In winter, 13-lined ground squirrels hibernate to conserve energy. In torpor, body temperature ($T_b$) is maintained at ~5°C, while metabolic rate (MR) is suppressed by ~95%, periodically interrupted by rapid arousals into interbout euthermia (IBE).

During arousals, up to 60% of the increase in MR is attributed to activation of ETS function in brown adipose tissue mitochondria through uncoupling protein 1 (UCP1). Free fatty acids (FFA) may also uncouple mitochondria in other tissues during arousal, and hibernators rely on lipid oxidation.

Do FFA uncouple oxidative metabolism in liver mitochondria?
- FFA-uncoupling may be mediated by UCP homologues, the Adenine Nucleotide Translocator or the Permeability Transition Pore

Does any uncoupling differs among hibernation states?
- Thermogenesis by the large, metabolically active liver could facilitate arousal

3. Research questions

4. Experimental design

O$_2$ consumption of isolated liver mitochondria
- State II respiration w/succinate (S) and rotenone (R)
- Uncoupling with palmitate (16:0 FFA)

Controls: Bovine serum albumin (BSA; binds FFA)
- Ethanol (solvent for palmitate)
- CCP (well-characterized synthetic uncoupler)

Blockers: Guanosine-5'-diphosphate (GDP; blocks UCPs)
- Atractylloside (Atra; blocks ANT)
- Cyclosporin A (CSA; blocks PTP)

6. FFA uncoupling is significantly higher during IBE compared to torpor

7. Conclusion: Liver thermogenesis by PTP-mediated FFA-uncoupling could facilitate arousal

Significantly higher FFA-induced uncoupling in IBE mitochondria could facilitate thermogenesis in the liver during arousal. BSA eliminated palmitate uncoupling in all hibernation states, indicating that the uncoupling was mediated entirely by FFA. Cyclosporin A also completely reversed the uncoupling, suggesting that FFA-uncoupling is facilitated through PTP.

Future direction: Does PTP expression or amount differ between torpor and IBE?