

# MOTS-c

(also written MOTSc)

RESEARCH USE ONLY

A tiny signal written in the mitochondria's own DNA, studied for how cells manage fuel.

NOT FDA APPROVED · EVIDENCE TIER D

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## 1 What the name stands for

**M**

**Mitochondrial**  
the cell's power plant

**O**

**Open reading frame**  
code that can be read into a protein

**T**

**Twelve**  
the "12" in 12S

**S**

**S (Svedberg)**  
a size unit: 12S names the RNA gene it hides in

**c**

**-c**  
the finders' label for this reading frame

All together: Mitochondrial Open-reading-frame of the Twelve-S rRNA gene, reading frame c. A short message hidden in the power plant's own instruction book.

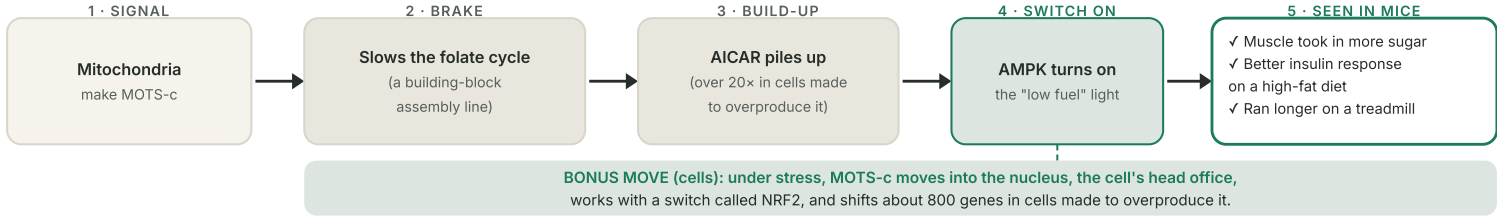
## 2 Description & origin

Most of a cell's DNA sits in the nucleus, its head office. But mitochondria, the cell's power plants, carry a small set of their own. For decades scientists thought it held only power-plant parts.

In 2015, Changhan Lee and Pinchas Cohen at USC showed it also codes a 16-amino-acid peptide: MOTS-c, the second signal like this ever found (after humanin, 2001). It shows up in human and mouse blood, so it may work across the body like a hormone. In mice, injected MOTS-c reached muscle. In people, not shown.

## 3 How it works (mechanism of action)

Think of a muscle cell as a factory. In cell and mouse studies, MOTS-c acts like a note from the power plant: "Fuel is tight. Use it smarter."



## 4 Research overview

**2015**

Discovered; blocks diet weight gain (male mice)

**2018**

Seen entering the nucleus (cells)

**2018-21**

First human trial: lookalike CB4211 (88 people)

**2021**

Exercise raises it (10 men); old mice fitter

**2026**

First trial of real MOTS-c begins

| AREA                                        | WHAT THE STUDIES FOUND                                                                                            |
|---------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| <b>Weight &amp; sugar</b> <span>mice</span> | Male mice on a high-fat diet gained less weight and kept a better insulin response. Female mice showed no effect. |
| <b>Fitness &amp; age</b> <span>mice</span>  | Mice ran longer at every age. Grip didn't improve in young mice; it did in old mice. Lifespan just trended up.    |
| <b>Exercise</b> <span>people</span>         | One bike ride raised it in muscle and blood (10 young men). A second study saw only a trend.                      |
| <b>Genes</b> <span>people</span>            | A variant found in Northeast Asian people was linked to more type 2 diabetes in men, mostly inactive men.         |

## Quick facts

|               |                                                                                            |
|---------------|--------------------------------------------------------------------------------------------|
| Type          | Peptide (a short chain of amino acids)                                                     |
| Size          | 16 amino acids · 2,174.6 g/mol                                                             |
| Sequence      | MRWQEMGYIFYPRKLR                                                                           |
| Origin        | Mitochondrial DNA (12S rRNA gene). Reported 2015, USC                                      |
| Key pathway   | AMPK, the cell's "low fuel" light <span>cells</span> <span>mice</span>                     |
| Direct target | CK2, an enzyme it binds and switches on <span>cells</span> <span>mice</span>               |
| Exercise      | Rose in muscle and blood after one bike ride <span>10 men</span>                           |
| Age           | In one study of men: lower in older men's blood, higher in their muscle                    |
| Human trials  | 2: one done (a lookalike), one recruiting                                                  |
| FDA (US)      | Not approved. July 2026 panel voted 7–5–2 for compounding, against FDA staff. No rule yet. |
| Sport         | Banned at all times by WADA (S4.4.1, AMPK activators)                                      |

## 5 How strong is the proof?

Cell studies strong

Mouse studies strong

Human blood & gene links some

Human trials of MOTS-c no results yet

Long-term safety data none yet

none some strong · our read

| HUMAN TRIAL                             | WHO, WHAT & STATUS                                                                                                                                                                                                                               |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>CB4211</b> <span>done</span>         | A lookalike, not MOTS-c. 2018–21, 88 people. Key part: 23 adults randomized (20 finished), with obesity and fatty liver, injected daily vs placebo, 4 weeks. <b>Company-reported only. Injection-site reactions 79% vs 33%. Formula dropped.</b> |
| <b>MOTS-MET</b> <span>recruiting</span> | Real MOTS-c. Began Feb 2026, Shenzhen. Plans 120 adults with prediabetes and overweight, injected daily vs placebo, 12 weeks. <b>Data collection ends Feb 2027 (est.). Dose not published.</b>                                                   |

## 6 Myths vs. the research

| WHAT YOU'LL HEAR                  | WHAT THE RESEARCH SHOWS                                                           |
|-----------------------------------|-----------------------------------------------------------------------------------|
| × "It's exercise in a bottle."    | ✓ Mice ran farther. No human study shows it replaces training.                    |
| × "It's a proven fat burner."     | ✓ It blocked weight gain in male mice. No fat-loss result in people is published. |
| × "It reverses aging."            | ✓ Old mice got fitter. Never shown in people.                                     |
| × "It's proven in people."        | ✓ One 4-week trial of a lookalike, company-reported. No MOTS-c results yet.       |
| × "It's natural, so it's safe."   | ✓ Long-term safety is unknown. FDA found no human exposure data.                  |
| × "It can replace diabetes meds." | ✓ Never tested with or against them.                                              |

## 7 How it's been studied

| IN            | HOW IT WAS USED IN STUDIES                                                                       |
|---------------|--------------------------------------------------------------------------------------------------|
| <b>Cells</b>  | Added to cells, or made by engineered cells, to trace each step.                                 |
| <b>Mice</b>   | Given by injection, in studies lasting from days to months.                                      |
| <b>People</b> | One finished lookalike trial (4 weeks) and one running MOTS-c trial (12 weeks), both vs placebo. |

**No dose has been established for any use.** The one MOTS-c trial hasn't published its dose, and FDA found no human safety data. PUURA doesn't give dosing or usage guidance. MOTS-c is sold for laboratory research only.

**The big learning lesson.** The cell's power plant has a voice of its own, and that's a recent finding. But nearly everything we know comes from cells and mice. The founding studies came from one group whose leaders held stock in a now-closed company that tested a lookalike. No human MOTS-c results before 2027. So treat MOTS-c as a research tool for studying how mitochondria talk to the rest of the cell. Each lot should match MRWQEMGYIFYPRKLR by mass on LC-MS, with purity by HPLC, and match its certificate.

Tiers: A approved · B late human trials · C early human data · D mostly animal/lab · E one lab. Key sources: Lee C et al. *Cell Metab* 2015;21:443–54 · Kim KH et al. *Cell Metab* 2018;28:516–524.e7 · Reynolds JC et al. *Nat Commun* 2021;12:470 · Zempo H et al. *Aging* 2021;13:1692–1717 · von Walden F et al. *J Appl Physiol* 2021;131:1035–42 · Kumagai H et al. *iScience* 2024;27:111212 · D'Souza RF et al. *Aging* 2020;12:5244–58 · ClinicalTrials.gov NCT03998514, NCT07505745 · CohBar SEC filings, Aug 2021 and FY2022 10-K · FDA PCAC briefing, MOTS-c, July 2026 · Federal Register 2026-07361 · WADA Prohibited List 2026, S4.4.1. **Research and education only.** Not medical advice. PUURA sells research compounds for laboratory use only, not for human or veterinary use, and nothing here recommends using any compound in people or animals. © 2026 PUURA LLC.