A Hunk of Burning Fat

Adiponectin-Cre; Tdtomato/GFP Brown Adipocytes

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**Adipose Tissue Energetics**

**White Adipose Tissue:**
- Storage.
- ~5% resting metabolic rate.
- Oxidative Stress $\rightarrow$ inflammation $\rightarrow$ insulin resistance.

**Brown Adipose Tissue:**
- Thermogenesis.
- Uncoupling (UCP1).
- Browning of white.
- Eat cake - be hot.
Eloise Aimee Parry, 21, Dies From Taking 'Diet Pills': What Is Dinitrophenol (DNP)?

The Huffington Post UK | By Natasha Hinde
Posted: 21/04/2015 10:44 BST | Updated: 21/04/2015 10:59 BST

Eloise Aimee Parry, a 21-year-old student, has died after taking "diet pills" she purchased on the internet.

On 12 April, Parry passed away in hospital after accidentally taking a lethal dose of dinitrophenol (DNP), a "very dangerous" chemical traditionally used in a range of industrial processes.

The student from Shrewsbury began to feel unwell around lunchtime and reportedly felt like she was "burning up from the inside". That afternoon, she died.

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Thermogenic chemicals are killer weight loss drugs

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Natural Thermogenesis
Conditional KO of CPT2

A

ATG

His372

TAG

Chr 4

B

CPT2 mRNA

Fold Change

CPT2+/+

CPT2^A^-^A^-

0.0

0.2

0.4

0.6

0.8

1.0

1.2

1.4

BAT

dWAT

gWAT

Liver

C

Adipo-Cre

+/+

b/+ f/f

CPT2

HSC 70

Brown Adipose

D

gWAT

iWAT

BAT

1^1^C Oleate Oxidation

1^1^C Oleate Oxidation

1^1^C Oleate Oxidation

WT KO

WT KO

WT KO

Adipose fatty acid oxidation is required for acute cold-induced thermogenesis.

The graph shows the body temperature (°C) over time (hr) for Control and Cpt2^A/- mice. The graph indicates that the body temperature decreases over time, with the Cpt2^A/- mice showing a lower temperature compared to the Control group. The images on the right show interscapular brown adipose tissue for WT and KO mice.
Loss of adipose fatty acid oxidation does not alter body weight

$n=13-18$
Loss of adipose fatty acid oxidation does not improve glucose intolerance.
Brown Adipose Tissue: Birth, Death and Resurrection

Mice lacking mitochondrial uncoupling protein are cold-sensitive but not obese

Sven Enerbäck††, Anders Jacobsson††, Elizabeth M. Simpson††, Carmen Guerra†, Hitoshi Yamashita††, Mary-Ellen Harper§ & Leslie P. Kozak†

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Cell Metabolism

Short Article

UCP1 Ablation Induces Obesity and Abolishes Diet-Induced Thermogenesis in Mice Exempt from Thermal Stress by Living at Thermoneutrality

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Thermoregulatory and metabolic phenotypes of mice lacking noradrenaline and adrenaline

Steven A. Thomas & Richard D. Palmiter
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Ambient temperature impacts physiology

- Standard housing generates a cold stress
  - Increased food intake
  - Increased Energy Expenditure

- Housing mice at thermoneutrality suppresses these phenotypes.

- Unclear exactly why thermoneutrality increases obesity in Ucp1KO mice.

Kokolus KM, Repasky EA et al. *PNAS* 110(50) 2013
Adipose fatty acid oxidation is dispensable for overall energy expenditure.
Loss of BAT in Cpt2^{A/-} mice following 12 weeks at thermoneutrality
Thermoneutrality does not make Cpt2<sup>A-/-</sup> mice obese prone.
Conclusions

• There is an autonomous requirement for adipose fatty acid oxidation in cold induced thermogenesis.
• Loss of adipose fatty acid oxidation does not result in changes in body weight or diabetes at any temperature.
• Loss of fatty acid oxidation alters fuel use without affecting overall energy expenditure.
• Does increasing brown adipose tissue mass have therapeutic potential for obesity or diabetes?

References:
Is there a therapeutic potential for increasing brown/beige adipocytes?

Control

Knockout

Drug 1

Drug 2

Only 10 days of treatment transforms white adipose tissue into a fat burning machine.
Wolfgang Lab

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