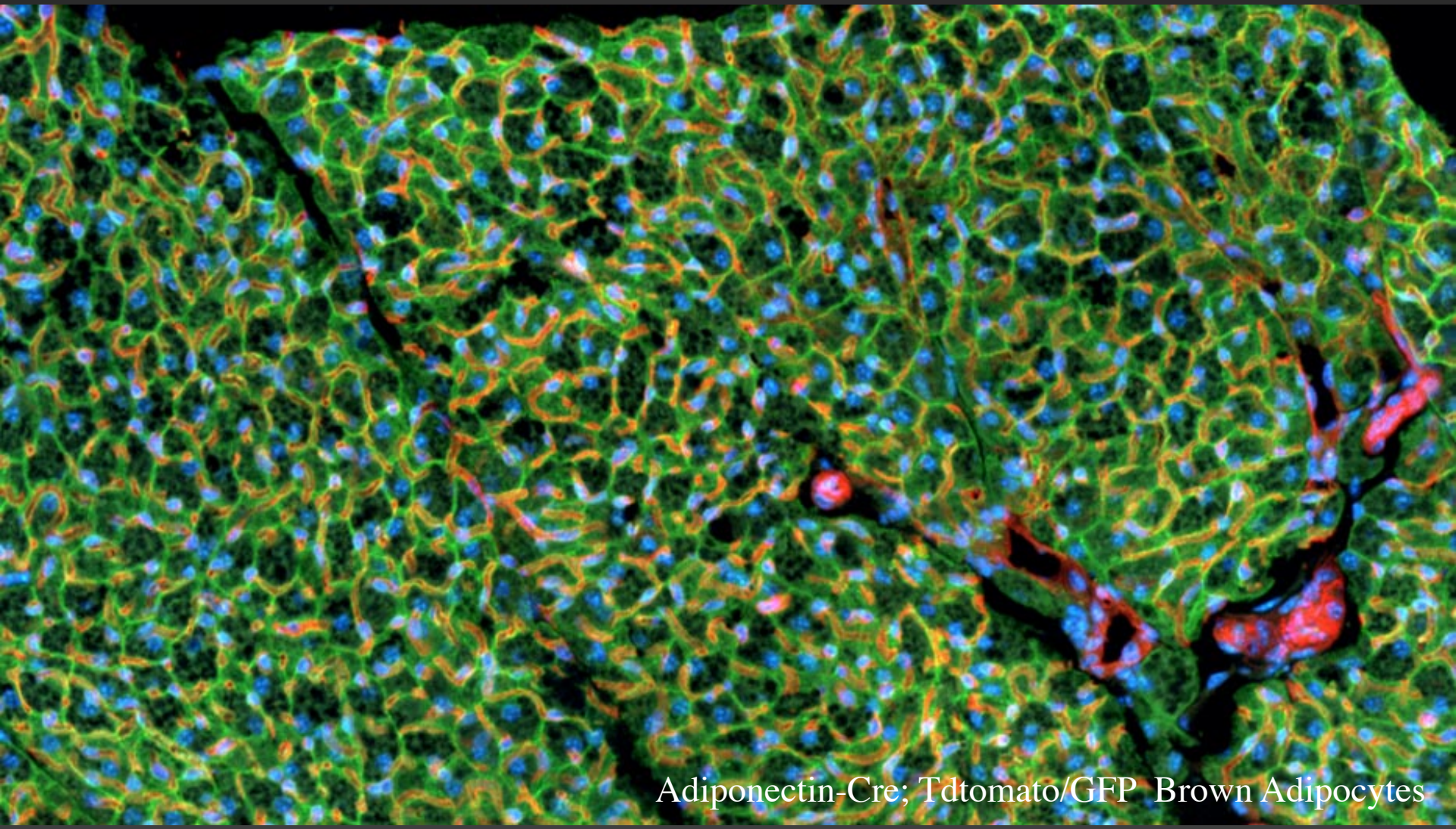
A Hunk of Burning Fat



Michael Wolfgang, PhD
Associate Professor

Department of Biological Chemistry
Johns Hopkins University

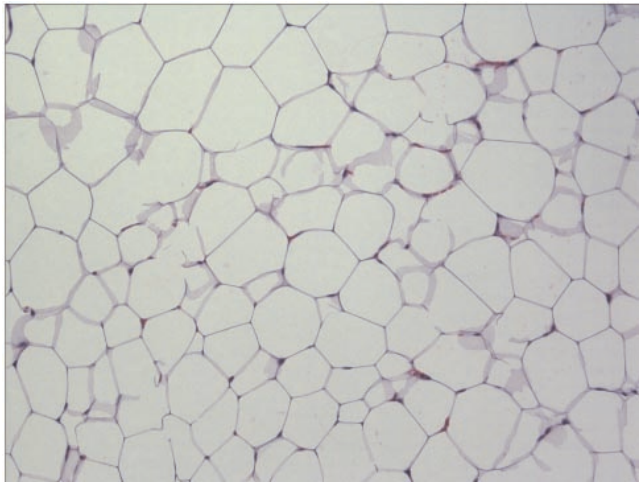
Adipose Tissue Energetics

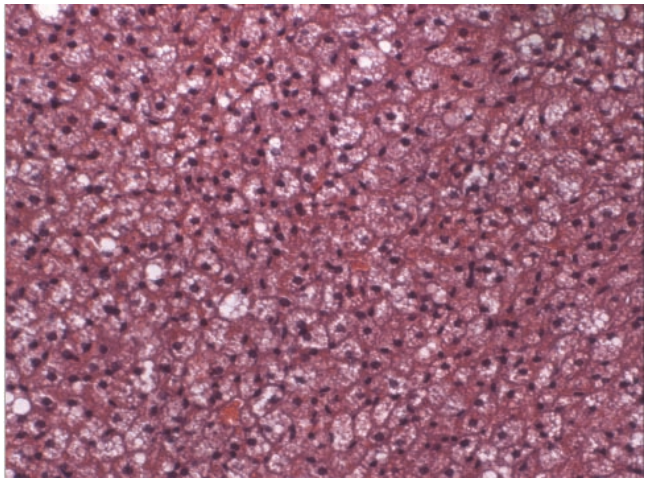
White Adipose Tissue:

- Storage.
- ~5% resting metabolic rate.
- Oxidative Stress->inflammation-> insulin resistance.

Brown Adipose Tissue:

- Thermogenesis.
- Uncoupling (UCP1).
- Browning of white.
- Eat cake-be hot.





Thermogenic chemicals are killer weight loss drugs

Eloise Aimee Parry, 21, Dies From Taking 'Diet Pills': What Is Dinitrophenol (DNP)?

The Huffington Post UK | By Natasha Hinde

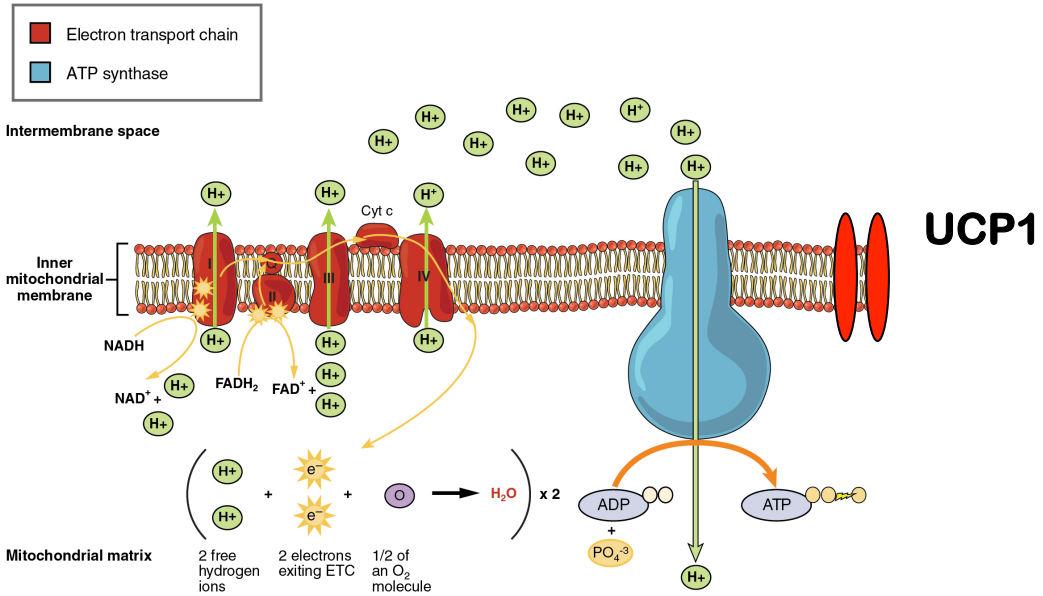
Posted: 21/04/2015 10:44 BST | Updated: 21/04/2015 10:59 BST

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

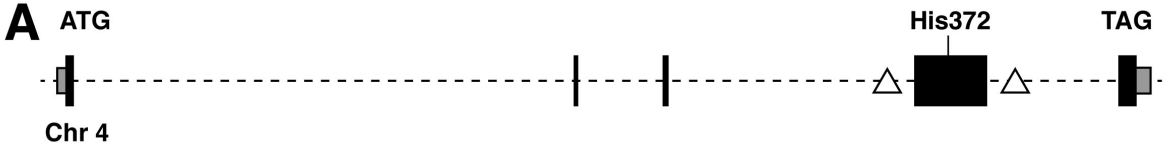
On 12 April, Parry passed away in hospital after accidentally taking a lethal dose of dinitrophenol (DNP), a "very dangerous" chemical traditionally used in a range of industrial processes.

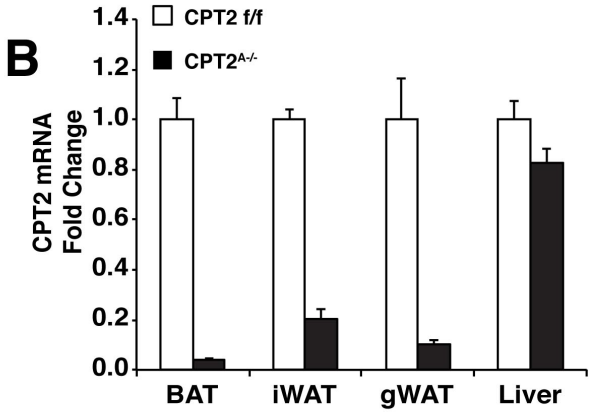
The student from Shrewsbury began to feel unwell around lunchtime and reportedly felt like she was "burning up from the inside". That afternoon, she died.

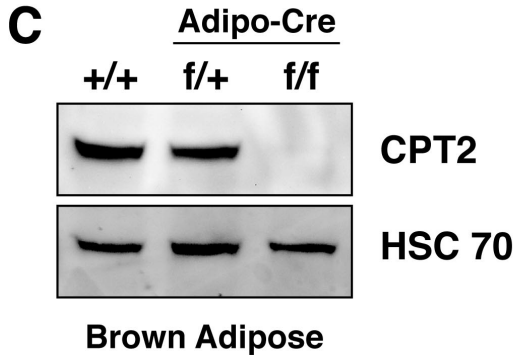
Natural Thermogenesis

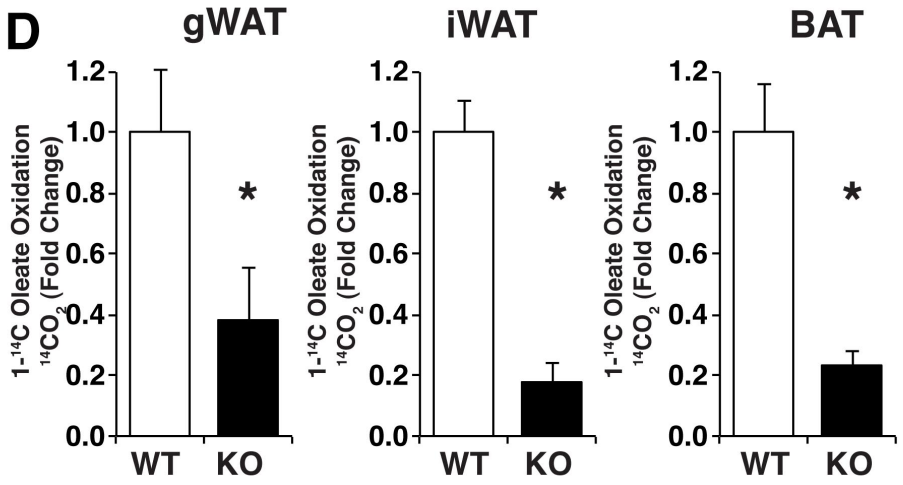


Conditional KO of CPT2



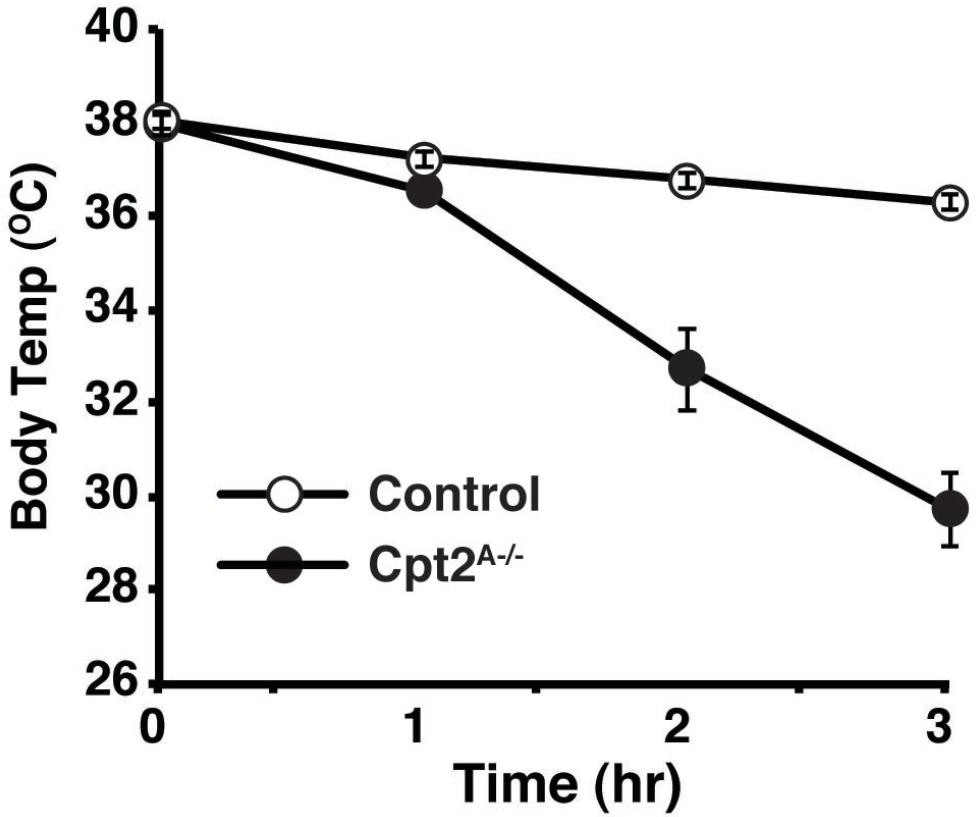


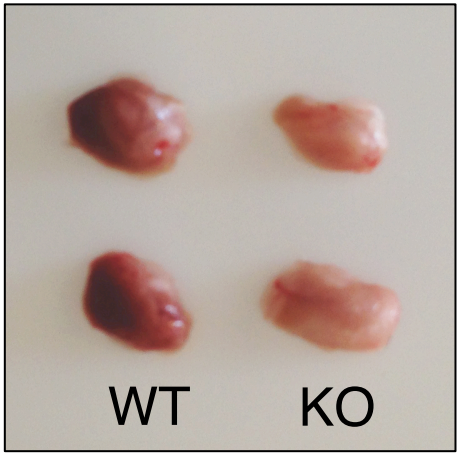




Lee J, Ellis JE, Wolfgang MJ. ***Cell Reports*** 2015; 10:266-279

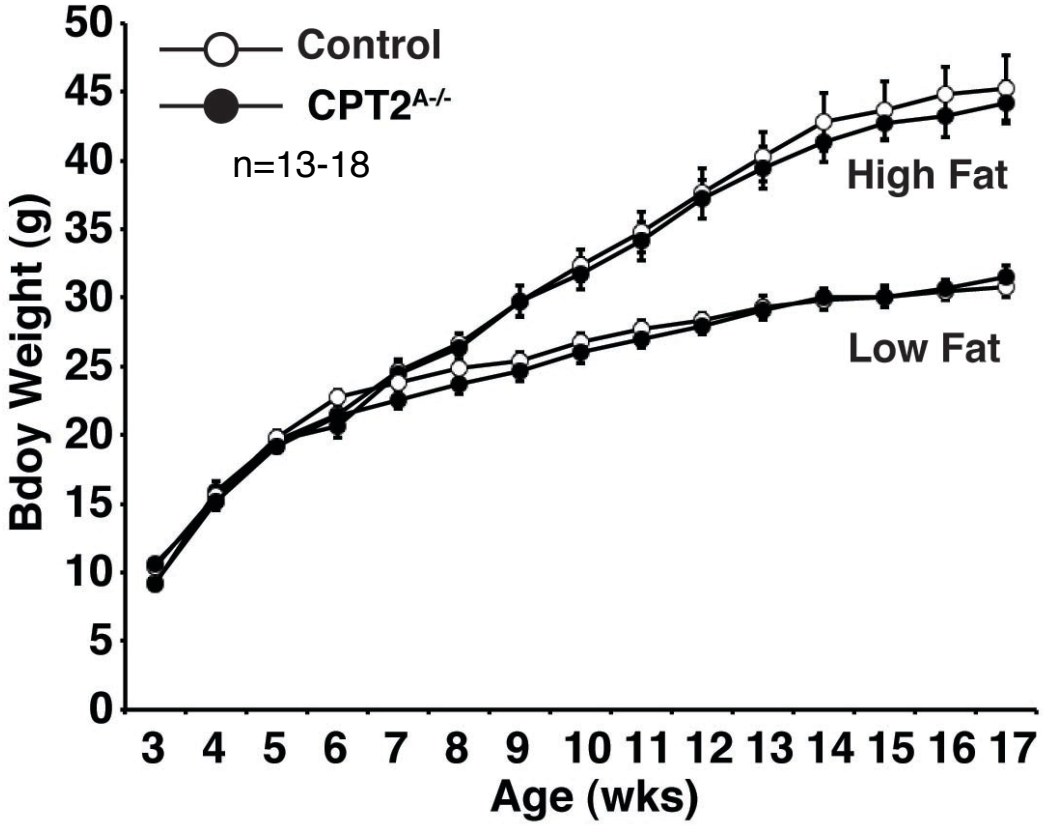
Adipose fatty acid oxidation is required for acute cold-induced thermogenesis



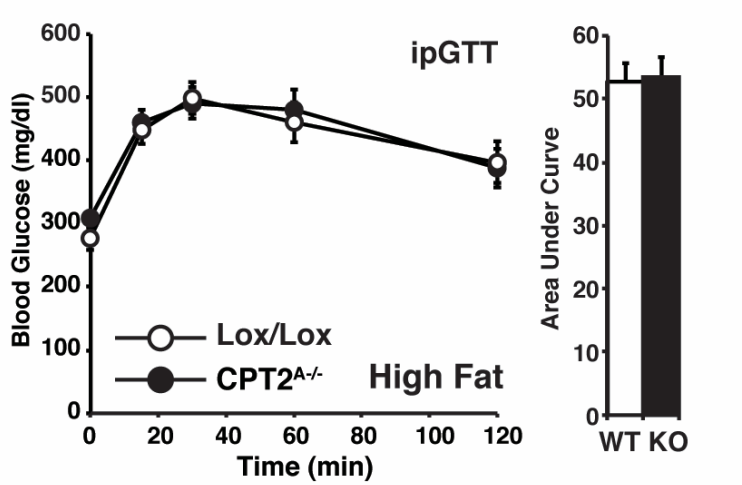


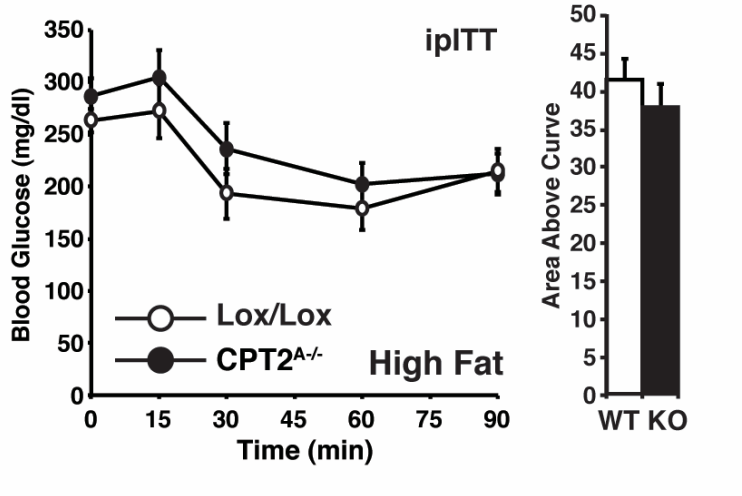
Interscapular
Brown Adipose Tissue

Loss of adipose fatty acid oxidation does not alter body weight



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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‡ *These authors contributed equally to this work.*

Thermoregulatory and metabolic phenotypes of mice lacking noradrenaline and adrenaline

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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

Helena M. Feldmann,[1] Valeria Golozoubova,[1,2] Barbara Cannon,[1] and Jan Nedergaard[1,*]
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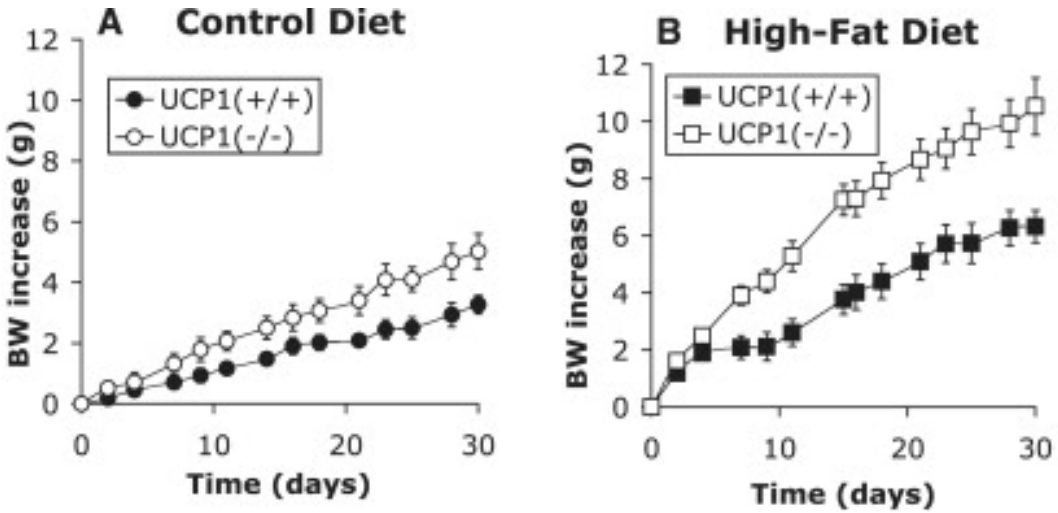
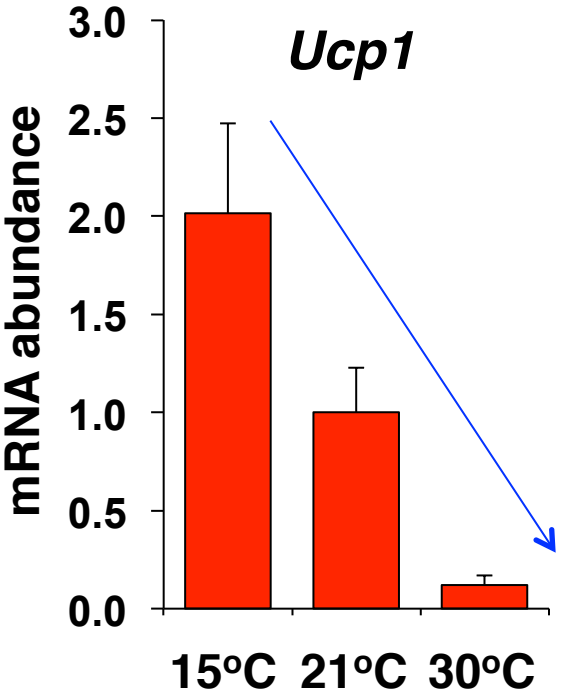
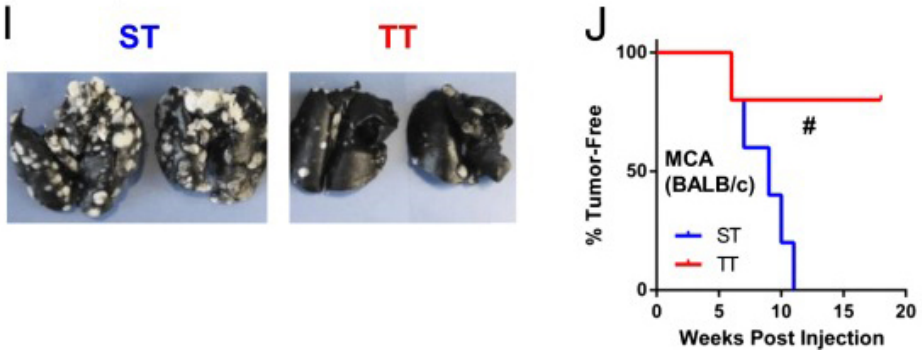
DOI 10.1016/j.cmet.2008.12.014



Ambient temperature impacts physiology

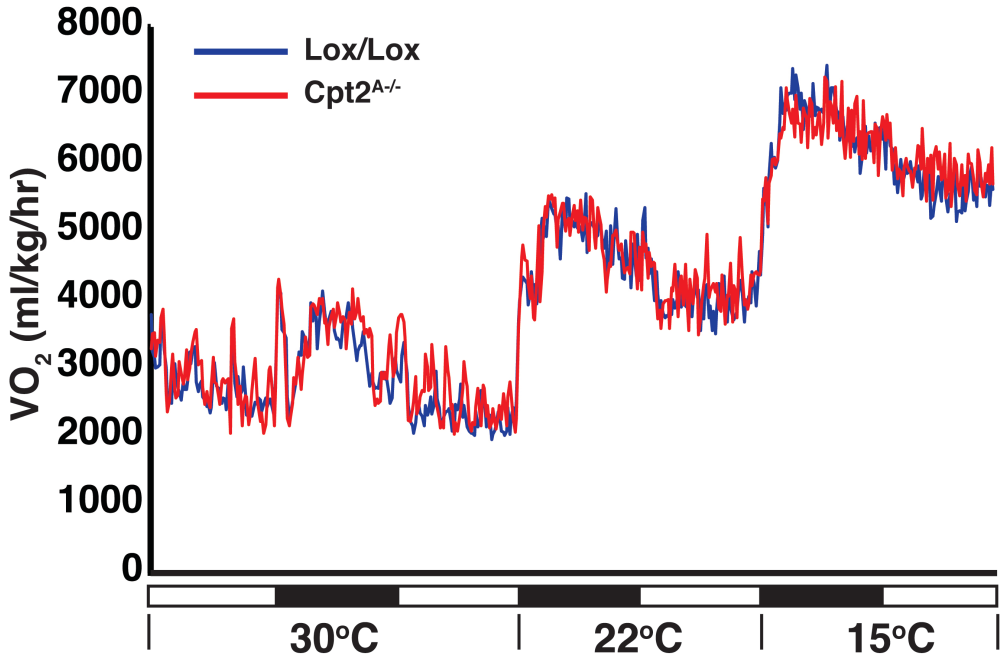


- Standard housing generates a cold stress
  - Increased food intake
  - Increased Energy Expenditure
- Housing mice at thermoneutrality suppresses these phenotypes.
- Unclear exactly why thermoneutrality increases obesity in Ucp1KO mice.

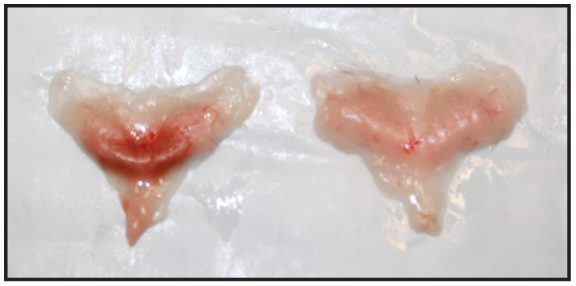


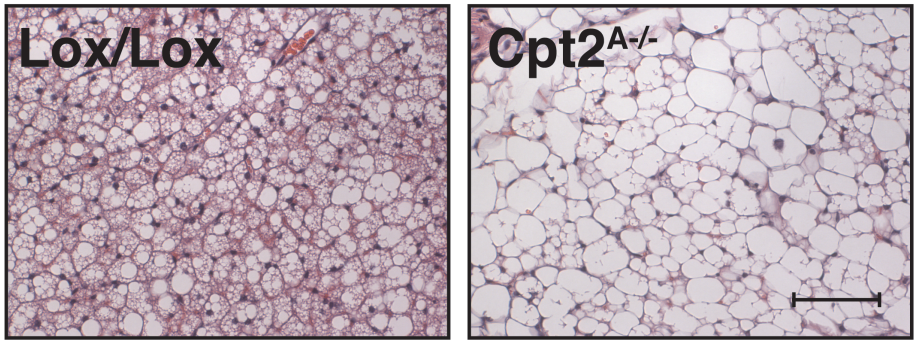
Kokolus KM, Repasky EA et al. ***PNAS*** 110(50) 2013

Adipose fatty acid oxidation is dispensable for overall energy expenditure.

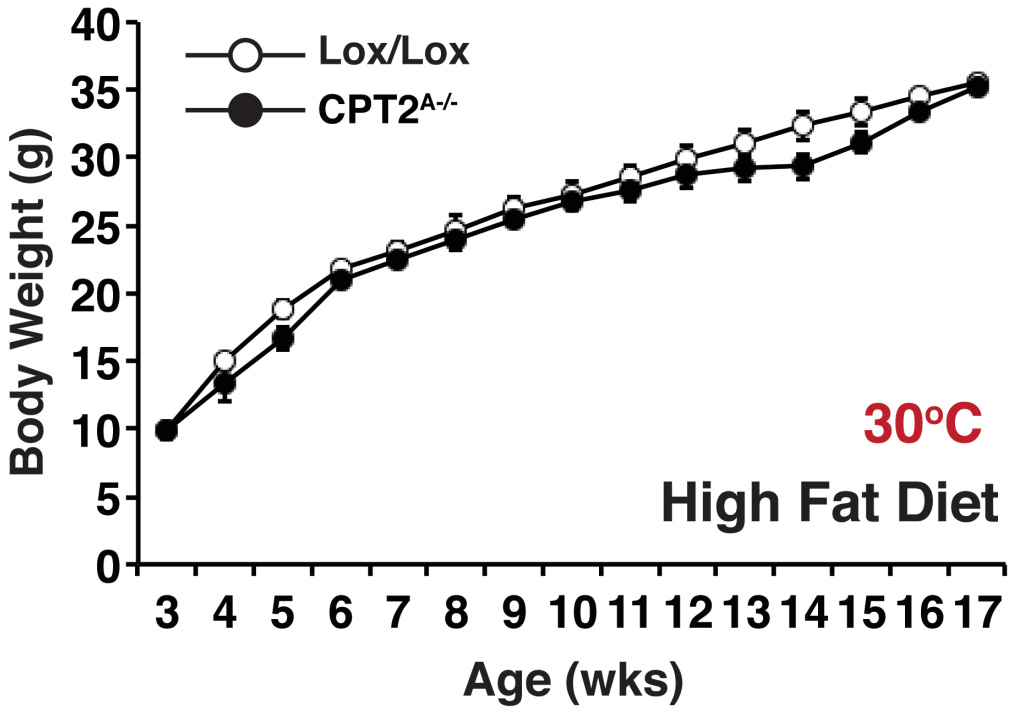


Loss of BAT in $Cpt2^{A-/-}$ mice following 12 weeks at thermoneutrality





Thermoneutrality does not make Cpt2$^{A-/-}$ 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?**

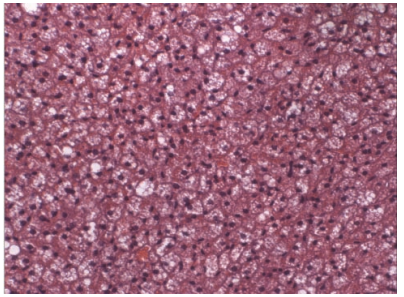
References:

Lee J, Ellis JE, Wolfgang MJ. ***Cell Reports*** 2015; 10:266-279

Lee J, Choi J, Aja S, Scafidi S, Wolfgang MJ. ***Cell Reports*** 2016; 14:1308-16

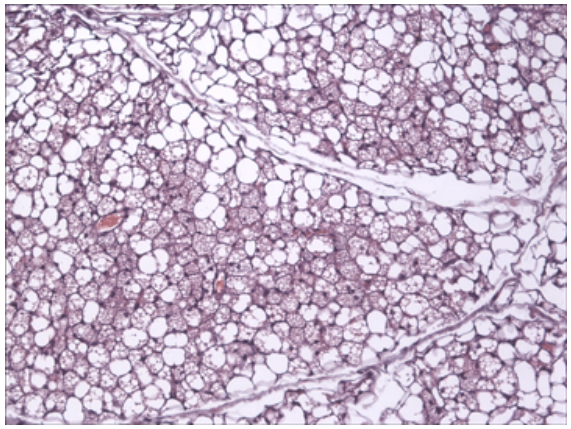
Lee J, Choi J, Scafidi S, Wolfgang MJ. ***Cell Reports*** 2016; In press

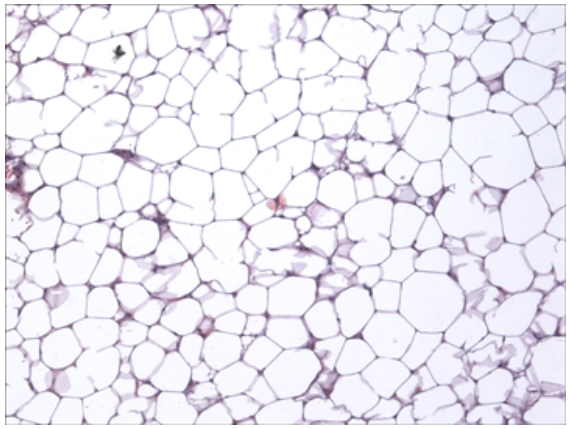
Is there a therapeutic potential for increasing brown/beige adipocytes?



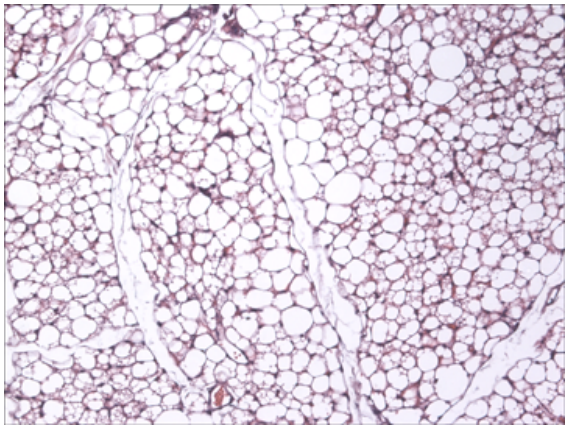
Control

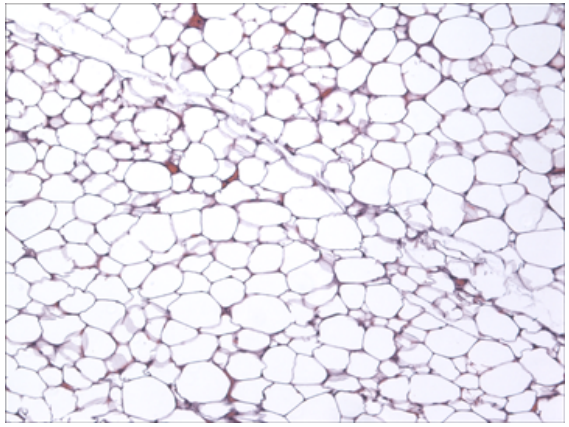
Knockout





Drug 1





Drug 2

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

Wolfgang Lab

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Joseph Choi, UMBC

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Ebru Selin Alpergin, Ph.D, Postdoctoral Fellow.

Susanna Scafidi, M.D. Department of Anesthesiology and Critical Care Medicine.

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