Reduced temperature sensitivity of brown adipose tissue mitochondrial respiration during torpor

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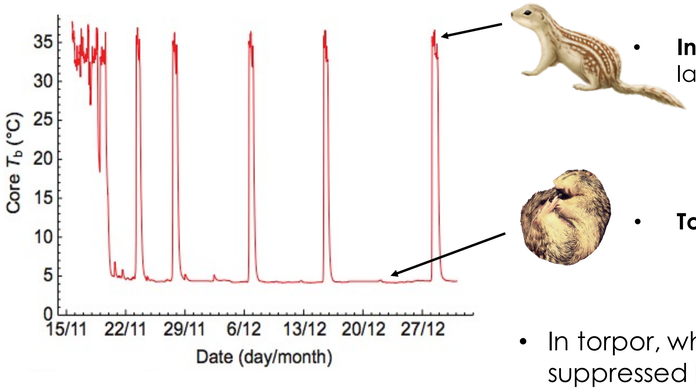
HIBERNATING GROUND SQUIRRELS AND METABOLISM

- The 13-lined ground squirrel, *Ictidomys tridecemlineatus*, is an obligate hibernator
- Hibernation season lasts from ~November to April
- During hibernation, squirrels cycle between two metabolic states:

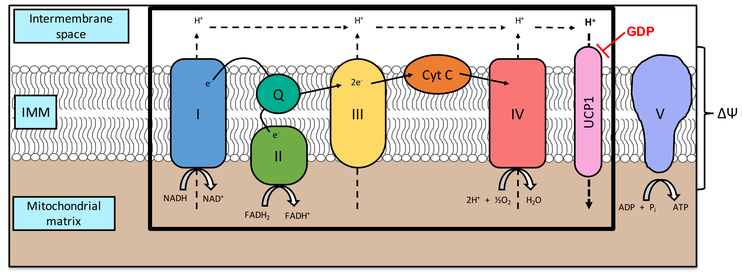


- **Interbout Euthermia (IBE)**: $T_b \approx 37°C$ and lasts for ~10-12 hours

- **Torpor**: $T_b \approx 5°C$ and lasts for ~10-14 days

- In torpor, whole animal metabolic rate is suppressed by >90% compared to IBE[1]

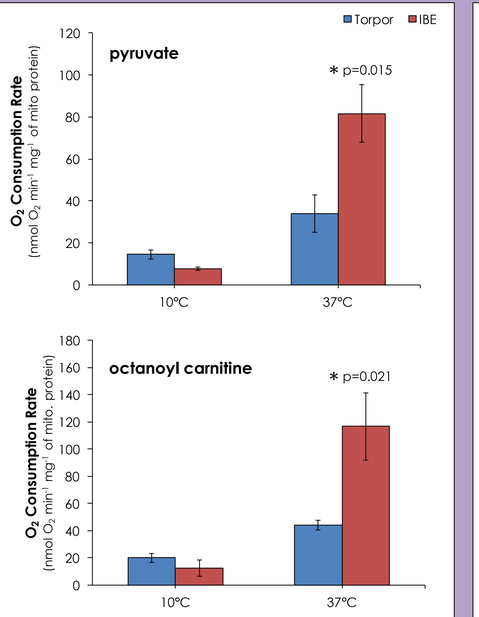
- During arousal from torpor, the whole animal metabolic rate increases ~20-fold, most of which is due to brown adipose tissue (BAT)[1]
- When stimulated by norepinephrine, BAT produces heat by uncoupling the electron transport system (ETS) function from ATP synthesis:
  - When activated by free fatty acids, **uncoupling protein-1 (UCP1)** causes futile cycling of protons across the inner mitochondrial membrane (IMM)
  - Heat is produced by the activity of ETS complexes I-IV to maintain the membrane potential(ΔΨ)



RESEARCH QUESTIONS AND GOALS

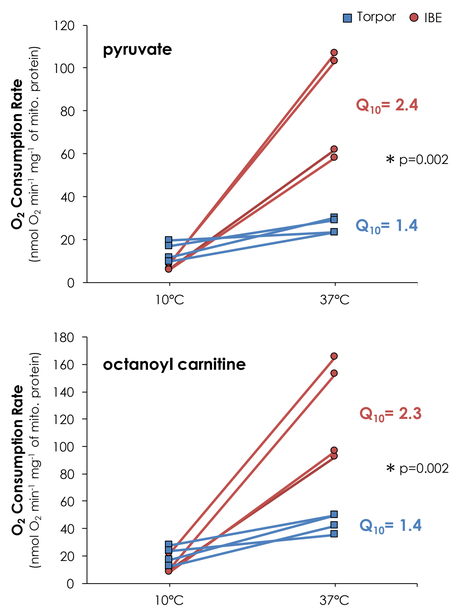
1. Is BAT mitochondrial metabolism suppressed in torpor?
   - Liver mitochondrial metabolism is actively suppressed in torpor by ~70%[1]
   - **Compare BAT mitochondrial respiration between torpor and IBE:**
     - **two fuels**: **pyruvate and octanoyl carnitine**(a medium chain fatty acid)
2. How does temperature effect BAT mitochondrial metabolism?
   - **Compare respiration at 10°C and 37°C** to approximate *in vivo* T_b
3. Are any respiration differences paralleled by differences in the maximal activities of ETS complexes?
   - **Enzyme assays at 10°C and 37°C** to approximate *in vivo* T_b

MITOCHONDRIAL RESPIRATION



Isolated BAT mitochondria, values are mean ± S.E.M.

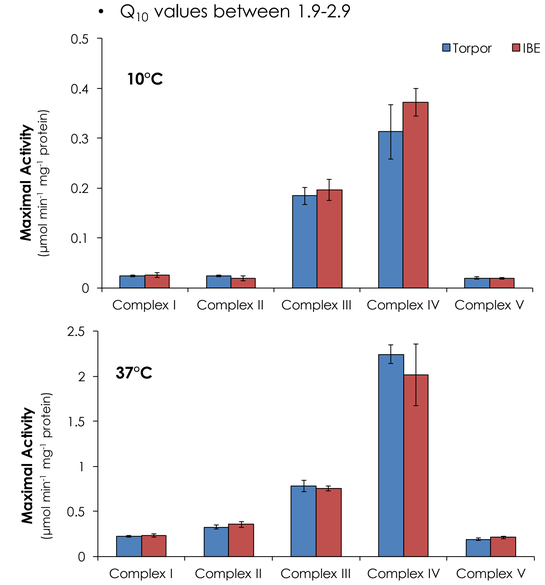
TEMPERATURE SENSITIVITY



Data points connected by a line are measurements taken from the same individual

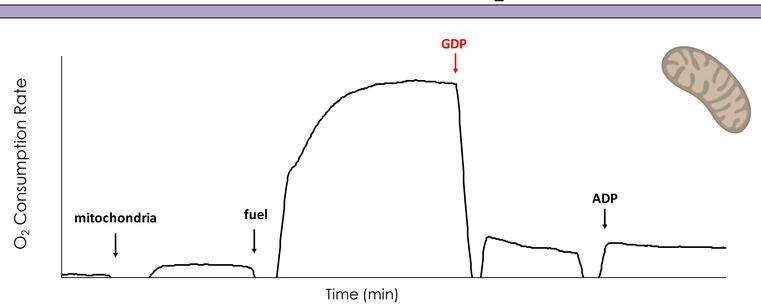
V_{max} OF ETS COMPLEXES

- No differences between torpor and IBE
- Q_{10} values between 1.9-2.9



Homogenized isolated BAT mitochondria, values are mean ± S.E.M.

MEASURING MITOCHONDRIAL O_2 CONSUMPTION



- addition of fuel produced high State 2 rate
- UCP1 activity inhibited by **guanosine 5'-diphosphate (GDP)**
- addition of ADP produced very low State 3 rate
  - indicative of low expression of Complex V in BAT mitochondria

CONCLUSIONS

- **BAT mitochondrial respiration changed between torpor and IBE:**
  - at 10°C, respiration rates tended to be higher in torpor compared with IBE
  - **BUT** at 37°C, respiration rates were **suppressed** by 62% in torpor compared with IBE
- **The respiration differences were NOT paralleled by enzymatic changes between torpor and IBE:**
  - Maximal activities (V_{max}) of the five ETS complexes did not differ between torpor and IBE
- **Mitochondrial respiration in torpor was less temperature sensitive than in IBE:**
  - Q_{10} significantly lower in torpor compared with IBE
- **Changes in mitochondrial membrane composition could account for our results**
  - Liver mitochondrial membrane phospholipid content changes between torpor and IBE[2]
  - Such changes in BAT would alter ETS enzyme activities and temperature sensitivity within the intact organelle

REFERENCES

1. **Muleme, H. M., Walpole, A. C., Staples, J. F.** (2006). Mitochondrial Metabolism in Hibernation : Metabolic Suppression , Temperature Effects , and Substrate Preferences. *Physiol. Biochem. Zool.* **79**, 474–483.
2. **Armstrong, C., Thomas, R. H., Price, E. R., Guglielmo, C. G., Staples, J. F.** (2011). Remodeling mitochondrial membranes during arousal from hibernation. *Physiol. Biochem. Zool.* **84**, 438–449.

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