Innovative Concepts in Drug Development

Targetting mitochondria

Substantiate **your commercial claims** through sound scientific testing.

Mitochondria are an active target in promoting skin beauty, reversing signs of aging, and protecting skin from environmental aggressors (pollutants, sun radiations).

ICDD provides you with innovative and state-of-the-art scientific solutions to demonstrate the efficacy of active ingredients or formulae on skin cell models.

Leader in mitochondrial testing, ICDD offers customized designs for your specific questions. Talk one on one with our scientists to harness the power of youth!

Enhance the value proposition of your product by the demonstration of mitochondrial activity in skin protection, beauty promotion, and cell energy.

Use the right biology

- Mitochondria are present in every cell of the body. They maintain cell homeostasis by controlling energy production, ion fluxes, and the rate-limiting step of steroidogenesis. They contribute to both free radical production and to anti-oxidant defenses. They represent a major target for cosmetic actives.
- Altered mitochondrial function and behavior have been recognized in age-associated skin alterations.

Use the right technology

- ICDD offers HTS and HCA industry-validated screening platforms to assess the safety and efficacy of active ingredients or complete formulae.
- For more pertinent and meaningful results, the mitochondrial function is analyzed inside a live cell—thus maintaining existing interactions—with fully integrated multiplexed bioassays.
- Results obtained are fully supported by proper statistics and interpreted with respect to the physiological context in which the experiments take place.
- Using the right model for the right question warrants that your *in vitro* results will better translate to *in vivo* results establishing your claims.

Use the right model

- ICDD has developed expertise in the development and validation of patient-derived cell models to increase result translatability. We favor primary cell models.

Use the right company

- ICDD is in business since 2007 and works with large, mid-size, and small cosmetic companies.
- ICDD works according to a quality statement in line with its mission and philosophy: providing you with the pharmacological mechanisms of action of your product at the cell level.
- ICDD's facilities and equipment are state-of-the-art, enabling human cell culture, mitochondrial testing in high throughput, computer-aided image acquisition, and image analysis with proprietary software to demonstrate the activity of products confided to us.
- Our scientists are experts in mitochondrial biology, combining more than 40 years of experience in assay development and data modeling.

Our expertise is at your disposal for customized bioassays to fit your specific needs.

Our technologies

Mitosafe®

- Mitochondrial function
- Functional bioassays
- Multiplexed targets assessed at the same time

- Non-permeabilized living cells
- No isolation of mitochondria required
- High throughput screening platform
- Customizable in pertinent cell models

➥ Identify active ingredients' mechanisms of action & efficacy

➥ Identifiy mitochondrial liabilities

Mitostream®

- Mitochondrial behavior
- Phenotypic outcome
- Resultant of dynamical interactions of mitochondrial targets with targets in other cell compartments

- Non-permeabilized primary living cells
- No isolation of mitochondria
- High content analysis platform

➥ Identify age signatures for different skin-type or ethnicity donors

➥ Establish age-reversal property of formulae

➥ Opt for a personalized approach to skin beauty

This catalog presents the different applications of our highly innovative & state-of-the-art technologies for the cosmetic industry. Contact us for more information.

Our models

Efficacy testing of skin care products

- Human primary cell biobank
  - Donor-derived cells
  - Fibroblasts, keratinocytes, melanocytes
  - Variety of age/gender/ethnicity
- More complex skin models available
  - 3D
  - Co-cultures
  - IPS-derived cells (neurons, etc.)
- Age models
  - Cell aging induced by environmental factors, modeled by addition of H_2O_2 in either cell type
  - Cell aging induced by physical stress with single or repeated exposure to UV or IR light in either cell type
  - Senescent cell model
- Pollution models
  - Exposure to urban pollutants
  - Young and mature skin cell models

➥ Ask us for the phenotype of these different models in terms of mitochondrial functionning patterns!

Substantiate your claims for:

- Anti-aging
- Anti-oxidation
- Protection from pollution
- Sun protection
- Energy modulation
- Slimming & toning
- Detox

➥ Don't see what you're looking for? Ask us to develop a customized model for your specific needs!

BBS

What

- Bioenergetic balance screen
- Multiplexed and integrated measurements of:
  - O_2 consumption rate
  - Cellular ATP level
  - Glycolysis level
  - Cell viability
- 2 culture conditions available:
  - Glucose-containing medium
  - Galactose-containing medium
- HTS/single point or dose response studies

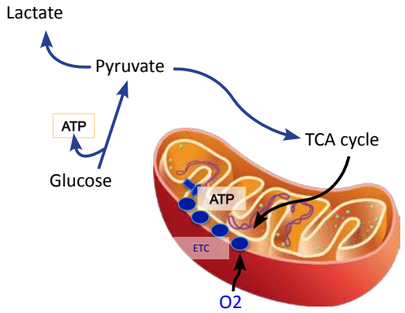
Value

- Demonstration of ingredient's MOA*
- Early detection of unwanted activity at the mitochondrial respiration level helps deselect compounds with toxicity liabilities
- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health

Mechanisms of action

Applications

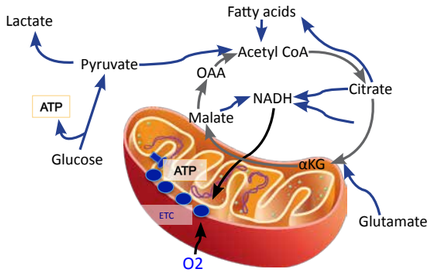
- Select energizing compounds to fight against physiological conditions in which reduced metabolism impacts skin health (firmness, youth)
- Identify ETC uncoupler, inhibitors, and energizing activities
- Define MOA that speak to your audience
- Validate energizing claims
- Reinforce anti-aging claims



BBS +

What

- Bioenergetic balance screen
- Integrated measurements of
  - O_2 consumption rate
  - Cellular ATP level
  - Glycolysis level
  - TCA cycle activity
  - Cell viability
- 4 culture conditions available:
  - Glucose-containing medium
  - Galactose-containing medium
  - Glutamine-containing medium
  - Glutamine-free medium
- HTS/dose response studies



Value

- A finer understanding of MOA* helps position your product with respect to final customer value
- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health

Applications

- Understand where the ATP comes from
- Measure interactions between mitochondrial respiration and central metabolism (glycolysis and beta oxidation) in live cells
- Model ingredient and/or formula response on mitochondrial respiration in the context of central metabolism
- Search for skin subtype specificities in ingredient's response
- Explore firmness claims

*Mechanisms of action

Redox balance

What

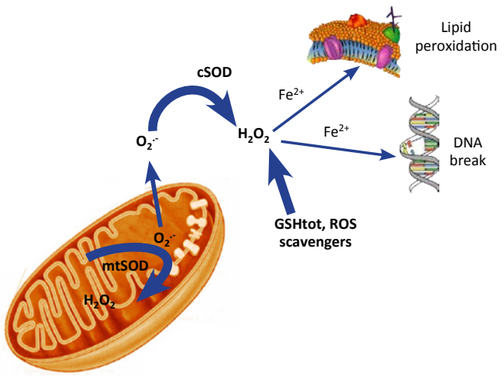
- Measurement of (any or all):
  - ROS mitochondrial production
  - Cytoplasm ROS accumulation
  - NADPH oxidase activity
  - MnSOD Cu/ZnSOD activities
  - Scavenging activity (Catalase/GSH)
  - Lipid peroxidation level (TBARS)
  - Protein carbonylation
  - Cell viability
- HTS/dose response studies
- Measure the direct pharmacological effect of ingredients on any of these markers at the basal level or after oxidative stress induction (chemical or physical stressors available)

Value

- Qualify actives with anti-oxidant activities in live cells
- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health

Applications

- Validate anti-oxidant and anti-aging claims
- Reverse age-induced elements characterized by increased oxydative stress, notably in skin cells and for some markers in skin explants
- Use our different models available to mimick age-induced increase in oxydative stress



mtDNA content*

What

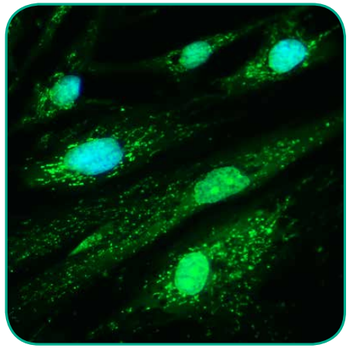
- Measurement of:
  - Mitochondrial DNA content
  - Mitochondrial mass
  - Mitochondrial biogenesis
  - Cell viability
  - Nucleus integrity/morphology (optional)
- Measure the direct pharmacological effect of ingredients on mtDNA content at the basal level or after oxidative stress induction (chemical or physical stressors available)
- qPCR objectivation of deletions within mtDNA available upon request

Value

- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health
- Provide quality visuals for your marketing team with this test based on image analyses

Applications

- UV, IR, and heat modulate mtDNA content in skin cells exposed to radiation: measure the activity of your compound in modulating mitochondrial network recovery from this type of physical stress
- Validate solar protection claims

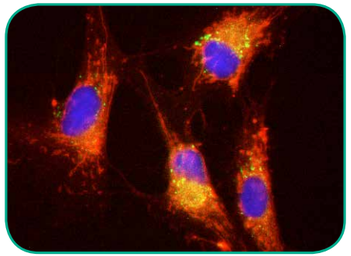


**We can also provide a better understanding of mtDNA quality control (mitophagy) after solar exposure.*

Mitophagy

What

- mtDNA quality control
- Measurement of (any or all):
  - Autophagic accumulation & autophagic flux
  - Western blot - LC3B
  - Mitochondrial co-localization at autophagosomes
  - Mitochondrial mass
  - Western blot - Tom20 and/or Mnf1/2
  - Cell viability
- Couples pharmacological effects of ingredients at autophagosome & mitochondrial networks with quantitative protein levels



Value

- Enhance the value of skincare products by demonstrating their efficacy in cell detoxification.
- Men & women have different response to toxicants and different mitophagy profiles: identify the right target population
- Aging impairs autophagy / mitophagy: evaluate your active's ability to repair it
- Mitophagy induction correlates with removal of UV-induced mtDNA damages
- Provide quality visuals for your marketing team with this test based on image analyses

Applications

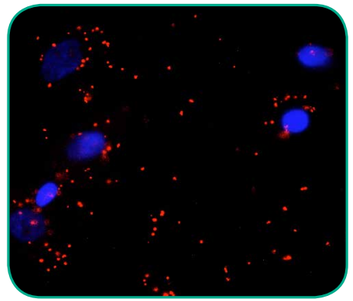
- Validate detox claims
- Validate claims of reparation of sun-induced damages
- Validate anti-aging claims
- Position your product on the right market

Endoplasmic reticulum (ER) stress

Endoplasmic reticulum (ER) and mitochondria are physically linked and signal through the mitochondria-associated membrane (MAM) to regulate the transfer of Ca^{2+} (a toxicant) from ER stores into the mitochondrial matrix, thereby affecting mitochondrial function and intracellular Ca^{2+} homeostasis. ER dysfunction further leads to the production of badly folded proteins, which accumulate and generate toxicity in the cell.

What

- Quantification of mitochondria & ER interactions
  - Proximity ligation assay to identify MAMs
  - Measurement of mitochondrial mass
  - Determination of changes in intracellular calcium concentrations (optional)
  - Cell viability
- UPR signaling pathways can also be measured to further understand the MOA* of your actives.



Value

- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health
- A finer understanding of MOA* helps position your product with respect to final customer value
- MAMs increase in cells that have built up oxidative stress: identify actives capable of detoxifying cells by reducing MAMs

Applications

- Validate detox claims
- Validate claims of reparation of sun-induced damages
- Validate anti-aging claims
- Position your product on the right market

*Mechanisms of action

Pollution-induced damages

What

- Evaluate actives on acute exposure to pollution induced alterations in mitochondrial behavior
- Two donor-derived cell models:
  - Young skin cells
  - Mature skin cells
- Models include measurement of
  - Cellular bioenergetics (BBS+ test)
  - Mitochondrial fusion-fission dynamics
  - Mitochondrial membrane permeability (mature model only)
  - Cell viability

Value

- Pollution differentially impacts young and mature skin: identify the right target population
- Understand the mechanism by which your actives impact pollution-induced damages
- Enhance the value of skincare products by demonstrating their efficacy in relevant mechanisms for skin beauty and health
- Provide quality visuals for your marketing team

Applications

- A finer understanding of MOA* helps position your product with respect to final customer value
- Select actives capable of protecting from or reversing damages induced by acute exposure to urban pollution and substantiate anti-pollution claims
- Position your product on the right market

➥ Partner with us to identify the effects of chronic pollution on skin cells and/or skin explant secretome to evaluate your actives ability to reverse and/or repair these effects at pertinent mitochondrial & inflammatory targets

**Mechanisms of action*

Reverse age-associated phenotype

What

- Donor-derived cell model to test age-induced alterations in mitochondrial behavior
- Measurement of specific signatures* using mitochondrial behavior
- Simultaneous measure of variables along four dimensions:
  - Motility
  - Morphology
  - Mitochondrial reticular network organization
  - Mitochondrial membrane permeability

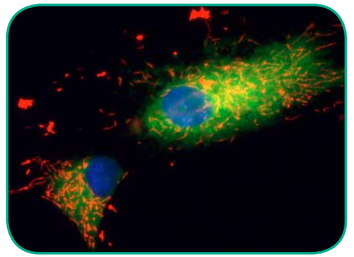
Value

- Better translate preclinical results to clinical performances
- Provide quality visuals (which can include video) for your marketing team

Applications

- Select age-associated phenotype modifying formulae
- Identify skin-type and/or population specific age signatures to match your targeted customer population
- Qualify and quantify your formula activity

➥ Partner with us to identify age signatures in pilot cohorts of patients that we have not yet studied using our proprietary models



**Signatures for neurodegenerative diseases have been obtained by ICDD and are in use in the pharmaceutical industry for disease-modifying drug selection.*

Specific gene and protein targets

What

- Quantitative capillary electrophoresis
- Protein expression level measurement in cell and tissue extracts
- qPCR
- Mitochondrial protein targets
- Non-mitochondrial protein targets
- Cell signaling
- Protein or nucleic acid analysis

Value

- Better understanding MOA* helps refine ingredient's indication
- Target validation

Applications

- Screen specific targets and signaling pathways associated with age, anti-oxidant activity and signaling, fat metabolism, sun protection, etc.

*Mechanism of action

Possible combinations

All of our bioassays are **fully customizable** and can be combined to answer your specific questions. Here are some of our recommendations:

You have an anti-aging claim

- Senescent or young + mature cell model
- Redox status (cROS)
- Mitochondrial respiration (BBS)
- mtDNA quality control (mitophagy)
- mtDNA content
- Mitochondria & ER interactions

You have an anti-oxidation claim

- Physical or chemical stressor
- Redox suite (all or any)

You have an anti-pollution claim

- Young and/or mature cell model
- Bioenergetics (BBS+)
- Fusion/fission balance
- Mitochondria membrane potential (mature)

You have an energy modulation claim

- Bioenergetics (BBS or BBS+)

You have a detox claim

- mtDNA quality control (mitophagy)
- Fusion/fission balance
- Redox status (cROS)
- Mitochondrial respiration (BBS)
- Mitochondria & ER interactions

You have a photo-protection claim

- UV, IR, or heat models
- Redox status (cROS and mtROS)
- mtDNA content
- mtDNA quality control (mitophagy)
- Bioenergetics (BBS)
- Mitochondria & ER interactions

You have a slimming/toning claim

- Mitochondrial respiration and fatty acid oxidation (BBS +)
- Lipid droplet accumulation
- UCP expresion

Screening package

Unsure what potential your actives have? Identify how to position them and which claims to explore further with our screening package!

What

- Explores at the same time several different cell models
- Includes:
  - The analysis of oxidative stress in senescent cells (fibroblasts) to identify **anti-age activity**
  - The analysis of oxidative stress after UV in fibroblasts to identify a **sun protection claim**
  - The analysis of chemically induced oxidative stress in fibroblast cells to assess **anti-oxidant activity**
  - The analysis of ATP, O2 consumption, and cell viability with our BBS- test to identify if your active modulates the **cellular bioenergetics**
  - Cell viability
  - Cell banking and data interpretation

Value

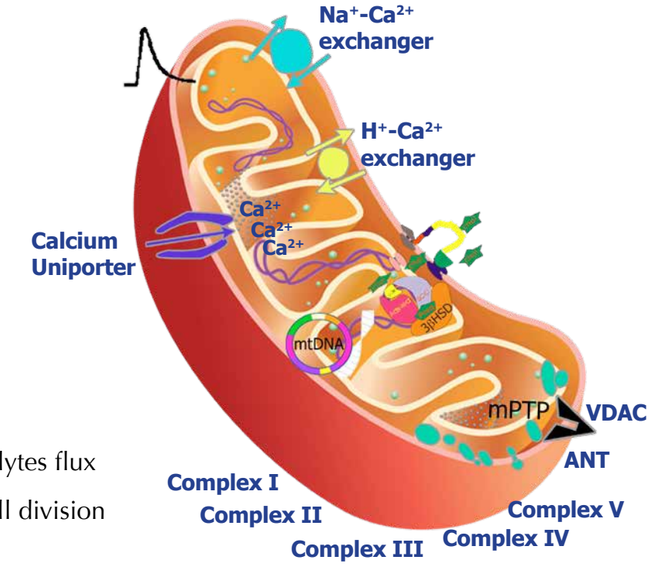
- Fast data return and cost-effectiveness for early positioning of active ingredients
- Know which claims to explore further and where to best invest your R&D resources

Applications

- Position your actives (or mixes) on the right claims

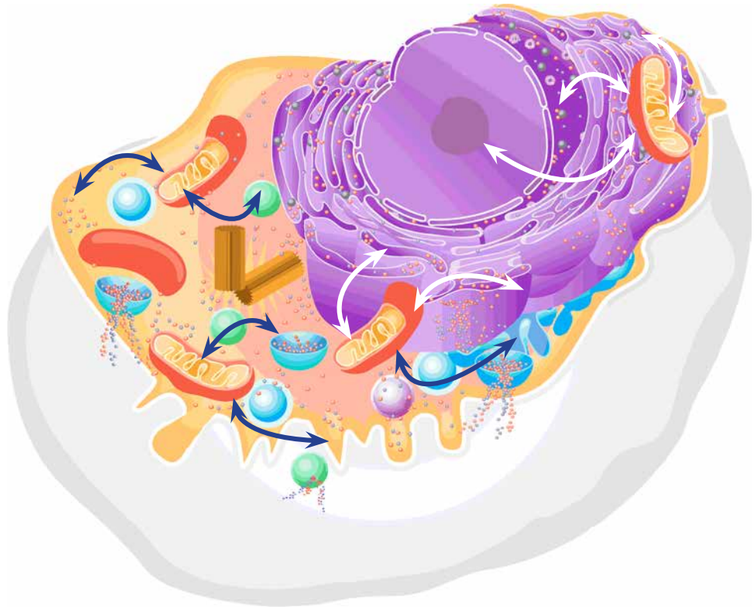
Mitochondrial Targets

- ✓ Energy conversion
  - pyruvate decarboxylation
  - fatty acids oxidation
  - respiration
- ✓ Apoptosis
- ✓ ROS production
- ✓ Non-nuclear genome
- ✓ Steroid hormones synthesis
- ✓ Regulation of the Ca^{2+} signaling
- ✓ Regulation of the cellular electrolytes flux
- ✓ Replication independent from cell division



Mitochondria control essential cell functions and provide pertinent molecular targets for active ingredients controlling cell energy, redox status, and mtDNA content.

Mitochondrial Interactions



Mitochondria interact with all cell compartments in a dynamical fashion. Monitoring these interactions through the analysis of mitochondrial behavior is a powerful readout of cell adaptability.

Make us your trusted partner

What are the next steps?

- Talk to one of our scientists to refine your question for a specific active ingredient
- Choose the right model to work with
- Choose the most pertinent assay or package
- Obtain a quote from ICDD
- Once the research expense is approved, the study starts with the review of a detailed study plan
- We include full statistical analyses to ensure that the observed changes are statistically significant
- Results are both compiled into a research report transmitted to you at the end of the study and presented to your team through a teleconference or during a visit to your site

We value your satisfaction in our scientists' rigor and expertise in the demonstration of your claims.

Quality statement

We offer customized services to meet your specific needs. Using our expertise, you can focus on what matters most: the safety and efficacy of your products using translatable human-based mitochondria testing.

The satisfaction of our clients and of our partners is our upmost priority. To this end, we guarantee our commitment regarding the quality of our services and the respect of our timeframes.

ICDD also guarantees the added value passed onto its customers and partners by its technologies. Our scientists truly listen to you to better answer your needs.

Keeping your trust is our best reward.

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