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A multi-tissue gene expression dataset for hibernating brown bears

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Abstract

Objectives Complex physiological adaptations often involve the coordination of molecular responses across multiple tissues. Establishing transcriptomic resources for non-traditional model organisms with phenotypes of interest can provide a foundation for understanding the genomic basis of these phenotypes, and the degree to which these resemble, or contrast, those of traditional model organisms. Here, we present a one-of-a-kind gene expression dataset generated from multiple tissues of two hibernating brown bears (*Ursus arctos*).

Data description This dataset is comprised of 26 samples collected from 13 tissues of two hibernating brown bears. These samples were collected opportunistically and are typically not possible to attain, resulting in a highly unique and valuable gene expression dataset. In combination with previously published datasets, this new transcriptomic resource will facilitate detailed investigation of hibernation physiology in bears, and the potential to translate aspects of this biology to treat human disease.

Keywords Gene expression, Hibernation, Transcriptomics, Brown bears

Objective

Multiple lineages of mammals, including ground squirrels [1–3], bears [4–6], and even several primates [7, 8], hibernate annually, during which metabolism is depressed, body temperature decreases to varying extents, and a suite of cellular and physiological changes culminate in the ability to survive periods of food scarcity [4, 5, 9–11]. Understanding how organisms both

achieve and reverse hibernation phenotypes may provide translational insight into novel treatments for numerous human diseases, such as the reversal of insulin resistance to avoid subsequent onset of diabetes in humans [12, 13].

Studies of gene expression have proved valuable for identifying genes and signaling pathways underlying hibernation phenotypes in key tissues. For example, early microarray studies in bear heart, liver, and muscle revealed differential expression of genes associated with protein biosynthesis and lipid metabolism during hibernation [14–17], and subsequent studies utilizing mRNA-seq have since further characterized massive changes in gene expression that occur during hibernation in liver, muscle, and adipose tissue in bears [18–20]. These studies have focused on a small number of tissues per individual at a time, and our understanding of whole-body changes in gene expression associated with hibernation is therefore lacking and largely unexplored.

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Table 1 Overview of data files/data sets

Label	Name of data file/data set	File types (file extension)	Data repository and identifier (DOI or accession number)
Data file 1	Sample information table	MS Excel file (.xlsx)	Figshare (https://doi.org/10.6084/m9.figshare.22574578.v1) [21]
Data file 2	Detailed methods information	MS Word file (.docx)	Figshare (https://doi.org/10.6084/m9.figshare.22574578.v1) [21]
Data set 1	Multi-tissue transcriptomic dataset for hibernating brown bears	FASTQ files (.fastq)	NCBI Sequence Read Archive (https://identifiers.org/bioproject:PRJNA835146) [22]

Here, we present an unprecedented transcriptomic dataset for 26 samples collected from 13 tissues of two hibernating brown bears (Table 1). These data were collected opportunistically rather than as part of a pre-designed experiment; as a result, this dataset is notably low in sample number (n=2 bears) and does not include powerful controls (i.e., samples from all tissues in non-hibernating bears). However, these samples are exceedingly unique and are typically impossible to attain, and therefore present an inherently valuable and unprecedented look at gene expression across multiple tissues in hibernating bears.

Data description

Sample collection
Tissues used in this study were collected during the necropsy of two adult male bears (individuals P and R) following euthanization in winter 2016. Both bears were born in captivity in 2011 at the Washington State University Bear Center. The bears were anesthetized using a mixture of Tiletamine/Zolazepam (Telazol) and dexmedetomidine and subsequently euthanized in January 2016 with Sodium pentobarbital euthanasia solution, 1 ml/10 lbs administered intravenously. Procedures were conducted by staff of the Washington State University College of Veterinary Medicine. Samples were collected by the necropsy team immediately post-mortem to minimize nucleic acid degradation; samples were then placed in RNAlater (Invitrogen, Carlsbad, CA, USA) for storage. The following tissues were sampled: lung (right and left), heart ventricle (left and right), heart atrium (left and right), small intestine, kidney medulla, kidney cortex, gall bladder, adipose, stomach, gastrocnemius, liver, skin, and spleen. See Data file 1 [21] for additional sample information. Samples were transported to the laboratory where they were stored at -80° C. Procedures for all experiments were approved by the Institutional Animal Care and Use Committee at Washington State University (Protocol #06468).

RNA extraction, library preparation, and sequencing
Tissue was homogenized using a TissueLyser LT (Qiagen, Redwood City, CA, USA) and RNA extractions were completed using the RNeasy fibrous tissue mini kit (Qiagen, Valencia, CA, USA) using a QIAcube (Qiagen). RNA yield and quality were assessed using a Qubit 2.0

(Invitrogen, Carlsbad, CA, USA) and Bioanalyzer 2100 (Agilent Technologies, Santa Clara, CA, USA), respectively. RNA-sequencing libraries were prepared using the Illumina TruSeq Stranded Total RNA Prep with Ribo-Zero Gold kit to remove rRNA according to the manufacturer's instructions (Part #15,031,048 Rev.E, Illumina, San Diego, CA, USA). The libraries were sequenced on one lane of an Illumina HiSeq 2500 with v4 reagents with 100 basepair (bp) paired-end reads. Additional detailed methods are available in Data file 2 [21]. Raw sequence data are available at NCBI BioProject PRJNA835146 (https://identifiers.org/bioproject:PRJNA835146) [22].

Limitations
- Small sample size (n=2).
- Lack of experimental controls (i.e., samples from non-hibernating bears).

Data availability
The data described in this Data note can be freely and openly accessed on the NCBI Short Read Archive under BioProject: PRJNA835146 (https://identifiers.org/bioproject:PRJNA835146). Please see Table 1 and references [19–21] for details and links to the data.

Declarations

Ethics approval and consent to participate
Procedures for all animal care and experiments were approved by the Institutional Animal Care and Use Committee (IACUC) at Washington State University (Protocol #06468). All methods were performed in accordance with the guidelines and regulations of this IACUC protocol.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Abbreviations
Not applicable.

References

1. Van Breukelen F, Martin SL. Invited review: molecular adaptations in mammalian hibernators: unique adaptations or generalized responses? J Appl Physiol. 2002;92:2640–7.
2. Davis DE. Hibernation and circannual rhythms of food consumption in marmots and ground squirrels. Q Rev Biol. 1976;51:477–514.
3. Barnes BM. Freeze avoidance in a mammal: body temperatures below 0 C in an arctic hibernator. Sci (80-). 1989;244:1593–5.
4. Hellgren EC. Physiology of hibernation in bears. Ursus. 1998;:467–77.
5. Hissa R, Siekkinen J, Hohtola E, Saarela S, Hakala A, Pudas J. Seasonal patterns in the physiology of the european brown bear (*Ursus arctos arctos*) in finland. Comp Biochem Physiol Part A Physiol. 1994;109:781–91.
6. Nelson RA, Folk GE Jr, Pfeiffer EW, Craighead JJ, Jonkel CJ, Steiger DL. Behavior, biochemistry, and hibernation in black, grizzly, and polar bears. Bears their Biol Manag. 1983;:284–90.
7. Dausmann KH, Glos J, Ganzhorn JU, Heldmaier G. Hibernation in a tropical primate. Nature. 2004;429:825–6.
8. Blanco MB, Dausmann KH, Faherty SL, Yoder AD. Tropical heterothermy is "cool": The expression of daily torpor and hibernation in primates. Evol Anthropol Issues, News, Rev. 2018;27:147–61.
9. Geiser F, Hibernation. Curr Biol. 2013;23:R188–93.
10. Wu CW, Biggar KK, Storey KB. Biochemical adaptations of mammalian hibernation: exploring squirrels as a perspective model for naturally induced reversible insulin resistance. Brazilian J Med Biol Res. 2013;46:1–13.
11. Storey KB. Mammalian hibernation. Hypoxia. 2003;:21–38.
12. Martin SL. Mammalian hibernation: a naturally reversible model for insulin resistance in man? Diabetes Vasc Dis Res. 2008;5:76–81.
13. Stenvinkel P, Jani AH, Johnson RJ. Hibernating bears (Ursidae): metabolic magicians of definite interest for the nephrologist. Kidney Int. 2013;83:207–12.
14. Fedorov VB, Goropashnaya AV, Tøien Ø, Stewart NC, Chang C, Wang H, et al. Modulation of gene expression in heart and liver of hibernating black bears (*Ursus americanus*). BMC Genomics. 2011;12:171.
15. Fedorov VB, Goropashnaya AV, Tøien Ø, Stewart NC, Gracey AY, Chang C, et al. Elevated expression of protein biosynthesis genes in liver and muscle of hibernating black bears (*Ursus americanus*). Physiol Genomics. 2009;37:108–18.
16. Fedorov VB, Goropashnaya AV, Stewart NC, Toien O, Chang C, Wang H, et al. Comparative functional genomics of adaptation to muscular disuse in hibernating mammals. Mol Ecol. 2014;23:5524–37.
17. Goropashnaya AV, Tøien Ø, Ramaraj T, Sundararajan A, Schilkey FD, Barnes BM, et al. Transcriptional changes and preservation of bone mass in hibernating black bears. Sci Rep. 2021;11:8281.
18. Jansen HT, Trojahn S, Saxton MW, Quackenbush CR, Hutzenbiler BDE, Nelson OL, et al. Hibernation induces widespread transcriptional remodeling in metabolic tissues of the grizzly bear. Commun Biol. 2019;2:1–10.
19. Tseng E, Underwood JG, Evans Hutzenbiler BD, Trojahn S, Kingham B, Shevchenko O, et al. Long-read isoform sequencing reveals tissue-specific isoform expression between active and hibernating brown bears (*Ursus arctos*). G3 Genes| Genomes| Genet; 2022.
20. Perry BW, Armstrong EE, Robbins CT, Jansen HT, Kelley JL. Temporal analysis of gene expression and isoform switching in brown bears (*Ursus arctos*). Integr Comp Biol. 2022;62:1802–11.
21. Perry BW, Saxton MW, Jansen HT, Quackenbush CR, Evans Hutzenbiler BD, Robbins CT, Kelley JL, Cornejo OE. Data file 2. Detailed methods information. Figshare. 2023. https://doi.org/10.6084/m9.figshare.22574578.
22. NCBI BioProject. (2023). https://identifiers.org/bioproject:PRJNA835146.

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