# AlphaFold-Based Modeling Supports Mechanistic Interpretation of Adipocyte-Derived NAA in Postprandial Thermoregulation

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**Our role: Creative Proteomics performed AlphaFold-based structural modeling and molecular docking analysis to evaluate a proposed interaction between N-acetylaspartate (NAA) and CAD. The analysis supported a mechanistic model in which NAA may engage the ATCase domain and promote CAD-associated de novo pyrimidine synthesis.**

## Background & Significance

N-acetylaspartate (NAA) is widely known as a major brain metabolite, yet its physiological functions outside the nervous system have remained unclear. This study shows that white adipose tissue (WAT) is a key regulator of circulating NAA and identifies adipocyte-derived NAA as an endocrine signal that influences postprandial body temperature and metabolic homeostasis.

## Research Gap

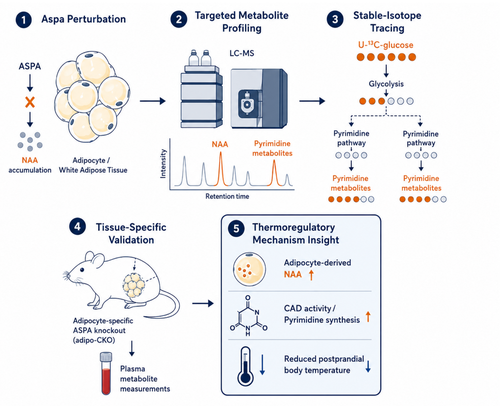
Although NAA is well studied in the central nervous system, its metabolic and physiological roles in peripheral tissues are not fully defined. In particular, it has remained unclear whether adipose-derived NAA contributes to systemic metabolite regulation, pyrimidine metabolism, or thermoregulatory control after feeding.

## Study Objective

To investigate how adipocyte-derived NAA contributes to systemic metabolic regulation and postprandial thermoregulation, and to explore whether structural modeling can provide a plausible molecular mechanism linking NAA to CAD-associated pyrimidine synthesis.

## Workflow

Aspa perturbation → targeted metabolite profiling → stable-isotope tracing → adipocyte-specific physiological validation → AlphaFold docking and mechanism modeling

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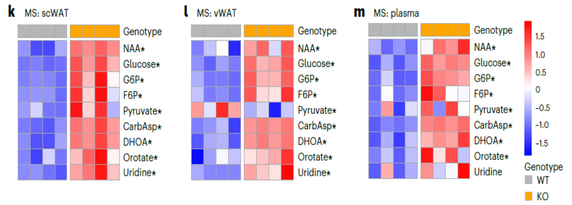
## Key Findings

### Finding 1 | Adipose ASPA governs systemic NAA and pyrimidine-related metabolite levels

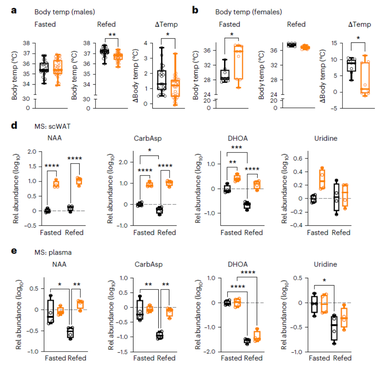
- Aspa was highly expressed in adipose tissue and increased during adipocyte differentiation.
- Whole-body Aspa deletion raised NAA levels in scWAT, vWAT, and plasma.
- Aspa knockout also increased glycolytic intermediates and pyrimidine-related metabolites, including CarbAsp, DHOA, orotate, and uridine, revealing a broad metabolic shift in WAT.




*Aspa deletion elevates NAA and reshapes pyrimidine-related metabolites in adipose tissue and plasma.*

### Finding 2 | Adipocyte-derived NAA Regulates Postprandial Temperature

- Adipocyte-specific Aspa deletion lowers postprandial body temperature.
- Plasma and WAT NAA levels increase in the refed state.
- Demonstrates endocrine function of adipocyte-derived NAA in thermoregulation.

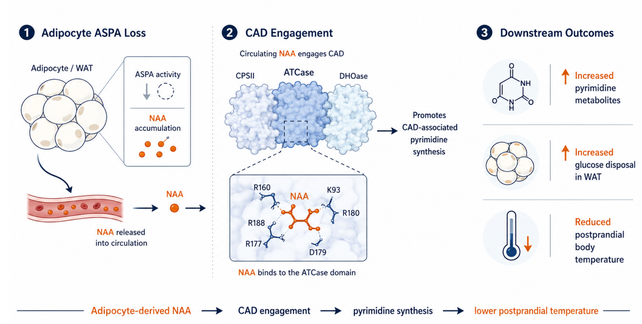



*Adipocyte-derived NAA acts as an endocrine signal, reducing postprandial temperature.*

### Finding 3 | Structural Modeling Supports A Proposed NAA-CAD Mechanistic Link

AlphaFold modeling supports NAA binding to the CAD ATCase domain. This interaction is consistent with enhanced CAD-associated pyrimidine synthesis.

The model links adipocyte-derived NAA to metabolic signaling and reduced postprandial body temperature.




*Structural modeling supported by Creative Proteomics links adipocyte-derived NAA to CAD engagement and enhanced pyrimidine synthesis, providing a mechanistic basis for systemic metabolic effects.*

## Our Contribution (Creative Proteomics)

Creative Proteomics performed **AlphaFold prediction and molecular docking** to evaluate interactions between adipocyte-derived NAA and the ATCase domain of CAD. This modeling provided mechanistic insight into how NAA may promote CAD-associated pyrimidine synthesis and regulates postprandial body temperature, supporting the interpretation of experimental observations and pathway-level effects.

### Why This Service Matters

- Provides molecular-level interpretation to help connect small-molecule signals with enzyme activity.
- Supports mechanism-focused hypotheses generation in complex metabolic and physiological studies.
- Enhances confidence in pathway-level conclusions drawn from experimental data.

### What Customers Gain

- Hypothesis-generating mechanistic insight into protein–metabolite interactions, helping prioritize follow-up experiments and reduce exploratory wet-lab burden.
- Integration with physiological and biochemical data to support interpretation of systemic effects.
- Actionable interpretation that can inform experimental design, pathway analysis, or mechanistic publications.
- Flexible, expert service tailored to specific proteins, small molecules, and research models.

## Why Choose Creative Proteomics

- Expertise in AlphaFold modeling and molecular docking for complex protein domains.
- Reliable structural modeling workflows combined with expert interpretation to support mechanism-focused research.
- Mechanism-oriented service: bridges experimental metabolite data with protein-level insights.
- Flexible and collaborative: analyses tailored to your experimental system, hypothesis, or model organism.

**Need to explore protein–metabolite interactions in your system?**

Creative Proteomics provides AlphaFold-based structural modeling and molecular docking workflows to support mechanism-focused studies, helping you evaluate metabolite effects on protein function and connect molecular hypotheses with physiological outcomes.

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