MOTS-c Research Summary

Research Library Summary — PHX Performance Research

For laboratory research use only. Not for human consumption. This summary describes published research and is not medical advice.

What the Research Suggests, in Plain Language

MOTS-c is a small peptide that the body makes naturally, coded by the genetic material inside mitochondria, the energy-producing parts of cells.

• In animal studies, mostly in mice, results suggest MOTS-c may be linked to better blood-sugar control, less weight gain on a high-fat diet, and more exercise endurance.

• In people, no published study has given MOTS-c to anyone. Human studies so far only measured the body's own MOTS-c levels, for example finding that levels rose after exercise.

• One human trial that gives MOTS-c is registered and recruiting. It has no results yet.

In short: the mouse results and the human measurement studies are separate lines of research. They do not show that MOTS-c is safe or effective in people.

Overview

MOTS-c is a mitochondrial-derived peptide encoded in the mitochondrial genome. It is not an approved drug.

What the Research Actually Presents

Mouse studies (animal models):

• Lee et al. Cell Metabolism 2015 (PMID 25738459): Mice given MOTS-c showed improved insulin sensitivity and increased exercise capacity in the models tested. Researchers also reported that MOTS-c treatment was associated with resistance to diet-induced obesity and improved metabolic markers in those mice.

• Subsequent mouse studies (many from Chinese groups): Animals receiving MOTS-c showed improved insulin sensitivity, reduced fat accumulation, and better exercise performance compared with control mice in the specific aging, obesity, and metabolic models used.

Human observational studies (no administration of MOTS-c):

• Sedentary adults who then performed exercise: Circulating (serum) MOTS-c levels increased measurably after the exercise sessions. These studies measured the body's own MOTS-c; they did not administer the peptide.

• Other human records in the catalog are primarily observational measurements of circulating MOTS-c levels at rest, after exercise, after heat exposure, or in relation to metformin. No published human trial has administered MOTS-c.

One registered phase 2a trial (NCT07505745) is recruiting; no results have been posted.

What the Research Suggests

In mouse models, MOTS-c administration produced measurable improvements in insulin sensitivity, resistance to diet-induced obesity, and exercise capacity under the conditions tested. These are animal findings only.

In humans, observational data show that the body's own circulating MOTS-c levels rise after exercise in previously sedentary adults. This does not test the effects of administering MOTS-c.

No published human administration studies exist. The animal results and the human observational exercise data are separate lines of evidence and do not establish that the same outcomes would occur if MOTS-c were given to people.

Mechanism and Signaling Pathways (as described in the literature)

Animal and mechanistic studies describe MOTS-c in the context of AMPK (AMP-activated protein kinase, a cellular energy sensor) activation, improved insulin signaling, and mitochondrial function in the mouse models examined. These descriptions remain limited to preclinical work.

Research Landscape

Catalog: 274 records — 5 records auto-tagged as human randomized controlled trials (RCTs): 4 randomized exercise, heat or metformin studies that measured the body's own MOTS-c (none administered MOTS-c), plus the registered phase 2a trial NCT07505745 (no results); 53 other human, 109 animal, 5 in-vitro, 54 reviews, 2 systematic reviews/meta-analyses, 46 other.

Key Studies

• Lee C et al. 2015 (Cell Metabolism): animal study (mice), metabolic and obesity models (PMID 25738459).

• von Walden F et al. 2021: human study measuring circulating MOTS-c after endurance exercise; no MOTS-c given (PMID 34351816).

• Dieli-Conwright CM et al. 2021: randomized exercise study in breast cancer survivors measuring circulating MOTS-c; no MOTS-c given (PMID 34413391).

• NCT07505745: registered phase 2a randomized, placebo-controlled trial; recruiting, no results.

Safety Findings Reported in the Studies

No human efficacy or safety data from administration of MOTS-c are present in the catalog.

Limitations and Evidence Gaps

No published human trials of administered MOTS-c. All administration data are from animal models. Human data are observational measurements of endogenous (the body's own) levels only.

Regulatory Status

Not an approved drug. Included in the Department of Health and Human Services (HHS) draft/interim 503A compounding enforcement-discretion policy (Federal Register 2026-22192, October 30, 2026). No final bulks-list rule.

References

Lee C et al. Cell Metabolism 2015 (PMID 25738459). von Walden F et al. 2021 (PMID 34351816). Dieli-Conwright CM et al. 2021 (PMID 34413391). NCT07505745 (recruiting, no results). Subsequent mouse studies and human observational studies listed in the research catalog.

Evidence reviewed through November 2026 (PHX research catalog snapshot of PubMed, ClinicalTrials.gov and Europe PMC).

For laboratory research use only. Not for human consumption. This summary describes published research and is not medical advice.