SYGNATURE DISCOVERY

CASE STUDY

Mitochondrial Function

Real World Data for Decision Makers in the CNS Diseases Space

INTRODUCTION

Mitochondria are vital organelles responsible for energy production within cells, with the brain being particularly dependent on this energy supply due to its high metabolic demands. Any disruption in energy production can result in damage or dysfunction in brain cells, underscoring the significance of modulating mitochondrial function in addressing neurodegenerative disorders.

Supporting Your Research

At Sygnature Discovery, we offer unparalleled expertise and specialized services in mitochondrial research, equipping researchers with cutting-edge tools to explore the therapeutic potential of targeting mitochondria.

Our extensive suite of mitochondrial function assays and advanced technologies is meticulously designed to cater to diverse research objectives precisely and efficiently. We provide a wide array of plate types and sizes and various readout methods and leverage various platforms to accommodate different experimental formats. With our innovative technologies and seasoned team of experts, we deliver comprehensive support for drug discovery initiatives targeting mitochondrial function.

Mitochondrial Dysfunction Platform

Our Mitochondrial Dysfunction Platform is equipped with a range of resources to facilitate your research needs:

Off-the-Shelf Reagents

We provide readily available reagents essential for mitochondrial function assays, ensuring convenience and efficiency in your experiments.

Cutting-Edge Technologies

Our platform integrates state-of-the-art technologies to enable precise and accurate measurements of mitochondrial function, allowing for in-depth analysis and interpretation of results.

Fluorescence-based Medium and High-Throughput Screening

Leveraging fluorescence-based screening methods, we offer both medium and high-throughput capabilities to accommodate various experimental scales, allowing for rapid screening of potential drug candidates targeting mitochondrial dysfunction.

Downstream Assay Cascades/Orthogonal Assays

In addition to primary screening, our platform supports downstream assay cascades and orthogonal assays to validate findings and ensure robustness of results. Examples include Seahorse, King Fisher, Echo platforms, Bio-Rad CFX, and Applied RT-PCR machines.

By harnessing these tools and technologies, our Mitochondrial Dysfunction Platform empowers researchers to gain comprehensive insights into mitochondrial function and its implications in disease pathology, facilitating the development of novel therapeutic interventions for neurodegenerative disorders and beyond.

Methods

- **Fluorescence and Luminescence Plate-Based Assays:** These assays are conducted using Envision® or Pherastar® plate readers, allowing for accurate and sensitive measurements of fluorescence and luminescence signals.
- **High Content Imaging Platforms:** Incucyte® and ImageXpress® are employed for quantifying fluorescence readouts of specific probes, enabling detailed analysis of cellular processes at the single-cell level.
- **Kinetics Experiments:** Kinetics experiments utilize Pherastar® plate readers to monitor dynamic changes over time, providing insights into temporal aspects of mitochondrial function and drug effects.

- **mRNA Extraction and RT-PCR:** RNA extraction and Real-Time PCR (RT-PCR) are performed using King Fisher®, Echo platforms, Bio-Rad CFX, and Applied RT-PCR machines, facilitating the analysis of gene expression profiles related to mitochondrial function.
- **Quality Control (QC) Conditions:** QC measures include the use of internal reference controls such as Staurosporin (STS), Carbonyl cyanide-p-trifluoromethoxy phenylhydrazone (FCCP), Hydrogen Peroxide (H2O2), or Digitonin, tailored to the specific experimental requirements. Additionally, standardized mitochondrial modulators (Figure 1) are available to ensure experiment consistency. By employing a diverse array of modulators with known mechanisms, researchers can precisely manipulate mitochondrial function to elucidate specific pathways involved in neurodegenerative disorders and evaluate the efficacy of potential therapeutic interventions.
- **Data Analysis:** Depending on the platform utilized for the experimental setup, data is analysed using various software tools. These include MARS Software, Bio-Rad CFX Maestro Software, MetaXpress Software, Wave Software, and Prism Version 9.0 (GraphPad), enabling robust statistical analysis and visualization of results.
- **Data Normalization:** Compound-induced changes are calculated by normalizing the findings from the agent of interest to the control (vehicle) group. Then, data is expressed as a percentage of the control group per day of experiments. In some assays, further normalization is performed relative to the total protein content or cell number, ensuring the accuracy and reliability of the results.

Mitochondrial Function Modulators

Modulators	MoA	[conc]
Rotenone (Rot)	Mitochondrial complex I inhibitor	Rot 200 nM Rot 1000 nM
Cyclosporin A (CSA)	Mitochondrial PTP inhibitor	CSA1: 1 µM CSAl: 10 µM
Mn(III)tetrakis(4-benzoic acid) porphyrin Chloride (MnTBAP; Mn)	Mitochondrial superoxide dismutase mimetic and superoxide scavenger	Mn1: 2 µM Mn2: 20 µM
N-Acetyl-L-cysteine (NAC)	Antioxidant and free radical scavenger	NAC1: 100 µM NAC2: 1 mM
Resveratrol (R)	Antioxidant and histone deacetylase modulator	R1: 250 nM R2: 500 nM
Ederavone (E)	Antioxidant	E1: 10 µM E2: 40 µM
Pioglitazone (P)	Selective PPARy agonist	P1: 1 µM P2: 10 µM

Figure 1

The table above lists and describes all modulators and concentrations standardized at Sygnature Discovery. These modulators serve as reference compounds to induce toxicity or protection in various models and against different insults. It's important to note that each modulator operates through distinct mechanisms of action, ensuring a comprehensive coverage of mitochondrial function and responses.

Assay Validation to Interrogate Mitochondrial Function

Understanding mitochondrial behaviour is paramount for advancing new treatments targeting age-related cognitive decline and neurodegenerative disorders. To achieve this, validating high-quality and robust assays capable of effectively interrogating mitochondrial function is crucial. With such assays and endpoints measured, researchers can obtain comprehensive insights into mitochondrial function, enabling the identification of novel therapeutic targets and the development of effective interventions for age-related cognitive decline and neurodegenerative disorders.

At Sygnature Discovery, various assays and endpoints are standardized, a critical measure for comprehensively evaluating mitochondrial function and health.

- Cellular toxicity
- ATP/ADP levels measurement
- NAD/NADH levels measurement
- Pyruvate/Lactate measurement
- Oxygen Consumption Rate
- Extracellular Acidification Rate
- Cytosolic calcium levels measurement
- Mitochondrial membrane potential measurement
- General oxidative stress levels measurement
- Mitochondrial superoxide levels measurement
- Lipid Peroxidation levels measurement
- Mitochondrial fission/fusion levels evaluation
- Mitochondrial Biogenesis levels evaluation
- Mitophagy

Cellular toxicity

Mitochondrial toxicity, which refers to damaged or dysfunctional mitochondria, often leads to cellular toxicity, ultimately resulting in cell death. Cell death induced by mitochondrial toxicity can manifest through various mechanisms, including apoptosis, necrosis, or autophagy. Understanding the interplay between mitochondrial dysfunction and cellular toxicity is crucial for elucidating the pathogenesis of diseases and developing effective therapeutic interventions.

At Sygnature Discovery, we leverage commercially available and standardized Off-the-Shelf Reagents to assess cellular viability. Our comprehensive approach includes using the CytoTox-Glo™ Assays (Figure 2) and CellTiter-Glo™ Assay from Promega to evaluate cell viability. We also employ CellTox™ Green Assays from Promega to enhance our understanding of cellular health further. These readily available reagents enable us to conduct mitochondrial function assays efficiently and assess cell viability, ensuring convenience and accuracy in your experimental processes.

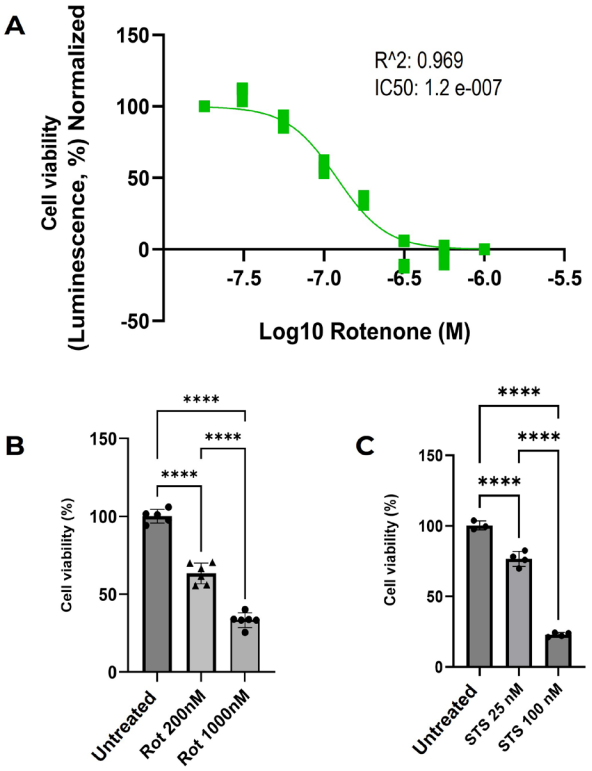


Figure 2

Cellular viability on Rotenone-treated SHSY5Y cells in the presence or absence of mitochondrial modulators. Cells were plated, and after 24 hrs were exposed to Rotenone (Rot) at different concentrations. As a positive control, neuroblastoma cell line was also treated w ith Staurosporin (STS) for 24 hrs at 25 nM and 100 nM. Data was expressed as a percentage of the control group. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant p<0.05; ****p<0.0001. It was also calculated de R^2 and IC50 for Rotenone using GraphPad software.

Measurement of metabolic-related energetic compounds

Because mitochondria's primary function is to generate the energy necessary for various cellular activities, we can monitor specific metabolites to infer the mitochondrial respiratory chain's efficiency and the cells' overall metabolic state. This information can be crucial for understanding disease mechanisms, especially in neurodegenerative diseases where mitochondrial dysfunction is a hallmark, and evaluating the potential efficacy of new therapeutic compounds targeting cellular metabolism.

The levels of several key energy-related metabolites can be measured to assess the bioenergetic health of cell cultures (Figures 3-5). These include:

- *ATP:* The direct source of energy for cellular processes. Its abundance gives us a snapshot of the cell's immediate energy supply.
- *NADH (Nicotinamide adenine dinucleotide):* A coenzyme that plays a critical role in energy production. It is a major electron donor in the production of ATP and serves as an indicator of oxidative stress and the metabolic state of the cell.
- *Pyruvate:* A key molecule in several metabolic pathways, but most notably, it marks the end product of glycolysis. In the presence of oxygen, pyruvate enters the mitochondria to be further processed for ATP production.
- *Lactate:* Typically produced from pyruvate under anaerobic conditions (when oxygen is limited). Lactate levels can indicate a shift in cellular metabolism, such as when cells rely on glycolysis instead of oxidative phosphorylation for energy production.

At Sygnature Discovery, we utilize commercially available and standardized Off-the-Shelf Reagents to measure and monitor changes in several energetic compounds (Figures 3-5). By employing these readily available reagents, we ensure convenience and efficiency in conducting mitochondrial function assays, thereby facilitating the progress of your experiments.

ATP and ADP Levels

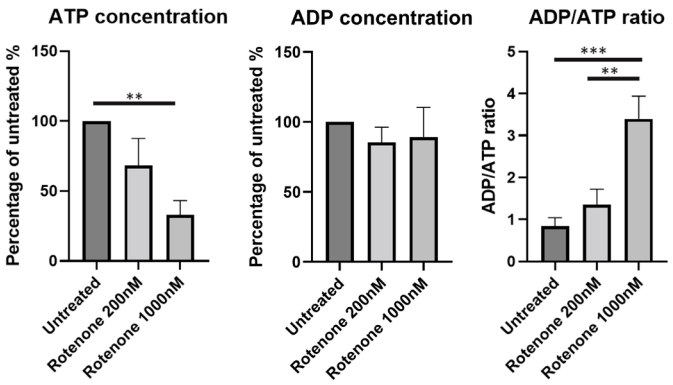


Figure 3

Representative bar graphics of ATP and ADP levels on Rotenone-treated SHSY5Y cells. Data was normalized to protein content, and it was expressed as a percentage of the control group. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant $p<0.05$; $^{**}p<0.01$, $^{***}p<0.001$.

NADH and NAD+ Levels

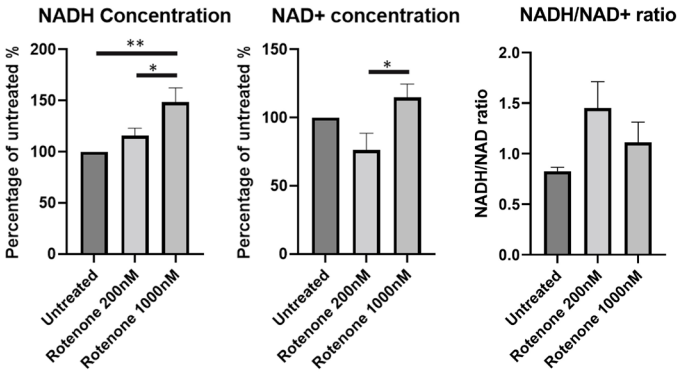


Figure 4

Representative bar graphics of NADH and NAD+ levels on Rotenone-treated SHSY5Y cells. Data was normalized to protein content, and it was expressed as a percentage of the control group. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant $p<0.05$; $^{*}p<0.05$, $^{**}p<0.01$.

Pyruvate and Lactate Levels

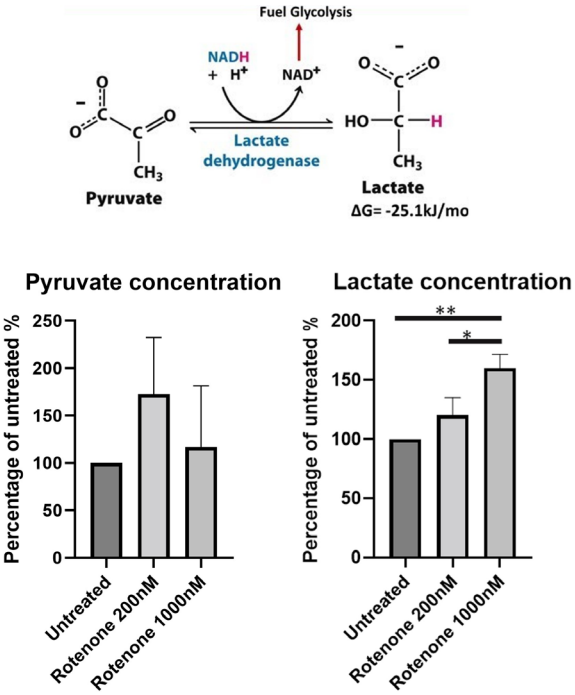


Figure 5

Representative bar graphics of Pyruvate and Lactate levels on Rotenone-treated SHSY5Y cells. Data was normalized to protein content, and it was expressed as a percentage of the control group. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant $p<0.05$; $^{*}p<0.05$, $^{**}p<0.01$.

Oxygen Consumption Rate and Metabolic status

Mitochondria produce ATP through a series of chemical reactions known as cellular respiration, which includes the electron transport chain. The efficiency of these processes is critical for maintaining cellular homeostasis that allows cells to live and function. Importantly, changes in mitochondrial membrane potential (MMP), calcium homeostasis, and oxidative stress are frequently associated with alterations in cellular respiration.

At Sygnature Discovery, oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) are measured using Seahorse XF Analyzers to evaluate mitochondrial respiration and glycolysis in real time, respectively. This platform allows the measurement of several mitochondrial respiration steps, namely basal respiration, maximum respiration, and spare respiratory capacity (Figure 6).

Seahorse Oxygen Consumption Rate (OCR) analysis

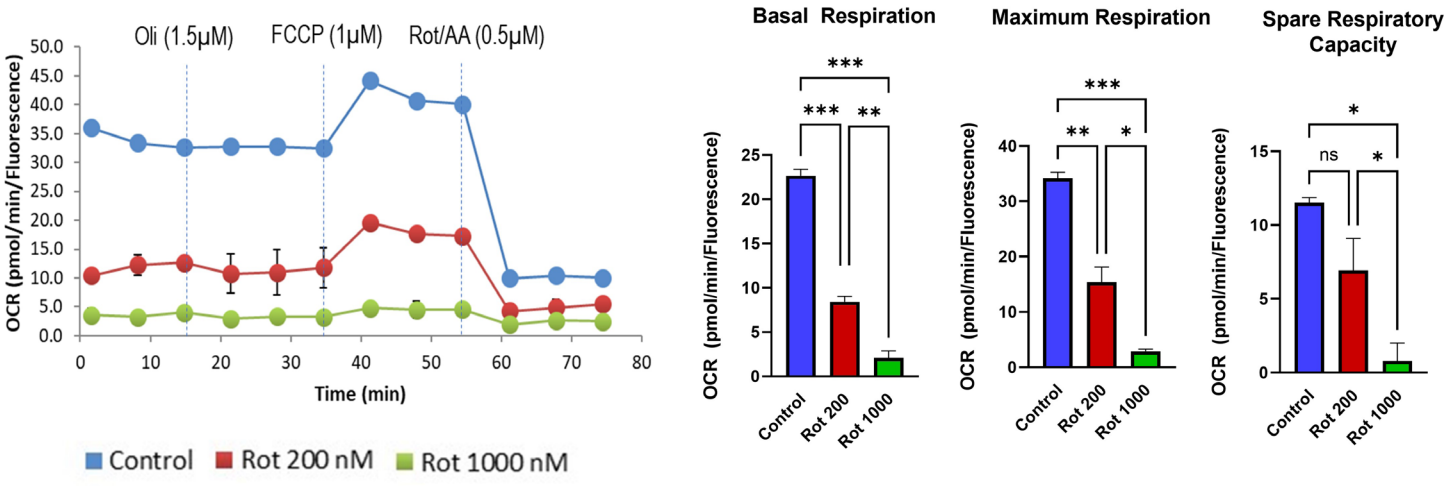


Figure 6

Representative line and bar graphics of Oxygen Consumption Rate (OCR) on Rotenone-treated SHSY5Y cells. As recommended, different pharmacological agents were injected throughout the assay, named Oligomycin (Oli) (1.5 µM), FCCP (1 µM), and a mix of Rotenone and Antimycin A (Rot/AA) (0.5 µM). OCR was normalized by cell number after cellular incubation with DAPI. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant p<0.05; *p<0.05, **p<0.01, ***p<0.001.

Assays using the Seahorse platform can be performed with adherent and non-adherent cells, even in tissue homogenates. At Sygnature, in addition to performing the Seahorse assay using SHSY5Y, experiments were performed in THP-1 cells, human fibroblasts, and human-derived microglia cells (MDMi) exposed to LPS, asshown in Figure 7.

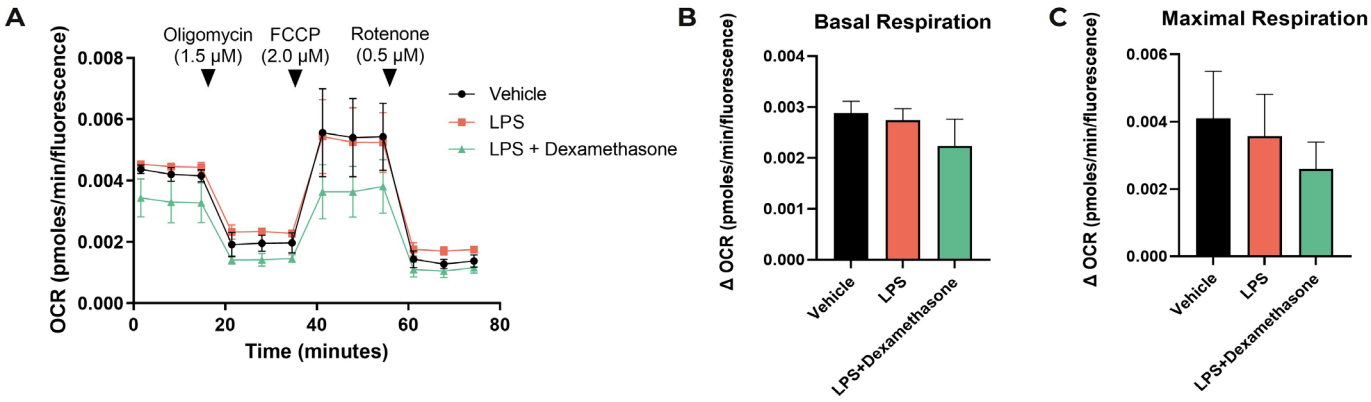


Figure 7

Representative line and bar graphics of Oxygen Consumption Rate (OCR) on LPS- and Dexamethasone-treated MDMi cells. Cells were exposed to LPS (100 ng/ml) for 24 hrs ± 1 hr Dexamethasone (1 µM). As recommended, different pharmacological agents were injected throughout the assay, named Oligomycin (Oli) (1.5 µM), FCCP (2 µM), and a mix of Rotenone and Antimycin A (Rot/AA) (0.5 µM). OCR was normalized by cell number after cellular incubation with DAPI. Statistics were performed using One-Way ANOVA followed by Turkey post-hoc test. It was considered significant $p<0.05$.

Assessing Mitochondrial Functional Parameters via Kinetic Experiments

In mitochondrial research, kinetic experiments play a pivotal role in unveiling the complexities of mitochondrial function (Figure 8). These assays, characterized by their robustness, reproducibility, and validation, are instrumental in assessing mitochondria's dynamical functional parameters.

Employing fluorescence probes adaptable across diverse plate reader platforms, we can meticulously track changes in mitochondrial behaviour over time. This method enables the precise evaluation of the mitochondrial functional status of healthy (control) and disease-affected cells.

At Sygnature, we measure cytosolic calcium levels, MMP, and oxidative stress using live cells loaded with specific fluorophores and in the presence of reference compounds. One example is the FCCP, a mitochondrial protonophore commonly used in kinetic readouts. It can depolarize the MMP, releasing mitochondrial calcium into the cytosol (Figure 8).

Cytosolic Calcium

Mitochondrial Membrane Potential (ΔΨm)

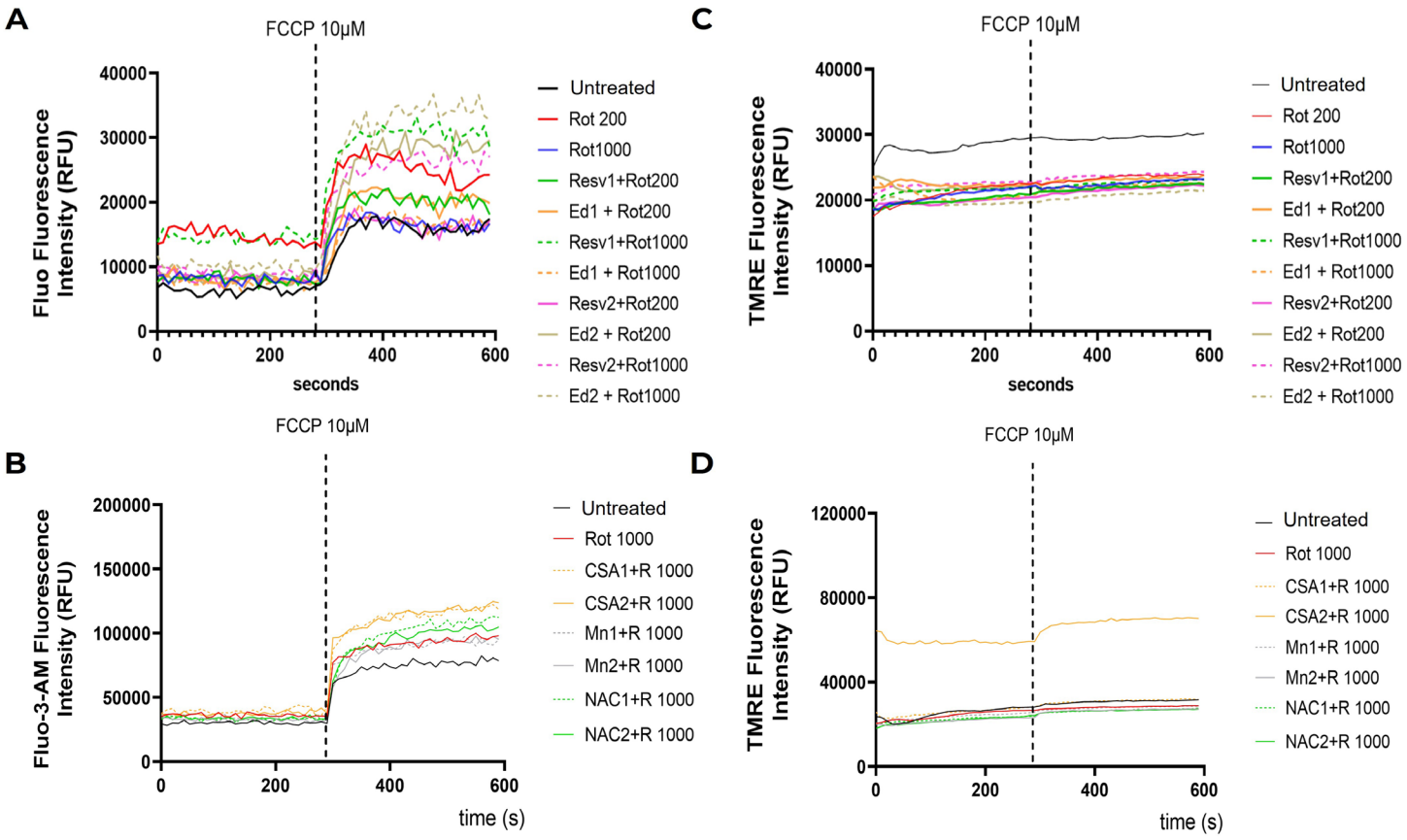


Figure 8

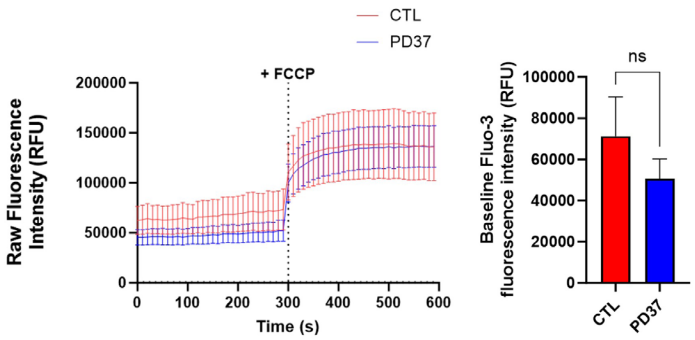
Representative line graphics of cytosolic calcium levels (A-B) and mitochondrial membrane potential (C-D) measurements in the SHSY5Y neuroblastomas cell line. The cells were pre-incubated with Rotenone and mitochondrial modulators (Figure 1). Kinetics readings were performed in the absence and presence of FCCP.

Cytosolic Calcium Levels

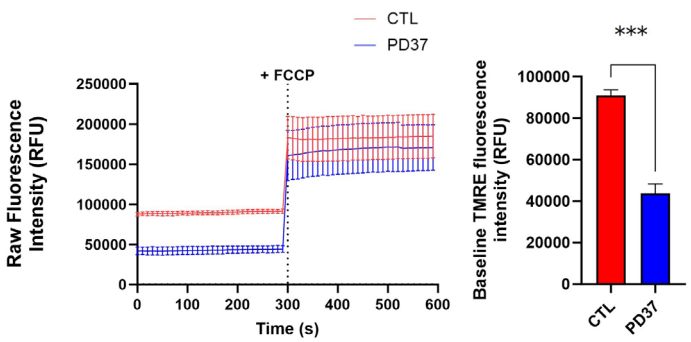
Specifically, regarding calcium homeostasis, changes in this parameter are associated with mitochondrial dysfunction and neuronal excitotoxicity. Mitochondria are one of the most crucial calcium buffering systems, and excess mitochondrial calcium uptake can trigger cell death mainly through changes in MMP and oxidative stress.

At Sygnature Discovery, cytosolic calcium changes are measured using the probe Fluo-3-AM (Figure 9). During kinetic experiments, both basal and after FCCP fluorescence can be acquired. Then, the delta (Δ) value is calculated by subtracting the normalized average value of the basal fluorescence (before FCCP) from the normalized average value 'after FCCP' for each sample. The Δ values reflect the increase in cytosolic calcium. The normalization of the fluorescence to 1, in the Δ graphic, is achieved by dividing the fluorescence obtained throughout the experiment by the mean of the first ten readings before FCCP. This normalization makes the FCCP-induced changes in calcium more apparent in the graph.

Basal Fluo-3 Fluorescence Analysis



Basal TMRE Fluorescence Analysis



Δ Fluo-3 Fluorescence Analysis

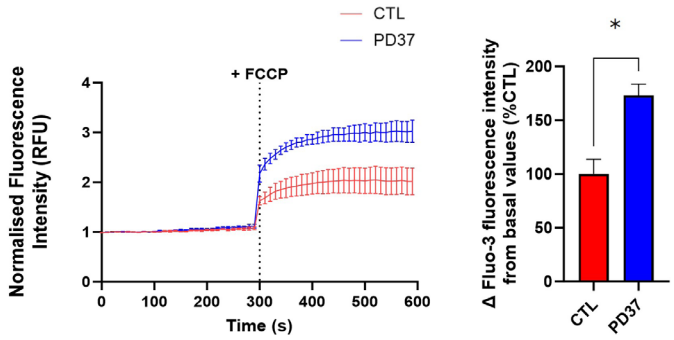


Figure 9

Representative line and bar graphics of control (healthy) and diseased fibroblasts incubated with Fluo-3-AM. Kinetics readings in the absence and presence of FCCP. Basal and delta (Δ) values are represented in both line and bar graphics. Fluo-3 fluorescence on Δ graphic was expressed as a percentage of the control group. PD37: Parkinson`s Disease cell line. Statistics were performed using the Student T-test. It was considered significant p<0.05; *p<0.05.

Δ TMRE Fluorescence Analysis

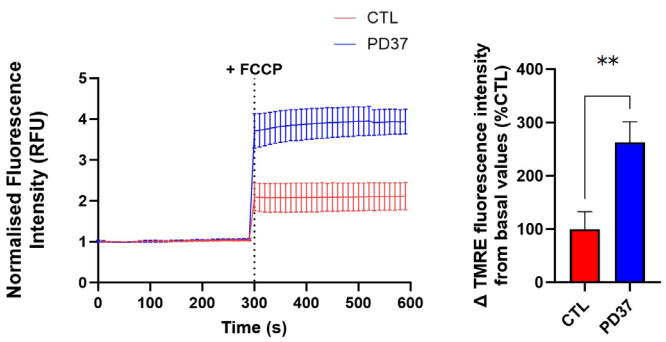


Figure 10

Representative line and bar graphics of control (healthy) and diseased fibroblasts incubated with TMRE. Kinetics readings in the absence and presence of FCCP. Basal and delta (Δ) values are represented in both line and bar graphics. TMRE fluorescence on Δ graphic was expressed as a percentage of the control group. PD37: Parkinson`s Disease cell line. Statistics were performed using the Student T-test. It was considered significant p<0.05; **p<0.01, ***p<0.001.

Mitochondrial Membrane Potential (MMP)

One of the most important outcomes of mitochondrial dysfunction is the collapse of MMP. Changes in the MMP result from alterations in the ion homeostasis inside the mitochondrial matrix, changes in the transport of electrons and protons, and also in the oxidative stress levels. Maintaining the MMP is crucial in controlling intracellular calcium levels in neurons by absorbing excess ions and ensuring appropriate calcium balance.

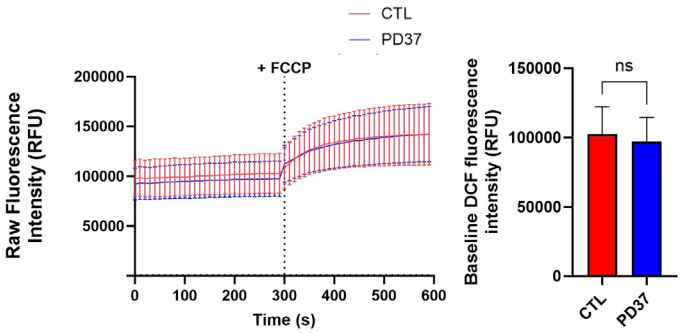
At Sygnature, MMP is measured using live cells loaded/incubated with the fluorophore TMRE (tetramethylrhodamine, ethyl ester) (Figure 10). During kinetic experiments, both basal and after FCCP fluorescence can be acquired. Then, the delta (Δ) value is calculated, reflecting the increase in cytosolic TMRE fluorescence after FCCP depolarises mitochondria. It will ultimately represent the ΔΨm for the mitochondrial membrane potential.

Oxidative Stress

Oxidative stress, characterized by an imbalance between excessive ROS production and the cell's antioxidant defences, is a prevalent factor in neurodegenerative diseases and contributes significantly to neuronal damage. While normal levels of ROS have signalling functions (such as in cellular proliferation, neuronal pruning, oxygen sensing and response to stress and inflammation), excessive production can lead to oxidative stress resulting in changes in MMP, calcium levels and energy production. Disturbances in the redox state of cells can also damage proteins, lipids, and DNA.

Here at Sygnature, oxidative stress is measured using live cells loaded/incubated with different fluorophores, such as H2DCFDA-AM (Figure 11). The principle used for measuring cytosolic calcium changes with Fluo-3-AM and MMP with TMRE can also be applied to DCF fluorescence to assess changes in oxidative stress. This involves recording basal fluorescence levels, followed by fluorescence after FCCP treatment, and calculating delta (Δ) values. This approach allows a clear visualization of FCCP's impact on oxidative stress.

Basal DCF Fluorescence Analysis



Δ DCF Fluorescence Analysis

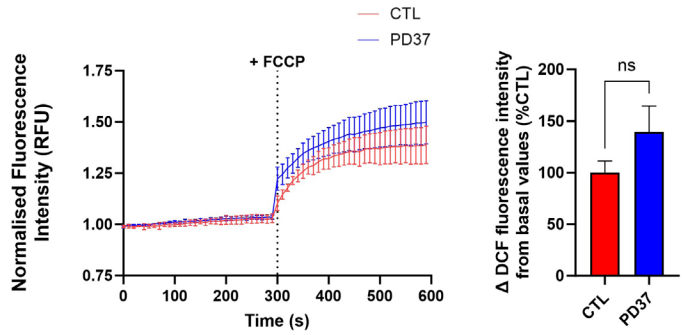


Figure 11

Representative line and bar graphics of control (healthy) and diseased fibroblasts incubated with H2DCFDA-AM. Kinetics readings in the absence and presence of FCCP. Basal and delta (Δ) values are represented in both line and bar graphics. DCF fluorescence on Δ graphic was expressed as a percentage of the control group. PD37: Parkinson`s Disease cell line. Statistics were performed using the Student T-test. It was considered significant p<0.05.

Mitochondrial Dynamics and Biogenesis

Mitochondria are organelles capable of adapting their format (shape), and quantity according to the energetic need of the cell in a specific moment or situation. This is particularly important in neurons, which require large amounts of energy. Moreover, abnormalities in mitochondrial dynamics can lead to the accumulation of damaged mitochondria, increased oxidative stress, and neuronal damage. Reduced biogenesis may compromise the cell's ability to replace damaged mitochondria, accumulating dysfunctional organelles. Therefore, the investigation of mitochondrial dynamics and biogenesis becomes crucial.

- Mitochondrial fusion allows for the exchange of genetic and protein material between mitochondria, promoting the mixing of healthy components and rescuing damaged ones.
- Mitochondrial fission, however, facilitates the removal of damaged or dysfunctional parts of mitochondria through processes like mitophagy (see below).

Mitochondrial biogenesis is the process of generating new mitochondria within cells. It involves the replication of mitochondrial DNA and synthesising proteins required for mitochondrial function.

At Sygnature, changes in mitochondrial dynamics and biogenesis are investigated through alterations in the transcription of genes related to all the aforementioned processes by real-time PCR (RT-PCR), named Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), mitochondrial transcription factor A (TFAM or mtTFA), Nuclear respiratory factor 1 (NRF1), Mitofusin 1 (MFN1), and Fission 1 (FIS1). Because the Nuclear factor erythroid 2-related factor 2 (NFE2L2), also known as nuclear factor erythroid-derived 2-like 2 (NRF2), is co-transcribed and regulated by PGC-1α and NRF1, it is usually evaluated concomitantly (Figure 12).

Mitochondrial biogenesis and fission/fusion gene expression

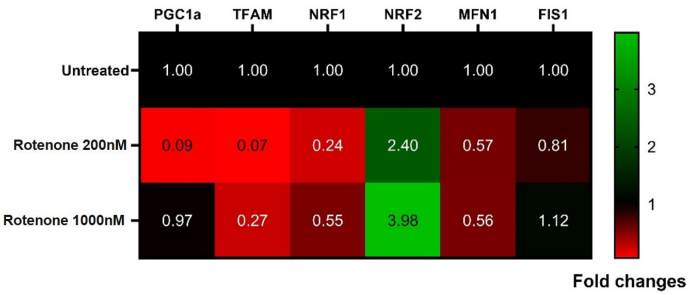


Figure 12

Relative expression of mitochondrial dynamics and biogenesis-related transcription factors in SHSY5Y cells exposed to Rotenone. Changes in gene expression are represented in the fold changes of the control group (untreated cells). Green: highest changes; Red: lowest changes.

At Sygnature, we also analysed mitochondrial dynamics and biogenesis in tissue homogenates via RT-PCR. This involved using cortex samples from P301S animal models (TGN Tau) and wild-type mice (Wt Tau) at the age of 5.6 months, as well as cortex samples from APP/PSEN1 animal models (TGN APP) and their wild-type counterparts (Wt APP) at 8 months old. Our investigation focused on the relative expression of PGC-1α, TFAM, and NFE2L2, as illustrated in Figure 13.

To obtain mRNA, we used automated tissue homogeniser Precellys®, and MagMAX™-96 Total RNA Isolation Kit. To set up RT-PCR, reagents were dispensed using automated Echo Liquid Handlers in 384-well plates and SyberGreen, and the reactions were performed using a BioRad C1000 Touch Thermocycler. Both ΔCt of the target gene and housekeeping were calculated, and the normalised gene expression was considered as 2-ΔΔCt (reaction efficiency ~100%) (Figure 13).

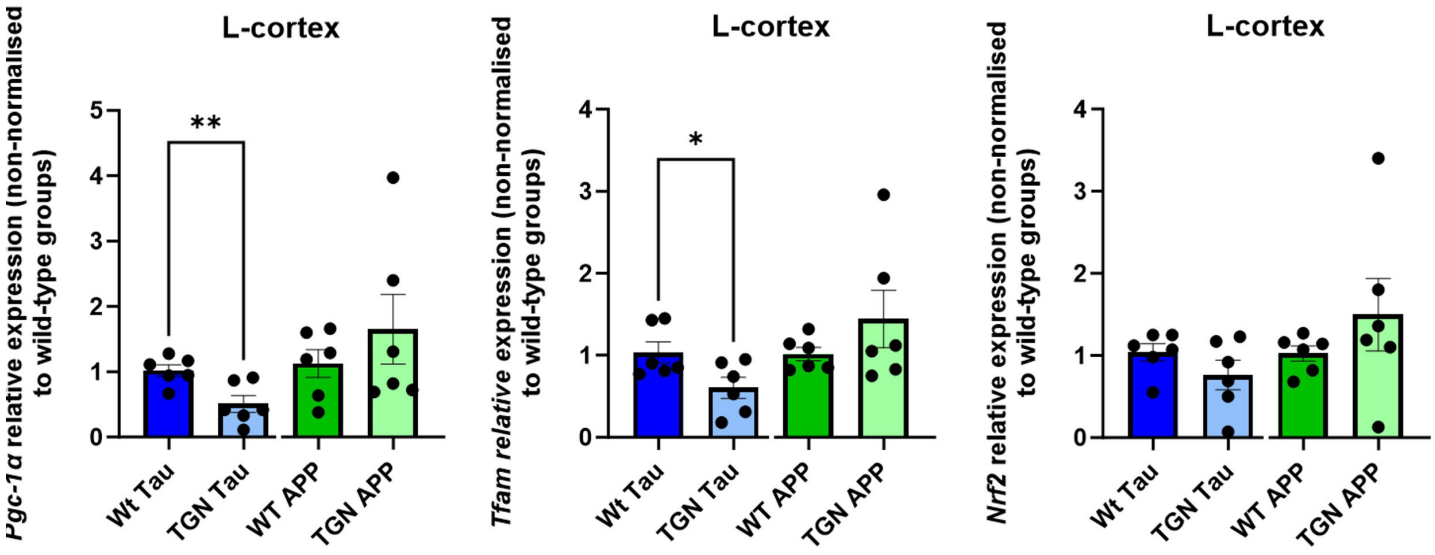


Figure 13

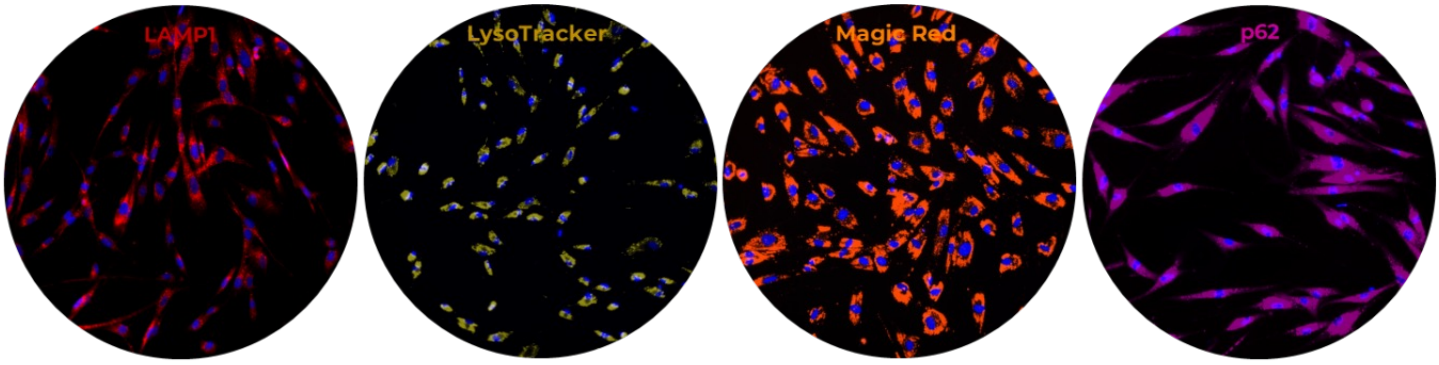
Relative expression of mitochondrial dynamics and biogenesis-related transcription factors in the brain of transgenics and wild-type mice. PGC-1α, TFAM, and NFE2L2 relative expression in the cortex of P301S animal model (TGN Tau) and wild-type mice (Wt Tau) at 5.6 months old and APP/PSEN1 animal model (TGN APP) and wild-type mice (Wt APP) at 8-month-old mice. Results in mean±SEM (n=3-6 per group). Statistical analysis was performed using the Student T-test between transgenic mice and their respective controls; *p<0.05, **p<0.01.

Mitochondria Quality Control

Enhancing mitochondrial degradation, or mitophagy, has gained attention as a promising therapeutic strategy for neurodegenerative diseases. This strategy focuses on modulating key regulatory proteins responsible for mitophagy, a selective form of autophagy that targets damaged or dysfunctional mitochondria for degradation. Mitophagy is crucial in neurodegeneration because it maintains mitochondrial quality and cellular homeostasis, thereby ensuring the proper functioning of neurons. Dysregulation of this process can lead to oxidative stress, impaired energy production, and heightened neuronal vulnerability to damage.

Lysosomes, spherical degradative organelles, are central to the cell's waste disposal and autophagy processes. Their function, including the content and activity of lysosomal enzymes, is pivotal in the mitochondrial quality control system.

At Sygnature, we assess lysosomal function and autophagy alongside mitochondrial content and morphology using immunostaining techniques and high-throughput imaging (see Figures 14-15). For lysosomal content and function, we utilize antibodies against LAMP-1—a glycoprotein located on the lysosomal membrane's inner surface. We also employ fluorescence probes such as LysoTracker™, which quantifies lysosomal acidity, and MagicRed®, which gauges Cathepsin B enzyme activity. Furthermore, autophagy flux is monitored by observing changes in p62 levels, while mitochondrial content and morphology are examined through variations in MitoTracker® fluorescence.



Lysosome Quantification and Lysosomal pH:
LAMP1 Immunostaining and LysoTracker Assay
LysoSensor Assay (pH fluctuations)

Enzymatic Activity:
Magic Red (Cathepsin B) Assay

Autophagy Flux:
p62 Immunostaining

Figure 14

Representative images of control fibroblasts stained with LAMP-1, Lysotracker™, MagicRed®, and p62. Cells were grown overnight and incubated with antibodies against LAMP-1 and p62 and with the fluorescent probes LysoTracker and MagicRed®.

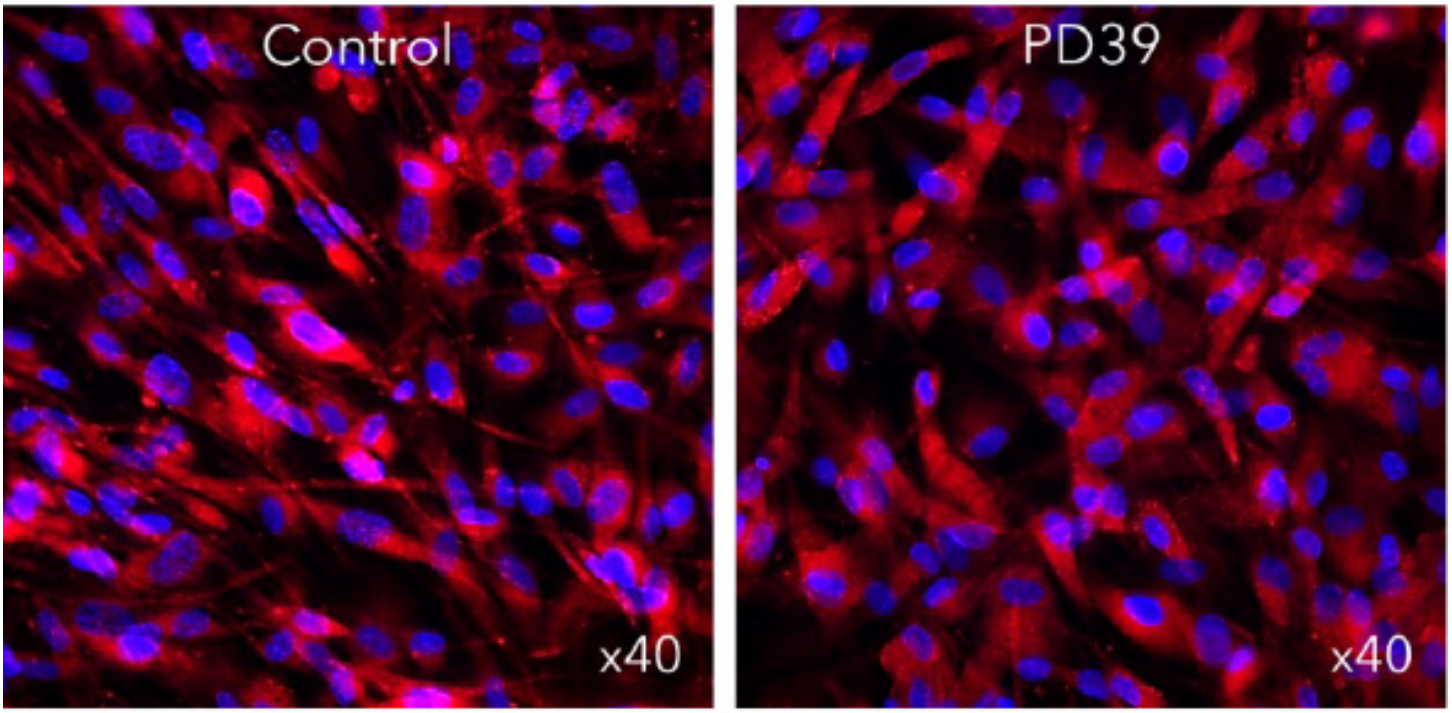


Figure 15

Representative images of fibroblasts stained with Mitotracker™. Cells were grown overnight and incubated with the fluorescent probe. Control and PD39 (Parkinson`s Disease) cell lines.

CONCLUSION

Advancing Neurodegeneration Research Through Mitochondrial Function Analysis

As we delve into the complexities of neurodegenerative diseases, it becomes increasingly clear that mitochondria play a central role in the vitality of brain cells and the pathogenesis of these conditions. At Sygnature Discovery, our commitment is underscored by our advanced Mitochondrial Dysfunction Platform. We have established a robust framework for investigating mitochondrial function and its implications in neurodegeneration, employing a broad spectrum of assays, state-of-the-art technologies, and stringent assay validation protocols.

By leveraging our expertise in fluorescence and luminescence plate-based assays, high-content imaging platforms, and kinetic experiments, we have gained valuable insights into the complex interactions between mitochondrial dysfunction and cellular toxicity. Our research has emphasized the importance of mitochondria in cellular energy production and the potential consequences of their dysfunction, including altered metabolic states, oxidative stress, and compromised neuronal viability. Our findings also highlight the critical role of mitochondrial dynamics, biogenesis, and quality control in maintaining cellular health, revealing the therapeutic potential of targeting these pathways in neurodegenerative diseases.

In conclusion, the comprehensive analysis capabilities of Sygnature Discovery's Mitochondrial Dysfunction Platform enable us to delve deeper into the intricacies of mitochondrial function and its correlation with neurodegenerative disorders. Researchers' collaborative efforts and ongoing advancements in mitochondrial science hold promise for developing innovative, effective treatments that can significantly improve the lives of those affected by these debilitating conditions.

For biotech companies looking to advance their research in neurodegenerative disorders and beyond, Sygnature Discovery is ready to collaborate and provide unparalleled support in mitochondrial research.

Contact us today to explore how our Mitochondrial Dysfunction Platform can accelerate your drug discovery efforts and drive meaningful advancements in therapeutics.

Visit the Sygnature Discovery website.
www.sygnaturediscovery.com