Toward torpor mechanisms: genome and gene expression in the meadow jumping mouse

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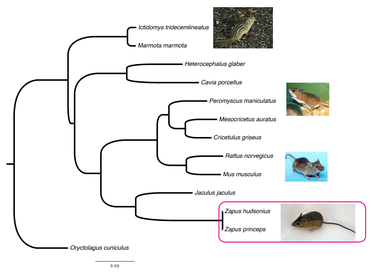
ABSTRACT

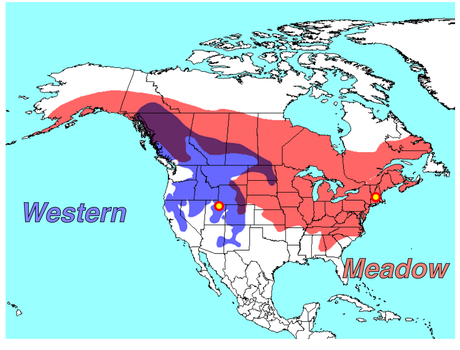
Hibernating mammals provide a natural example of torpor, a state of depressed metabolism with many potential applications. The meadow jumping mouse (*Zapus hudsonius*) is a small North American rodent that hibernates in response to shortened day length. These animals can thus be induced to hibernate in a laboratory setting and to enter torpor when fasted. Assembly of the meadow jumping mouse genome allows comparative analysis with other hibernating and non-hibernating species and provides the ability to study gene expression during torpor. To understand the cell-autonomous response to cold, meadow jumping mouse cells were exposed to temperatures typical of active (37°C) and hibernating (6°C) animals and subjected to mRNA sequencing. Expression changes were found in genes involved in growth signaling, transcription, and the circadian clock, among others. These results provide a baseline for understanding the relative contribution of cold temperature to the changes in gene expression observed during torpor in hibernating mammals. Interestingly, the observed changes are not analogous to the cold shock response of unicellular organisms and suggest that hibernating mammals may not employ a unique cell-based response to cold temperature when compared to non-hibernators.

1. Jumping Mice: Hibernating Rodents

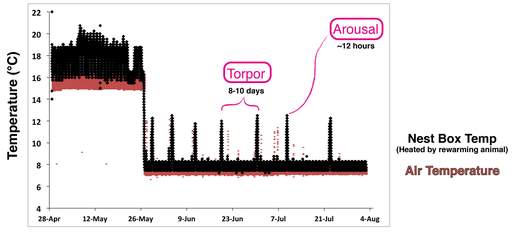
Phylogeny



Range



Torpor and Periodic Arousals



2. Inducing Hibernation in the Lab: Day Length & Temperature

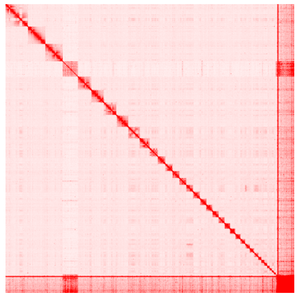
Meadow jumping mice prepare for hibernation based on environmental cues – primarily day length. The mice fatten up and hibernate during simulated fall and winter conditions, but remain reproductively active as long as they are housed in simulated summer conditions.

3. Draft Jumping Mouse Genomes

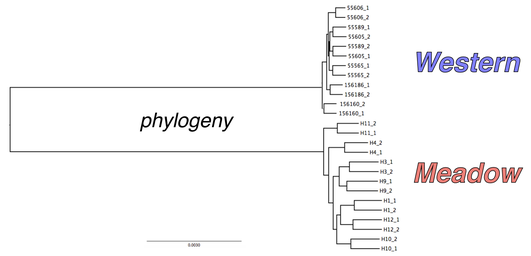
Current Z. hudsonius Draft Assembly

2.7 Gb **estimated genome size**
60.4 Mb **scaffold *N50***
~22,000 **genes**

Hi-C Contact Matrix



Lower Coverage Whole Genomes



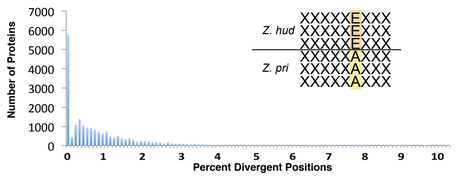
4. Comparative Genomics: *Zapus hudsonius & Zapus princeps*

What can we learn about hibernation via comparative genomics?

	Western Jumping Mouse *Zapus princeps*	Meadow Jumping Mouse *Zapus hudsonius*
Long Photoperiod Inhibits Fall Fattening:	**NO**	**YES**
Home Elevation:	**2300-2700 m (7600-8750 feet)**	**70 m (225 feet)**
Individuals Sequenced for Whole Genomes:	**7**	**7**

Major Urinary Proteins
Vomeronasal Receptors
Leptin
Hemoglobin

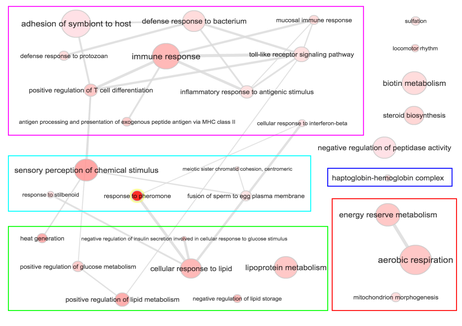
Identify Divergent Genes:
Find mutations that became fixed in both species



Significantly Diverged:
1697 / ~22,000 proteins

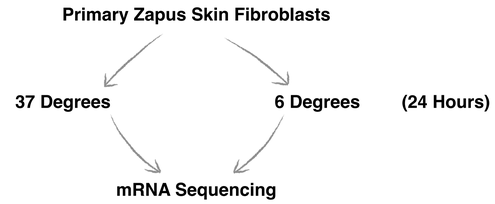
Criteria:
- Fixation Index > 0.8 in both species
- Enriched ($p < 0.05$) in divergent positions

Gene Ontology Analysis



5. Cell Response to Hibernation Temperature

How does cold temperature change gene expression in isolated cells?



Differentially Expressed Genes

Fold Change in Cold	q Value	Gene
0.306	0.011	Rad52
0.231	0.037	BC035947
0.016	0.037	Actg1
0.207	0.037	Ran
0.885	0.037	Cachd1
0.378	0.037	Nol4l
5.954	0.037	Eloc
1.374	0.038	Tmem165
0.894	0.038	Gps1
1.729	0.038	Bgn
0.126	0.038	Kcnd3
0.119	0.043	Srp54
0.835	0.044	FTSJ3
1.436	0.046	Pcmtd1
3.818	0.047	Tmem50b

Top Enriched GO Term

cellular response to transforming growth factor beta stimulus

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