LVL UP RX · CLIENT EDUCATION SERIES

MOTS-c

Mitochondrial Open Reading Frame of the 12S rRNA Type-c

Exercise Mimetic · Metabolic Regulator · Longevity Signal

A complete research guide to MOTS-c — the mitochondria-derived peptide that activates the same cellular pathways as exercise, encoded in your own mitochondrial DNA.

FOR RESEARCH PURPOSES ONLY

LVL UP RX

Client Education Series

Everything you need to know about MOTS-c and mitochondrial metabolic optimization

> *MOTS-c is not coded in your nuclear DNA like most proteins — it's encoded in your mitochondrial DNA, the ancient energy genome of the cell. It is your body's own built-in performance optimizer, and it declines with age just like every other critical metabolic signal.*

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Mitochondrial-Derived Peptide

What Is MOTS-c?

The peptide encoded in your mitochondrial DNA — not your nuclear genome

MOTS-c (Mitochondrial Open Reading Frame of the 12S rRNA Type-c) is a 16-amino-acid peptide encoded within the 12S ribosomal RNA gene of human mitochondrial DNA. This makes it fundamentally unlike every other research peptide in the LVL UP RX catalog — it is not derived from a protein, a growth factor, or a hormonal precursor. It is a signal produced by the mitochondria themselves.

First identified in 2015 by researchers at the University of Southern California, MOTS-c was discovered during a search for functional peptides hidden within what was previously thought to be non-coding regions of mitochondrial DNA. Its discovery fundamentally changed our understanding of mitochondrial biology — demonstrating that mitochondria are not just passive energy factories, but active signaling organelles that communicate with the rest of the cell and the body.

MOTS-c travels from mitochondria to the nucleus, where it directly regulates gene expression in response to metabolic stress — particularly the kind of stress created by exercise. This is the foundation of its classification as an 'exercise mimetic': it activates the same cellular programs that physical training triggers, through the same molecular pathway.

16aa	2015	mtDNA	AMPK
AMINO ACIDS	**DISCOVERED**	**ENCODED IN**	**ACTIVATES**
mitochondrial peptide	USC research team	not nuclear genome	the exercise pathway

What Makes MOTS-c Unique

Every other peptide in the LVL UP RX catalog is derived from nuclear-coded proteins — they mimic hormones, growth factors, or protective proteins that the body produces in specific tissues. MOTS-c is different in three fundamental ways:

Mitochondrial Origin

MOTS-c is coded in mitochondrial DNA — an entirely separate genome from the nuclear DNA that codes for most proteins. Mitochondria evolved from ancient bacteria and retain their own DNA, their own ribosomes, and their own gene expression machinery. MOTS-c is one of the first peptides discovered to be encoded in this ancient genome and to function as a systemic hormonal signal.

Nuclear Translocation

After being synthesized in the mitochondria, MOTS-c translocates to the nucleus — crossing two membrane barriers to directly regulate nuclear gene expression. This nucleus-to-mitochondria communication is a newly discovered signaling axis with profound implications for understanding how energy status is communicated across the cell.

Metabolic Stress Sensor

MOTS-c levels in the body respond dynamically to metabolic stress — rising during fasting, exercise, and caloric restriction. It acts as a cellular sensor of energy demand, coordinating metabolic adaptations in response to the body's energy needs. Supplementing MOTS-c essentially signals to the body that it is under the beneficial metabolic stress of exercise — even at rest.

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THE SCIENCE

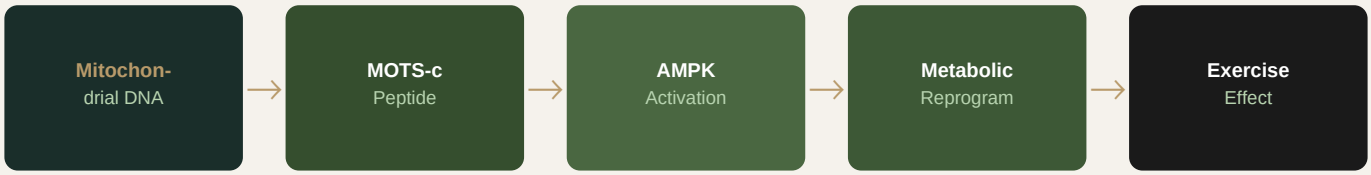
AMPK, Mitochondrial Biogenesis & Metabolic Reprogramming

The Science Behind MOTS-c

How mitochondrial signaling reshapes cellular metabolism

The Mitochondria → AMPK → Nucleus Pathway

The central mechanism of MOTS-c action can be summarized as a three-step cascade:



AMPK Activation — The Master Metabolic Switch

MOTS-c's primary molecular target is AMPK (AMP-activated protein kinase) — often called the 'master regulator of cellular energy homeostasis.' AMPK is activated whenever cellular energy is low (low ATP, high AMP ratio) — exactly the state created by exercise. When MOTS-c activates AMPK, it triggers a cascade of metabolic adaptations: increased glucose uptake, enhanced fatty acid oxidation, inhibited fat synthesis, and stimulated mitochondrial biogenesis. This is the same AMPK pathway activated by exercise, metformin, and caloric restriction — three of the most well-studied longevity interventions in science.

Mitochondrial Biogenesis

One of AMPK activation's most consequential downstream effects is stimulation of PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha) — the master regulator of mitochondrial biogenesis. PGC-1α activation causes cells to produce more mitochondria. More mitochondria means greater cellular capacity for energy production, fat oxidation, and metabolic efficiency. MOTS-c essentially tells cells to build more energy factories — a direct mechanism for improved endurance and metabolic health.

Folate Cycle & One-Carbon Metabolism

MOTS-c also inhibits the folate cycle — a metabolic pathway involved in nucleotide synthesis and methyl group donation. This inhibition activates AMPK through a distinct secondary mechanism, and is thought to contribute to MOTS-c's effects on insulin sensitivity and glucose metabolism, particularly in the context of aging and metabolic disease research.

Anti-Inflammatory Gene Regulation

In the nucleus, MOTS-c directly modulates the expression of genes involved in inflammatory signaling — suppressing NF-κB activity and reducing the chronic low-grade inflammation associated with aging, obesity, and metabolic syndrome. This 'inflammaging' suppression is considered one of its key longevity-relevant mechanisms.

Insulin Sensitivity Improvement

Through AMPK activation and its effects on glucose transporter expression (particularly GLUT4 translocation to the cell surface), MOTS-c improves the ability of muscle and fat cells to take up glucose in response to insulin — directly improving insulin sensitivity independent of weight loss, making it uniquely valuable in metabolic health research.

3

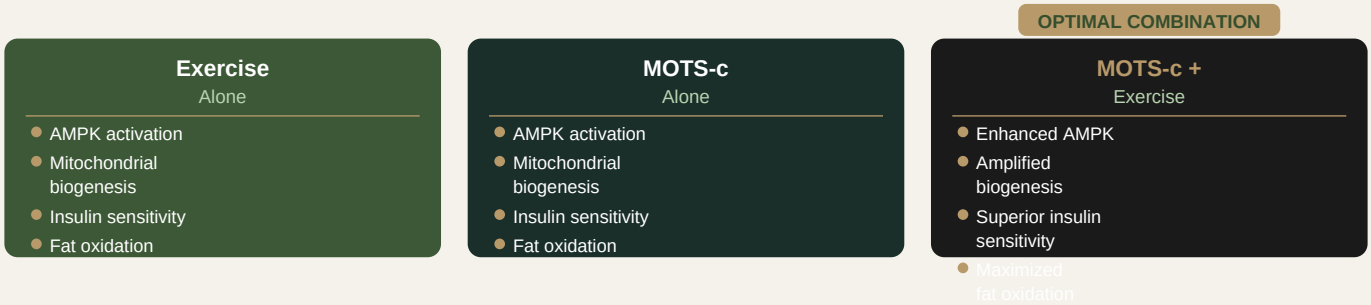
THE EXERCISE MIMETIC

Activating the Body's Training Response Without Training

MOTS-c as an Exercise Mimetic

Why researchers call it a 'workout in a molecule'

The term 'exercise mimetic' refers to compounds that activate the same molecular pathways that physical exercise triggers — without requiring the mechanical work of exercise itself. MOTS-c is one of only a handful of compounds that genuinely earns this classification, because its primary mechanism — AMPK activation via mitochondrial signaling — is the exact pathway through which exercise produces its most important metabolic benefits.



What Exercise and MOTS-c Share

When you exercise, your muscles rapidly consume ATP. The resulting drop in ATP and rise in AMP activates AMPK — triggering the same cascade that MOTS-c initiates directly. Both produce the following downstream effects:

- GLUT4 translocation to the cell surface — increasing glucose uptake by muscle cells
- Enhanced fatty acid transport into mitochondria — accelerating fat burning
- Increased mitochondrial density through PGC-1α/mitochondrial biogenesis
- Improved insulin sensitivity in skeletal muscle
- Suppression of inflammatory gene expression
- Enhanced endurance capacity through metabolic efficiency gains

What MOTS-c Can Do That Exercise Cannot

While MOTS-c does not replace the mechanical benefits of exercise (cardiovascular conditioning, bone density from impact, motor skill development), it can deliver metabolic benefits in contexts where exercise is limited:

- Individuals with mobility limitations, injury, or post-surgical restrictions
- Elderly populations where exercise capacity is significantly reduced
- Metabolic correction independent of physical activity — relevant for severe insulin resistance where exercise alone is insufficient
- Amplifying the metabolic response to exercise beyond what training alone achieves — the combination of MOTS-c and exercise produces greater AMPK activation than either alone
- During caloric restriction periods where exercise intensity may be reduced

IMPORTANT DISTINCTION: MOTS-c is an exercise mimetic — not an exercise replacement. The optimal research protocol combines MOTS-c supplementation with physical training, producing synergistic metabolic benefits greater than either intervention alone.

MT

MOTS-c Mitochondrial-Derived Peptide

Exercise Mimetic · Metabolic Regulator · Longevity Signal

Key Benefits of MOTS-c

Research-supported areas of effect

Metabolic Health & Insulin Sensitivity

The most extensively studied area of MOTS-c research:

- Significant improvement in insulin sensitivity — documented in multiple rodent and emerging human research models
- Enhanced glucose uptake by skeletal muscle independent of insulin signaling alone
- Reduced fasting blood glucose and improved post-meal glucose management
- Reversal of high-fat diet-induced insulin resistance in preclinical models
- Relevant to type 2 diabetes research — MOTS-c levels are lower in diabetic individuals
- Improved glucose homeostasis even without dietary changes in research subjects

Exercise Performance & Endurance

- Increased exercise capacity and running endurance in research models — dramatic improvements in treadmill performance documented
- Enhanced fat oxidation during exercise — greater proportion of fat burned as fuel
- Reduced exercise-induced fatigue through improved metabolic efficiency
- Faster recovery between training sessions through mitochondrial support
- Particularly relevant for endurance athletes and age-related decline in performance

Body Composition

- Anti-obesity effects documented in high-fat diet research models
- Reduced fat mass accumulation through enhanced fat oxidation
- Muscle preservation during caloric restriction — AMPK activation supports lean mass maintenance
- Improved muscle-to-fat ratio over sustained use
- Synergistic fat loss effects when combined with Retatrutide

Longevity & Healthy Aging

- MOTS-c levels naturally decline with age — levels are significantly lower in older adults compared to young adults
- Administration has extended lifespan and healthspan in multiple preclinical models
- Reduces markers of biological aging including inflammatory cytokines and oxidative stress markers
- Supports mitochondrial quality and function — a primary driver of cellular aging
- Potential relevance to age-related muscle loss (sarcopenia) research

BENEFIT AREA	KEY MECHANISM	RESEARCH STATUS
Insulin Sensitivity	AMPK/GLUT4 activation	Strong preclinical; emerging human
Exercise Performance	Mitochondrial biogenesis	Documented in animal models

MOTS-c

Key Benefits — What the Research Suggests

Fat Loss	Enhanced fat oxidation, AMPK	Preclinical + mechanistic data
Muscle Preservation	AMPK-mediated protein sparing	Preclinical evidence
Longevity	Anti-inflammatory, mitochondrial	Active research area
Blood Sugar Control	Glucose uptake enhancement	Multiple preclinical studies

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WHO IS IT FOR?

Ideal Candidates & Use Cases

Who Is MOTS-c For?

Ideal research candidates across multiple health goals

Athletes & Performance-Focused Individuals

Those seeking enhanced endurance, improved metabolic efficiency during training, faster recovery, and better fat oxidation. MOTS-c amplifies the metabolic response to training — producing greater mitochondrial adaptation and performance gains from the same workout volume. Particularly relevant for endurance athletes and those in cutting phases who want to preserve muscle while maximizing fat oxidation.

Metabolic Health & Insulin Resistance

Individuals dealing with insulin resistance, pre-diabetes, metabolic syndrome, or blood sugar dysregulation. MOTS-c addresses the mitochondrial dysfunction and impaired AMPK signaling that underlie these conditions — working at the root mechanism rather than just managing symptoms. Research shows particular promise for individuals where exercise alone has been insufficient.

Biohackers & Longevity Researchers

MOTS-c is encoded in mitochondrial DNA — one of the most ancient and consequential genomes in the cell. Its role as a longevity signal, its anti-inflammatory properties, and its ability to activate the same pathways as caloric restriction and exercise make it one of the most scientifically fascinating compounds in the longevity space.

45+ Anti-Aging Consumers

MOTS-c levels decline significantly with age — the same pattern seen with NAD+ and other critical metabolic signals. Restoring youthful MOTS-c levels may support mitochondrial health, muscle preservation, metabolic rate maintenance, and the resistance to metabolic disease that characterizes younger physiology.

Weight Loss & Body Recomposition

Individuals using Retatrutide or other fat-loss protocols who want to maximize muscle preservation and metabolic rate during the process. MOTS-c's AMPK activation supports lean mass retention and enhances fat oxidation — making it the ideal metabolic companion to caloric restriction or GLP-1 protocols.

Limited Exercise Capacity

Those with mobility limitations, chronic injury, post-surgical restrictions, or age-related exercise limitations who want to access some of the metabolic benefits of physical training through MOTS-c's exercise-mimetic properties. While not a replacement for movement, it can support metabolic health in those who cannot exercise at sufficient intensity.

Protocols & Delivery

How MOTS-c is administered in research contexts

MOTS-c is administered via subcutaneous (SubQ) injection. As a small peptide with systemic effects, it has favorable bioavailability via this route and is well-tolerated in research contexts. Timing relative to exercise appears to influence the magnitude of its metabolic effects.

Timing Considerations

- Pre-workout administration (30–60 min before training): may amplify the exercise-induced AMPK response, producing synergistic metabolic effects beyond either alone
- Morning fasted administration: aligns with natural circadian AMPK activity and supports metabolic benefits throughout the day
- Post-workout is also used in some research protocols — timing appears flexible compared to compounds where timing is critical (e.g., GH secretagogues)
- Consistent daily or every-other-day administration is more common than single weekly injections due to the shorter half-life

ASPECT	DETAILS
Delivery Method	Subcutaneous (SubQ) injection using insulin syringe
Injection Sites	Abdomen, thigh, or deltoid — rotate sites
Frequency	Daily or every other day is most common in research protocols
Best Timing	Pre-workout (30–60 min prior) or morning fasted state
Reconstitution	Add bacteriostatic water slowly; swirl gently; do not shake
Storage	Refrigerate after reconstitution; use within 30–60 days; never freeze
Cycling	Can be used continuously; 8–12 week cycles with 4-week rest also used

MOTS-c has a shorter half-life than longer-acting peptides like CJC-1295 (DAC) — making more frequent, smaller administrations preferable to less frequent larger doses. This mirrors the body's natural pulsatile pattern of endogenous MOTS-c release during exercise and metabolic stress.

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STACKING MOTS-C

Synergistic Combinations for Amplified Results

Stacking MOTS-c

Intelligent combinations for enhanced outcomes

MOTS-c is one of the most stackable compounds in the catalog — its AMPK/mitochondrial mechanism is complementary to virtually every other metabolic and performance compound.

— The Mitochondrial Power Stack

MOTS-c + NAD+

The most direct and synergistic pairing in the catalog. NAD+ is the fuel that powers mitochondrial ATP production — the raw material the mitochondria need to function. MOTS-c is the signaling molecule that tells mitochondria to multiply and operate more efficiently. Together, NAD+ provides the substrate and MOTS-c provides the stimulus — producing a mitochondrial optimization that neither compound achieves alone. Considered the gold standard energy and longevity stack.

BEST FOR: *Biohackers · Longevity · Chronic fatigue · Athletic performance · 45+ consumers*

— The Body Recomposition Stack

MOTS-c + Retatrutide

Retatrutide drives fat loss through triple receptor agonism. MOTS-c amplifies fat oxidation through AMPK activation and preserves lean muscle through metabolic reprogramming. The combination produces maximum fat loss with minimum muscle loss — the defining goal of body recomposition. MOTS-c also helps counteract the metabolic slowdown that can accompany aggressive caloric restriction.

BEST FOR: *Body recomposition · Weight loss · Muscle preservation · Metabolic syndrome*

— The Performance & Longevity Stack

MOTS-c + CJC-1295 / Ipamorelin

CJC-1295 and Ipamorelin restore youthful GH output — supporting muscle growth, fat metabolism, sleep quality, and tissue repair. MOTS-c adds exercise-mimetic metabolic reprogramming and mitochondrial biogenesis. Together they address the hormonal and mitochondrial dimensions of performance and anti-aging simultaneously.

BEST FOR: *Performance athletes · Anti-aging · Muscle · Sleep optimization · 35+ consumers*

— The Complete Metabolic Transformation Stack

MOTS-c + NAD+ + Retatrutide

The most comprehensive metabolic optimization protocol in the LVL UP RX catalog. Retatrutide drives unparalleled fat loss through three receptor pathways. MOTS-c preserves muscle, amplifies fat oxidation, and maintains metabolic rate. NAD+ keeps cellular energy production high during the deficit and supports mitochondrial health throughout. Every major variable in metabolic transformation is addressed simultaneously.

BEST FOR: *Maximum fat loss · Full body recomposition · Premium metabolic protocol*

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WHAT TO EXPECT

Timeline, Results & Realistic Outcomes

What to Expect

A realistic, research-grounded timeline for MOTS-c

MOTS-c's effects build progressively as mitochondrial biogenesis accumulates and metabolic reprogramming takes hold. Energy improvements and exercise performance gains tend to emerge first. Insulin sensitivity and body composition changes develop over weeks of consistent use. Longevity and anti-aging effects accumulate over months.

TIMEFRAME	METABOLIC EFFECTS	PERFORMANCE EFFECTS	LONGEVITY EFFECTS
Week 1–2	Improved energy levels; early insulin sensitivity gains	Enhanced workout energy; reduced fatigue during training	Anti-inflammatory effects beginning
Week 3–4	Measurable glucose metabolism improvements	Noticeable endurance gains; faster recovery	Mitochondrial biogenesis accumulating
Week 6–8	Significant insulin sensitivity improvement	Clear performance increases; better fat oxidation	Reduced inflammatory markers
Week 10–12	Body composition shifts; reduced metabolic syndrome markers	Peak performance benefits; mitochondrial density up	Systemic anti-aging effects building
Ongoing	Sustained metabolic health; longevity benefits accumulate	Maintained performance gains with continued use	Long-term mitochondrial health and resilience

EXERCISE AMPLIFICATION: *Research subjects using MOTS-c alongside a training program consistently show greater metabolic adaptations than those exercising without it. For optimal results, MOTS-c should be used in conjunction with regular physical activity — not as a substitute for it.*

Side Effect Profile

MOTS-c has a favorable tolerability profile in research contexts. As an endogenous peptide encoded in the body's own mitochondrial DNA, it is well-recognized by human biology:

- Injection site: mild temporary redness or swelling; resolves quickly
- No documented hormonal disruption — MOTS-c does not affect sex hormones, cortisol, or the HPG/HPA axes
- No receptor desensitization documented at research-appropriate doses
- Mild hypoglycemia is theoretically possible in individuals with pre-existing insulin sensitivity; monitor blood glucose if diabetic or on glucose-lowering medication
- Generally considered one of the most well-tolerated compounds in the metabolic peptide category
- No known negative interactions with most supplements or common medications at standard doses

As with all research compounds, individual responses vary. Consult a qualified healthcare provider before beginning any MOTS-c protocol, particularly if managing diabetes, metabolic disease, or taking glucose-lowering medications.

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RESEARCH NOTES

Important Information & Compliance

Research Notes & Disclaimer

Please read carefully.

All products offered by LVL UP RX are sold strictly as research compounds for investigational use only. They are not intended for human consumption and are not approved by the FDA or any equivalent regulatory authority for therapeutic, preventive, or diagnostic use in humans.

The Research Landscape

MOTS-c is a rapidly growing area of metabolic and longevity research. The foundational 2015 discovery paper by Lee et al. in Cell Metabolism established its role as a mitochondrial hormone with systemic metabolic effects. Subsequent research has validated its AMPK-activating mechanism, exercise-mimetic properties, and anti-aging effects in multiple preclinical models. Human clinical trials are limited but emerging. This guide presents findings accurately and without exaggeration.

What We Will Never Claim

- That MOTS-c treats, cures, or prevents any disease or medical condition
- That MOTS-c is FDA approved or safe for human use as medicine
- That MOTS-c replaces exercise — it is an exercise mimetic and complement, not a substitute
- That results are guaranteed — individual responses vary significantly
- That this compound replaces medical treatment or professional healthcare guidance

Selected Research References

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• Woodhead, J.S.T. et al. (2023). MOTS-c treatment and exercise are not additive in maintaining skeletal muscle function in a model of hind limb unloading. Frontiers in Physiology.

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> *MOTS-c represents one of the most fascinating discoveries in mitochondrial biology in decades. At LVL UP RX, we believe understanding the science is what separates informed research decisions from guesswork. We're here to provide both.*

LVL UP RX · PEPTIDES · SCIENCE-BACKED. RESULTS-DRIVEN.

For research use only. Not for human consumption. Consult a qualified healthcare professional.

Research Notes

Important Information & Compliance