MOTS-c

Mitochondrial-Derived Microprotein

What It Is & What It Does

MOTS-c is a tiny protein that's unusual because it's coded by your mitochondrial DNA, not your regular DNA — and your muscle naturally makes a lot more of it during and after exercise. It works by flipping on the same cellular energy switch (AMPK) that hard exercise and fasting activate, which is why it's often called an exercise mimetic, though that label oversells what it actually does on its own.

What The Research Shows

- In one study, muscle levels of MOTS-c increased almost 12-fold after a single bout of exercise — but this spike is specifically tied to short, high-intensity effort, not gentle movement like walking or yoga.
- A single dose given 10 minutes before an exercise test improved running performance by 12% (time) and 15% (distance) in animal research — the timing of the dose relative to exercise actually mattered in the one study that tested it.
- Separately, repeated dosing alone with no exercise at all improved how efficiently mitochondria produce energy and reduced cellular oxidative damage in a mouse study — the one effect that doesn't require exercise to show up.
- Is one of 7 peptides currently under FDA Pharmacy Compounding Advisory Committee review, which could expand legal compounding access if the review is favorable.

Men's & Women's Health Research

Men / General

- A University of Auckland study measured MOTS-c directly in the muscle and blood of healthy men across age groups: circulating (blood) MOTS-c actually declined with age, but muscle-level MOTS-c was about 1.5x higher in older men (70-81) and middle-aged men (45-55) than in young men (18-30), and was tied to the mix of muscle fiber types present.
- In mice, MOTS-c (and a related peptide, Humanin) protected sperm-producing testicular tissue from damage caused by chemotherapy given before puberty — studied specifically as a fertility-preservation approach for male cancer survivors.
- Much of the foundational exercise/performance research (the treadmill and AMPK studies) was originally conducted in male mice and young male human subjects, so the 'core' mechanism data skews more heavily toward men than women.

Women

- Women with PCOS (polycystic ovary syndrome) show significantly lower MOTS-c in both blood and skeletal muscle than women without PCOS (40 PCOS patients vs. 40 matched healthy women), linked in the study to the mitochondrial dysfunction seen in PCOS's metabolic symptoms.
- In pregnant women, MOTS-c was measurably higher in mothers and newborns in cases of obesity, and lower in cases of thyroid disorder — and a mother's blood level closely tracked her baby's umbilical cord blood level, suggesting it crosses to the baby.
- A 16-week exercise study in breast cancer survivors found MOTS-c levels changed with aerobic and resistance training, and that the response differed between Hispanic and non-Hispanic White participants — an ethnicity-linked difference, not just a sex-linked one.
- Preliminary fertility-focused research (less rigorous than the studies above) has proposed MOTS-c could improve egg quality in IVF for women with advanced maternal age, obesity, or insulin resistance, by supporting the mitochondria inside the egg cell — this is an early, less-established line of research compared to the PCOS and pregnancy findings.

Reported Side Effects

- No major adverse events reported in the available (mostly animal) research
- No established human safety profile from controlled dosing trials

Regulatory Status

Not FDA-approved. Currently under FDA Pharmacy Compounding Advisory Committee review as one of 7 peptides being considered for expanded compounding access.

Tumor Growth Research Note — MOTS-c

Category: No Documented Mechanism of Concern

MOTS-c's documented mechanism (AMPK activation, mitochondrial efficiency) is not one of the four pathways tumors typically hijack to grow (blood supply, growth signaling, spread, resistance to cell death). No cancer-risk signal has been raised in the available MOTS-c literature to date. This is stated as a genuine finding of "no documented mechanism of concern," not an assumption of safety — the compound simply hasn't been linked to tumor-promoting pathways in current research.

MOTS-c

2026 PCAC update

July 2026 FDA Advisory Vote

On July 23-24, 2026, the FDA's Pharmacy Compounding Advisory Committee (PCAC) met to vote on whether seven previously-restricted peptides should be added to the Section 503A Bulk Drug Substances list -- the list that determines what compounding pharmacies can legally prepare from a prescription. This is separate from, and later than, the April 2026 reinstatement to FDA Category 1 covered elsewhere in this document.

On July 23, 2026, PCAC voted 7-5 (two abstentions) to recommend MOTS-c for the 503A Bulks List, the narrowest margin of the four peptides reviewed that day.

A favorable PCAC vote is a recommendation, not a legal change. The FDA is not bound by it, and any formal addition to the 503A Bulks List still requires notice-and-comment rulemaking, a process that can take well over a year. As of this update, none of the peptides discussed below are legal to compound under 503A.