Drug Development

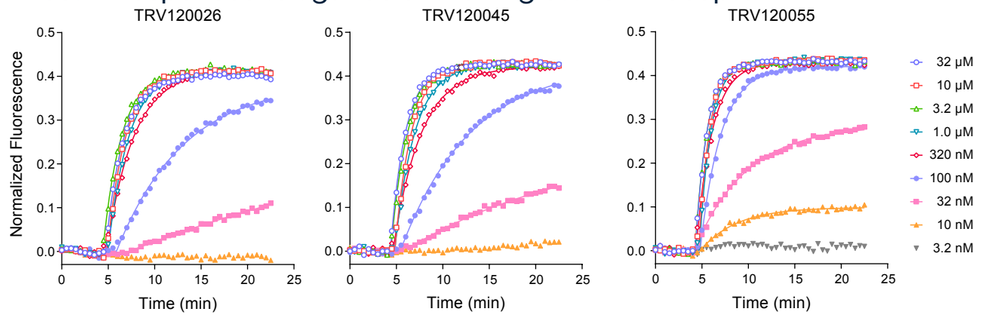


Unique Advantages

+ Ability to monitor cell signals in real time in any cell type with high S/N.
+ Multiplexing single red and green biosensors to detect simultaneous pathways.
+ High quality, real time data simplifies kinetic analysis of signaling bias.
+ Cost effective and biologically relevant information for SAR.
+ No need to FRET or BRET

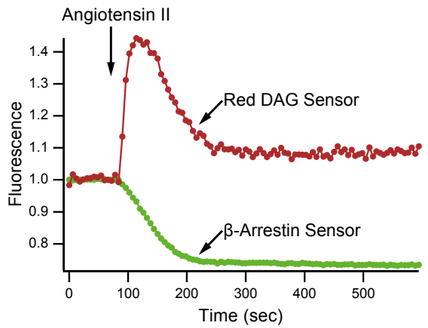
Real Time Data & Kinetic Analysis

Arrestin Responses to ligands of the Angiotensin Receptor



Establish a dose curve for each concentration in a single well to establish effective dosing. Multiplex red and green sensors to report simultaneous changes in multiple second messengers in the same cell population. Unambiguously indicate pathway selectivity to enable better predictions of both efficacy, potency and off-target effects.

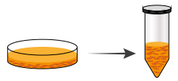
+ **GPCR**
+ **Ligand Bias**
+ **Phosphodiesterases**
+ **Cell stress and toxicity**
+ **Optogenetics**



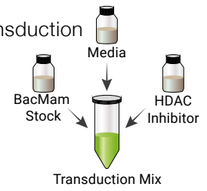
simple protocol steps

Day 1: Transduce and Plate Cells

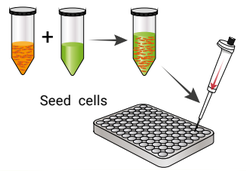
Step 1
Prepare Cells



Step 2
Prepare Viral Transduction Reaction

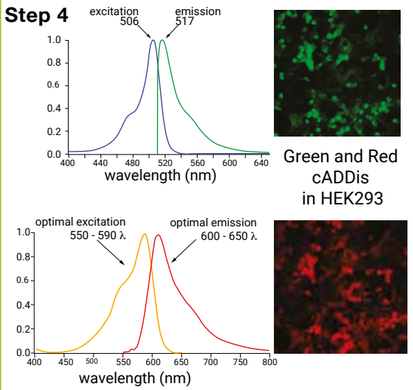


Step 3
Mix Cells and Transduction Mix



Day 2: Measure Fluorescence

Step 4

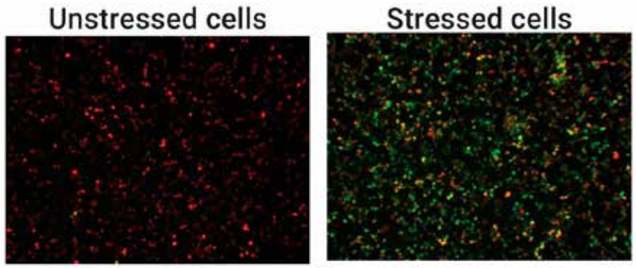


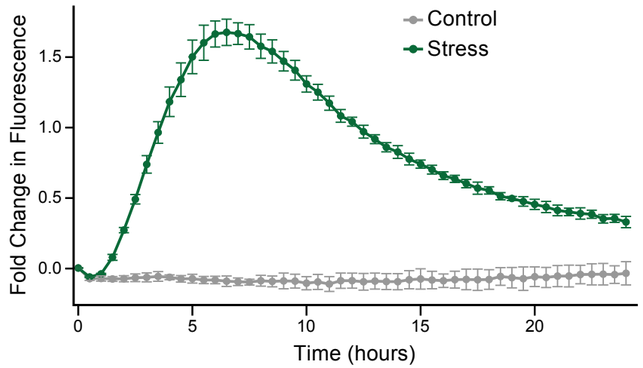
Reversible Assay for Cell Stress & Toxicty

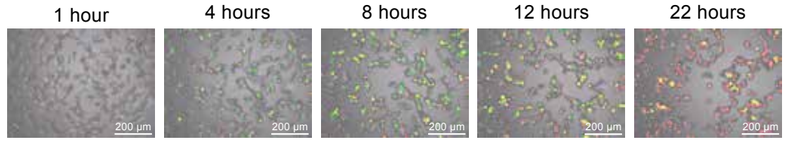
The Cell Stress Assay produces a bright green fluorescent protein when the cell endures endoplasmic reticulum (ER) stress or undergoes the unfolded protein response (UPR). This robust assay can be detected on standard fluorescence plate readers or imaging systems.

+ Discover a bright fluorescent assay for detecting ER-mediated stress and the UPR.
+ Reveal disrupted signals that underlie neurotoxicity and neurodegeneration.
+ Identify compounds that reverse cell stress.

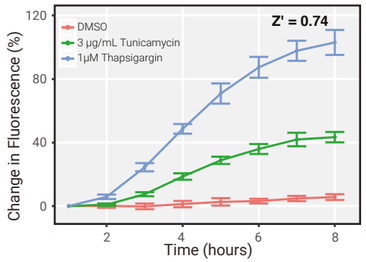
2-COLOR RATIOMETRIC STRESS ASSAY





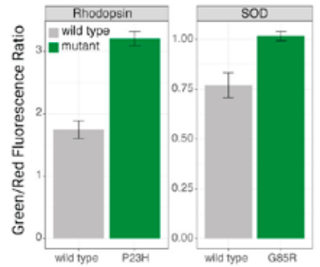


DETECTING CHEMICAL STRESS



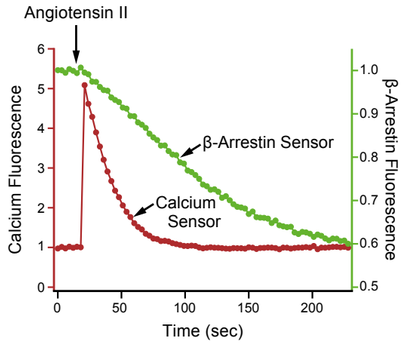
HEK293T cells expressing the cell stress sensor were treated with either the antibiotic tunicamycin or the SERCA pump inhibitor thapsigargin. Data were collected beginning after one hour to allow fluorescence to stablize after drug addition.

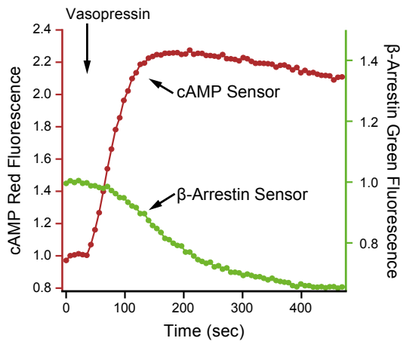
DETECTING GENETIC STRESS



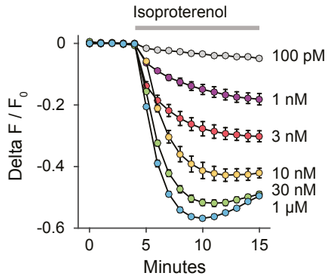
HEK293T cells expressing the cell stress sensor and either the wild type (WT) or a mutant version of rhodopsin or superoxide dismutase (SOD). Each disease mutant protein is a known mutation resulting in misfolded or aggregated protein. Rhodopsin P23H results in Retinitis Pigmentosa, and SOD G85R results in ALS. Cells anlyzed after 18 hours of expression.

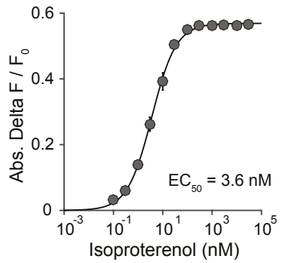
Monitor arrestin and G-protein pathways simultaneously

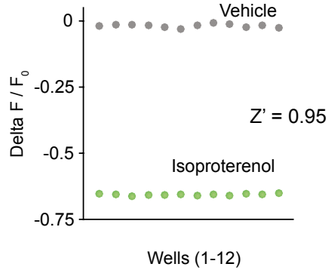




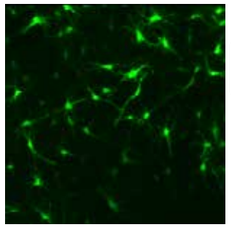
Unprecedented signal-to-noise



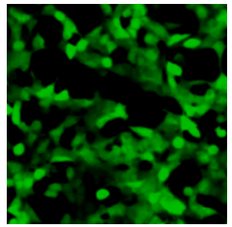




Directly measure drug responses in any cell type



iPSC-derived neurons



HEK 293

Detect robust fluorescence on a plate reader or imaging system

+ Molecular Devices FLIPR and Flexstation
+ Biotek Synergy MX
+ BioTek Cytation and Lionheart
+ BMG CLARIOstar and PheraStar
+ Tecan Infinite 500
+ Hamamatsu FDSS
+ Epifluorescence microscopes

Montana Molecular

Scientific Publications

T.A. Baldwin, et al. Insights into the Regulatory Properties of Human Adenylyl Cyclase Type 9. **Molecular Pharmacology, 2019**

X. Chen, et al. Phenylephrine, a common cold remedy active ingredient, suppresses uterine contractions through cAMP signalling. **Scientific Reports Aug. 2018.**

P. Tewson, et al. Assay for Detecting Gi-Mediated Decreases in cAMP in Living Cells. **SLAS. July 10, 2018.**

N. H. Wray, et al. NMDAR-independent, cAMP-dependent antidepressant actions of ketamine. **Molecular Psychiatry. April 2, 2018.**

T. Buranda, et al. A High-Throughput Flow Cytometry Screen Identifies Molecules that Inhibit Hantavirus Cell Entry. **SLAS Discovery. April 2, 2018.**

H. Zou, et al. PDE8: A Novel Target in Airway Smooth Muscle. **American Journal of Respiratory Cell and Molecular Biology. Vol. 58, No. 4. April 01 2018.**

T.B. Johnstone, et al. PDE8 is Expressed in Human Airway Smooth Muscle and Selectively Regulates cAMP Signaling by 2AR-AC6. **American Journal of Respiratory Cell and Molecular Biology. Dec. 2017.**

T.Togo. Cell membrane disruption stimulates cAMP and Ca2+ signaling to potentiate cell membrane resealing in neighboring cells. **Biology Open. November 1, 2017.**

K.A. McCrink, et al. -Arrestin2 Improves Post-Myocardial Infarction Heart Failure via Sarco(endo)plasmic Reticulum Ca2+-ATPase-Dependent Positive Inotropy in Cardiomyocytes. **Hypertension. Nov. 2017.**

H. Ohno, et al. Dynamics of Presynaptic Diacylglycerol in a Sensory Neuron Encode Differences between Past and Current Stimulus Intensity. **Cell Reports, Vol. 20, Issue 10. Sept. 2017.**

L.Liu, et al. Gq sensitizes TRPM8 to inhibition by PI(4,5)P2 depletion upon receptor activation. **BioRxiv. Sept. 2018.**

Q. Wang, et al. Regulator of G protein signaling G5-R7 is a crucial activator of muscarinic M3 receptor-stimulated insulin secretion. **FASEB J. Jul. 7,2017.**

SLAS 2019 Events

Q & A with Sam Hoare—Pharmechanics
Mon. Feb 4, 1:00 - 1:15 Booth #1548

Exhibitor Tutorial
Dual channel kinetic assays for detecting ligand bias at GPCRs
Tues. Feb 5, 9:30 - 10:15 Room 152A
Kevin Harlen—Principal Investigator, Montana Molecular
Anne Marie Quinn—CEO, Montana Molecular
Carl Peters—Senior Applications Scientist, BMG Labtech

BioTek Poster Presentation
Monitoring cellular stress response and inhibition of GPCR-dependent calcium signaling using kinetic imaging and expressed biosensors
Tues. Feb 5, 5:00 - 6:00 #1128-D
Peter Banks—Scientific Director, BioTek Instruments

Podium Presentation
Cell Stress Biosensors for Rapid, Live-Cell Detection of Neurotoxic and Cardiotoxic Compounds in iPSC-Derived Neurons and Cardiomyocytes
Wed. Feb 6, 10 - 10:30 Room 145AB
Kevin Harlen—Principal Investigator, Montana Molecular

Pharmechanics Poster Presentation
Measuring biased agonism with a kinetic analysis platform for real time data from fluorescent biosensors
Tues. Feb 5, 5:00 - 6:00 #1218-D
Sam Hoare—CEO, Pharmechanics