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PATIENT GUIDE

MOTS c *for metabolic health*

MOTS c is a small peptide encoded in the DNA of the mitochondria. Animal studies link it to metabolism and exercise capacity, and no published study has yet given it to a person.

COMPOUND	CLASS	ROUTES	RESEARCH	SOURCES
MOTS c (16 aa)	Mitochondrial peptide	Injection	Mostly animal	27 · PMID linked

§ 01

Overview

MOTS c is a very small peptide, only 16 amino acids long, that your own mitochondria make. Mitochondria are the parts of your cells that turn food into usable energy, and the discovery that they also release signaling peptides like MOTS c changed how researchers think about metabolism and aging. In laboratory and animal studies MOTS c behaves like a signal that helps the body handle fuel, and its levels rise with exercise and tend to fall with age.[1] [2]

This guide sets out what that research has and has not shown. Almost all of the research that gave MOTS c to a living body was done in mice, and the human studies to date have measured the body's own MOTS c without testing it as a medicine. Every source is listed at the end with a link so you can read it yourself.

16	**Amino acids long.** MOTS c is a 16 amino acid peptide encoded within the mitochondrial 12S rRNA gene. It was discovered in 2015 and named for its origin, the mitochondrial open reading frame of the 12S rRNA type c.[1]
11.9x	**Rise after one workout.** In 10 healthy young men, a single bout of cycling raised MOTS c measured inside muscle about 11.9 times over the pre exercise level, and roughly 1.5 times in the blood.[2]
Nucleus	**It can act on your genes.** Under metabolic stress, MOTS c moves into the cell nucleus and helps switch on protective, antioxidant related genes, which is unusual for a mitochondrial peptide.[3]
Falls with age	**Levels change over life.** In a study of 104 healthy men, the amount of MOTS c circulating in the blood was lower in older men than in younger men.[4]

§ 02

What MOTS c is

Most of the signals in your body are made from instructions in the nucleus, the cell's main library of DNA, but MOTS c is written into the small, separate genome that lives inside your mitochondria, in a stretch of the 12S rRNA gene. The peptide is read out in the cell body, can be found in many tissues and in the blood, and appears to be highly conserved across species,

which usually suggests a function the body relies on.[1][5]

Because its main target seems to be skeletal muscle, and because it rises with exercise, researchers sometimes describe MOTS c as an exercise mimetic, meaning a molecule that reproduces some of the signals exercise sends.[1][2][6] The term describes what it does in the laboratory, and taking it has not been shown to equal exercising. The synthetic version used in research is the same 16 amino acid sequence, prepared either as the free peptide or as an acetate salt.[7]

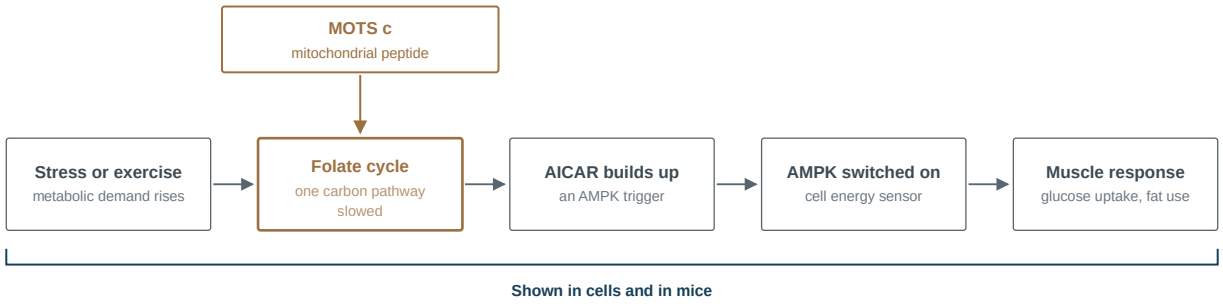
MOTS C AT A GLANCE	
Name	MOTS c
Full name	Mitochondrial open reading frame of the 12S rRNA type c[1]
Structure	A peptide of 16 amino acids (Met Arg Trp Gln Glu Met Gly Tyr Ile Phe Tyr Pro Arg Lys Leu Arg); sold as the free peptide or an acetate salt[7]
Origin	Encoded in the mitochondrial genome, not the nucleus; made naturally in the body and also made synthetically[1]
Class	A mitochondrial derived peptide, one of a small family that includes humanin[6]
How it is given	Studied in animals as an injection under the skin or into the abdomen; no form has been tested in people[7]

§ 03

How MOTS c works

The best worked out idea comes from cell and mouse studies, and it centers on an energy sensor called AMPK. AMPK acts as a switch that cells flip when they need to make and spend energy efficiently, the same switch that exercise and the diabetes drug metformin are known to engage.[1][6]

In those studies, MOTS c slows down part of a chemical assembly line called the folate cycle. When that line slows, a molecule called AICAR builds up, and AICAR is a known trigger for AMPK. Once AMPK is switched on, skeletal muscle takes up more glucose, and in cell studies fat burning also rose.[1] Separately, when a cell is under stress, MOTS c can move into the nucleus and help turn on genes that defend against oxidative stress, working alongside a master regulator called NRF2.[3]



In cells and mice, MOTS c works through the AMPK energy pathway. MOTS c slows the folate cycle, which lets AICAR accumulate and switch on AMPK, the cell's energy sensor, in skeletal muscle.[1] Under stress it can also enter the nucleus and help turn on antioxidant genes.[3] Whether either chain works the same way in the human body has not been measured.

This chain was mapped mainly in cells and in mice, and the exact molecule that MOTS c first latches onto is still unknown, which the FDA noted in its 2026 review.[8] Not every experiment has been positive either. In one cell study using cells that carried a disease causing mitochondrial mutation, adding MOTS c did not improve mitochondrial function at all.[9]

KEY POINT

The AMPK pathway is a strong, repeatable laboratory finding, and it explains why MOTS c is studied for metabolism, muscle and exercise. The evidence for it comes from cells and animals, so a benefit in people has not been established.[1][8]

§ 04

What the research shows

The published work on MOTS c is large and growing quickly, and it falls into two very different groups. Studies that gave MOTS c to an animal are where the benefits have been seen. Studies in people measured the body's own MOTS c, and they show associations without testing whether it works as a treatment.

What the evidence supports

In mice, giving MOTS c changes metabolism in consistent ways. The founding study showed that MOTS c prevented diet induced obesity and improved insulin sensitivity in mice, raising whole body insulin sensitivity by roughly 30 percent in one test, and it traced the effect to the AMPK pathway in skeletal muscle.[1] A later study found that MOTS c improved treadmill performance in young, middle aged and old mice, and that old mice treated with it ran about twice as long as untreated old mice; the same paper confirmed that exercise raises MOTS c in people.[2] In other animal models, MOTS c reduced bone loss after ovary removal,[10] protected against vascular calcification,[11] and reduced muscle wasting signals.[12] These findings have been repeated, though with few exceptions they come from mice.

What is not yet known

No published study has given MOTS c to a person, and every human result describes the body's own MOTS c. Those studies show that circulating MOTS c falls with age,[4] rises with exercise,[2][13] and tends to be lower in some metabolic and vascular conditions, including obesity in boys,[14] coronary endothelial dysfunction,[15] and obstructive sleep apnea.[16] A natural variant of the MOTS c gene, called K14Q, that makes a weaker version of the peptide has been linked to a higher rate of type 2 diabetes in men of Japanese descent.[17] These associations suggest MOTS c is part of how the body responds to metabolic stress, but they do not show that giving MOTS c changes health in people.

WHAT THE HUMAN STUDIES MEASURED Every human study measured the body's own MOTS c, and none gave it as a treatment

STUDY	N	WHO	WHAT IT FOUND
Reynolds et al, 2021[2]	10	Healthy young men, one exercise session	Muscle MOTS c rose about 11.9 times and blood MOTS c about 1.5 times; blood levels were back to baseline after 4 hours of rest
von Walden et al, 2021[13]	30	Adults; endurance or resistance exercise	Endurance exercise showed a trend to raise blood MOTS c; resting levels did not track age
D'Souza et al, 2020[4]	104	Healthy young, middle aged and older men	Blood MOTS c lower in older men; muscle MOTS c higher with age
Du et al, 2018[14]	97	Obese and healthy children	MOTS c lower in obese boys, linked to insulin resistance markers

STUDY	N	WHO	WHAT IT FOUND
Baylan and Yarar, 2021 [16]	90	Obstructive sleep apnea and controls	Serum MOTS c lower with sleep apnea and fell as severity rose
Zempo et al, 2021 [17]	27,527	Japanese and Japanese American cohorts, genetic analysis	A weaker MOTS c variant (K14Q) linked to more type 2 diabetes in men

SUMMARY

MOTS c rests on a strong and repeated body of cell and animal research and on a consistent set of human observations that connect it to metabolism, fitness and age. No published study has yet given MOTS c to a person and measured anything afterward, so it is promising in the laboratory and unproven as a treatment in people.

§ 05

How MOTS c is given

MOTS c has been studied by only a few routes, and no regulator anywhere has set a dose for people. Because no human study has given MOTS c, there is no human dose to point to; where a dose appears below it is the dose used in an animal study, labelled as such, and any dose used in your care is set by your physician.[8] Under the federal compounding policy, pharmacies may prepare MOTS c acetate only as an injection under the skin or into the muscle. [19]

Injection under the skin

This is the route proposed when MOTS c was put forward to the FDA for compounding, as 5 mg and 10 mg vials for injection under the skin, and it is the route the federal policy now allows.[8] [19] It has not been studied in people. In the animal work, mice generally received MOTS c into the abdomen (an injection into the belly cavity that is practical in mice but not used in people) at doses such as 0.5 to 15 milligrams per kilogram; these cannot be translated into a human dose. [1] [2] As with any injection, some redness or tenderness where the needle went in is possible.

Injection into the muscle

The federal policy also allows MOTS c acetate to be compounded for injection into the muscle.[19] As with the injection under the skin, there is no published human study of MOTS c given this way, so your physician would set any dose and schedule. [8]

By mouth

Taking MOTS c as a capsule is not a realistic option today. In an animal study, MOTS c taken by mouth gave no significant benefit, and researchers had to engineer a modified, cell penetrating version to get it to work by that route.[20] The federal policy does not cover MOTS c by mouth. [19]

Routes outside the policy

You may see MOTS c marketed as part of an intravenous drip or a blend with other peptides. A vein infusion has not been studied in people and is not a route the federal policy covers for MOTS c, and the policy covers only single ingredient products, so any blend falls outside it.[19] In human blood tested in a dish, MOTS c was also broken down quickly, which raises a real question about how much of an injected dose stays active and for how long. [21]

COMPARING THE OPTIONS				
	UNDER THE SKIN	INTO THE MUSCLE	BY MOUTH	INTO A VEIN OR AS A BLEND
How it is given	Small injection	Injection in clinic	Capsule	Infusion or mixed product
Covered by the policy	YES [19]	YES [19]	NO [19]	NO [19]
Human research	None published [8]	None published [8]	Not effective in animals [20]	None published [8]
Published dose in people	None; set by physician	None; set by physician	None	None

Your physician can help you decide whether MOTS c fits your goals, and if so, which approved route and schedule make sense for you.

§ 06

What to expect

The benefits people hear about, such as better metabolism and exercise capacity, come from mice, where MOTS c was given over days to weeks and researchers measured running time, body weight and blood sugar. [1] [2] The human studies did not give MOTS c and did not measure how anyone felt; they measured the body's own MOTS c in blood or muscle. [8]

No published timeline exists for how soon a person would notice anything, because that has never been tested. If you and your physician decide to proceed, we treat it as a defined trial with a clear goal written down at the start and a date to review it.

DURING A COURSE

- If you are using injections, you will be shown how to give them and how to store the vials.
- Keep a simple note of your energy, exercise and any changes you are tracking, so we can look at them together.
- Tell us about anything that feels unusual, including redness or swelling at an injection site that does not settle.

§ 07

Safety

The safety of MOTS c in people is unknown, because it has not been given to people in a published study. In its 2026 review the FDA found no clinical studies and no human exposure data for MOTS c by any route, and its adverse event database held no reports, although the agency noted that pharmacies compounding for individual patients generally do not report side effects to it. [8] The FDA also found no animal toxicity studies of MOTS c. [8] In one long term mouse study, treated mice kept a body weight similar to untreated mice, although they ate less, [2] and animals cannot tell us about the uncommon or long term risks that matter to people.

MOTS c is a peptide given by injection, and the FDA raised a general concern that injected peptides can, in principle, provoke an immune response, a concern it could not rule out because the quality data were incomplete. [8] The quality and purity of the preparation also matter a great deal for any compounded peptide, which is one reason the federal policy requires a tested ingredient source. [19]

TELL YOUR PHYSICIAN BEFORE STARTING IF ANY OF THESE APPLY

- You are pregnant, trying to conceive, or breastfeeding.
- You have diabetes or take any medicine that lowers blood sugar, since MOTS c acts on glucose handling in animals.
- You have a current or past cancer diagnosis, or you are under surveillance for one.
- You have had an allergic reaction to an injected medicine or peptide before.
- You compete in a sport that tests for drugs.
- You take any prescription medication, over the counter product or supplement. Please bring the full list.

Long term safety data on MOTS c in people do not exist, because there is no published human use of any length.[8] For that reason we review how you are doing at set points.

§ 08

Is this right for you

MOTS c may suit some patients who are interested in metabolic health and comfortable with early, mostly animal evidence, and it is not the right starting point for others. The purpose of your consultation is to work out which group you are in.

Before we begin

- [ ] A review of your medical history, current medications and supplements
- [ ] Blood pressure, weight, and a short history of your activity and energy
- [ ] Baseline bloodwork, including glucose and metabolic markers, so that anything we see later can be compared against a starting point
- [ ] A clear note of what you are hoping to feel or change, written down, so we can tell together whether it worked

If you are coming to us because of fatigue, weight or blood sugar concerns, we will look for findable and treatable causes first. Those problems often have specific treatments with strong evidence behind them, and finding one of those would serve you better than a peptide that has not been tested in people.

Reviewing your progress

We will reassess against your documented starting point after a defined period. If you are doing well, we will plan together whether and how to continue. If you are not, we will say so and look at other options. You are welcome to stop at any time.

QUESTIONS TO ASK YOUR PHYSICIAN

What has actually been shown in people, and what has only been shown in animals? How will we measure whether this is working for me? What would make you recommend stopping? Which approved options should I consider first?

§ 09

Regulatory status

MOTS c is not approved by the U.S. Food and Drug Administration for any indication. It is not part of any FDA approved medicine and has no official United States Pharmacopeia standard.[8] Since 30 October 2026, a federal enforcement discretion policy from the U.S. Department of Health and Human Services has allowed licensed pharmacies to compound MOTS c acetate under strict conditions. [18] [19] The conditions that matter most to you are these:

- The preparation is made on a prescription written for you personally, by a state licensed pharmacy or physician.
- MOTS c is its only active ingredient. Blends and stacks are not covered.
- It is given only as an injection under the skin or into the muscle.
- The ingredient comes from an FDA registered manufacturer and carries a certificate of analysis.
- Serious side effects and quality problems are reported to the FDA.

The policy is temporary. It applies until the FDA addresses MOTS c in a final rule on the list of substances pharmacies may use in compounding, and it may be revisited. It is also not an approval. The policy itself states that compounded drugs are not FDA approved and that the FDA does not review their safety, effectiveness or quality before they are sold.[18] Prescribing a compounded or unapproved preparation is lawful and common in American medicine, and it is a decision your physician makes with you. It does mean no regulator has reviewed this preparation for your use, and you should know that before you consent.

The policy follows earlier steps in the FDA's review. In April 2026 the FDA updated its list of bulk substances that may present significant safety risks, and MOTS c is now shown there as withdrawn from that category.[22] In July 2026 the FDA's Pharmacy Compounding Advisory Committee considered MOTS c for obesity and osteoporosis and voted 7 to 5 to recommend adding it to the list of substances pharmacies may use in compounding, although FDA staff had recommended against it. [23] [8] The committee's vote is advisory. The FDA must still make its own decision and complete a formal rulemaking process.

If you compete in sport, please know that MOTS c is named on the 2026 World Anti Doping Agency Prohibited List, in section S4.4.1 among activators of the enzyme AMPK, and it is prohibited at all times, both in and out of competition.[24] The federal compounding policy does not change this. If you are subject to drug testing, please tell us before starting, and check your own organization's rules.

If you would like details about the preparation used in your treatment, please ask.

§ 10

Common questions

Has MOTS c been tested in people?

Not as a treatment. No published study has given MOTS c to a person; the FDA confirmed this in its 2026 review.[8] The human studies that exist measured the body's own MOTS c in blood or muscle and found that it rises with exercise and falls with age. [2] [4] Those findings do not show that giving MOTS c helps.

Is it safe to try, and what side effects should I expect?

The safety of MOTS c in people is unknown, because it has not been given to people in a published study, and the FDA found no human safety data and no adverse event reports.[8] The animal studies were not designed to test safety, and the FDA found no animal toxicity studies. [8] As with any injection, the most likely experience is some redness or tenderness where the needle went in.

How soon will I notice a difference?

The studies did not measure that. The benefits seen with MOTS c, in metabolism and exercise capacity, were measured in mice, and no human study has tracked how a person feels on it.[1] [2] [8] We suggest treating it as a defined trial with a clear goal and a review date.

How is it given, and for how long?

Under the current federal policy, compounded MOTS c acetate is given as an injection under the skin or into the muscle.[19] No regulator has set a dose or a course length for people, and there is no human study to base one on, so your physician sets both with you.[8]

Can I take it together with other peptides?

The federal policy covers only preparations with a single active ingredient, so a blend or stack that contains MOTS c falls outside it.[19] If you already take other peptides or supplements, please bring the full list so your physician can review them with you.

Who should not use it?

Anyone who is pregnant, trying to conceive or breastfeeding should talk with their physician before starting, as should anyone with diabetes or on medicines that lower blood sugar, since MOTS c acts on glucose handling in animals.[1] A current or past cancer diagnosis, a history of reacting to an injected medicine, and competing in a tested sport are all reasons to discuss it carefully first.

How will we know if it is working?

Before you begin, we will write down with you what you are hoping to change and record a starting point, including baseline bloodwork and metabolic markers. After a defined period we will reassess against that starting point and decide together whether to continue. Because no human study has defined what to expect or when, this shared record is how we judge it for you.[8]

Where is a compounded medicine made, and who oversees it?

Federal law sets out two kinds of compounding. Under section 503A, a state licensed pharmacy or physician prepares a medicine for one patient against that patient's own prescription, and the state board of pharmacy carries the day to day oversight while the FDA inspects for cause and on surveillance.[25] Under section 503B, an outsourcing facility registers with the FDA, works to federal manufacturing quality standards, reports adverse events and the products it makes to the agency, and is inspected by the FDA on a risk based schedule; it may also supply a clinic directly rather than for one named patient.[26] We use both kinds, and which one prepares your medicine depends on the preparation. For MOTS c the October 2026 federal policy applies to section 503A compounding only.[18]

Is a compounded medicine the same as an FDA approved one?

No, and the difference matters. A compounded preparation is not FDA approved, and the agency does not check its safety, effectiveness or quality before it is sold, which is why an approved product is the first choice whenever one fits your situation.[25] What a prescription from a licensed pharmacy or a registered outsourcing facility does give you is a named prescriber, a facility answerable to a state board or to the FDA, ingredients that meet federal requirements, and a route for reporting a problem. A vial bought online and labelled for research use only has none of that: the FDA treats those products as unapproved new drugs when they are meant for people, and has written to the companies selling them.[27] Please do not use one.

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