NOVEL RESEARCH

Biochemistry and Molecular Biology of Environmental Stress

Dr. Ken Storey's Lab – Biology/Biochemistry/Neuroscience

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Our research program is aimed at discovering the cellular and molecular mechanisms that allow both vertebrates and invertebrate extremophiles to cope with severe environmental stresses. Our specific interests include gene regulation responses to metabolic rate depression. Novel areas of research include microRNA regulation in new and interesting animals, novel neuronal mitochondrial peptide regulation, as well as the circadian rhythms of hibernators.

At night, Red Devil squid hunt in warm oxygenated surface waters but descend into the ocean's depths in daytime where they must endure hypoxia, high-pressure and near freezing conditions. To survive, squid lower their metabolic rate and use microRNAs to help suppress & reorganize gene expression. This study evaluates the importance of microRNA action in adaptation to this extreme environment.

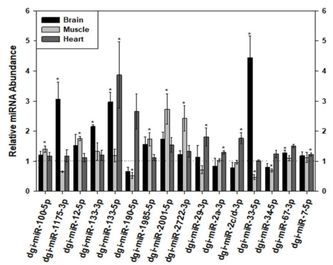
HYPOXIC + HYPOMETABOLIC SQUID:

Squid descend into the ocean's oxygen minimum zone to avoid predators, but must deal with:

- Severe hypoxia
- High pressure
- Very cold water

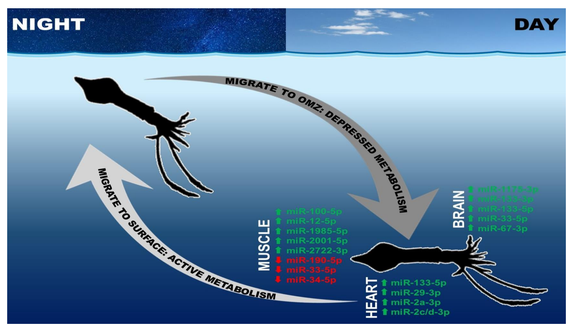
MICRORNAS:

- Short non-coding RNAs of ~22 nt in length.
- **miRNA + mRNA = translational repression OR mRNA degradation**



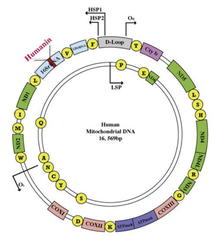
IN HYPOXIA WE FOUND:

- Tissue-specific miRNA expression in heart, muscle & brain.
- MicroRNA targets were involved in processes including regeneration, anti-apoptosis, and energy conservation.



Hadj-Moussa *et al.* (2018). *BBA- Gene Regulatory Mechanisms*. Submitted.

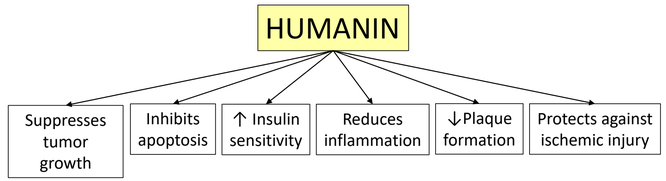
A novel mitochondrial peptide encoded in the 16S rRNA was discovered in 2001 in the unaffected brain areas of an Alzheimer's disease patient. This peptide was found to have neuroprotective functions by reducing damaged caused by amyloid plaques. Recently, the squirrel-specific analogue has been characterised and shown to be differentially in aroused vs hibernating animals.

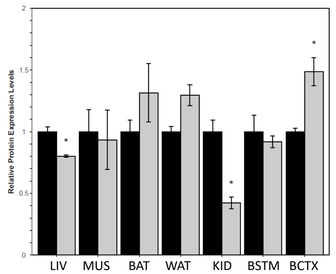


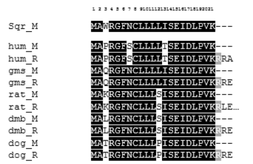
HUMANIN:

- Human mitochondrial peptide found in unaffected Alzheimer's brains.
- Multiple analogues exist in other vertebrates
- Sequence conservation high among mammals.

Left: The human mitochondrial genome and the humanin ORF.
Middle: 3D model of humanin.





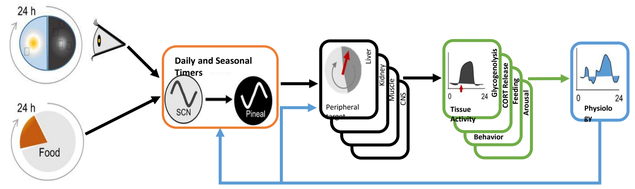


Above: Humanin analogues found in other vertebrate species. Multiple sequence alignment showing similar amino acid sequences. Identical amino acids highlighted in black, similar amino acids in grey. "M" indicates peptide translated with mitochondrial code, "R" indicates peptide translated with standard code.

Above: Normalized Squirrelin relative protein levels in the liver, muscle, brown adipose, white adipose, kidney, brainstem and brain cortex of aroused vs torpid ground squirrels. (n = 4 independent trials on tissue from different animals). Asterisk (*) denotes significant change ($p < 0.05$) (From Szereszewski and Storey, 2018).

Under harsh winter conditions, many mammals hibernate allowing for substantial energy savings by reducing their body temperature and metabolic demands. The implication of the biological clock, or circadian rhythms, with respect to hibernation have long been debated. Here we show tissue-specific regulation of the clock genes during hibernation in the 13-lined ground squirrel.

CIRCADIAN RHYTHMS



Circadian (daily) rhythmicity occurs in many physiological processes including body temperature, sleep, and metabolism. Peripheral circadian clocks have been linked to organ-specific energy metabolism, warranting their investigation in hibernation, wherein body temperature, torpor bout duration, euthermic interval length, and torpor entry speed may be affected by the circadian clock.

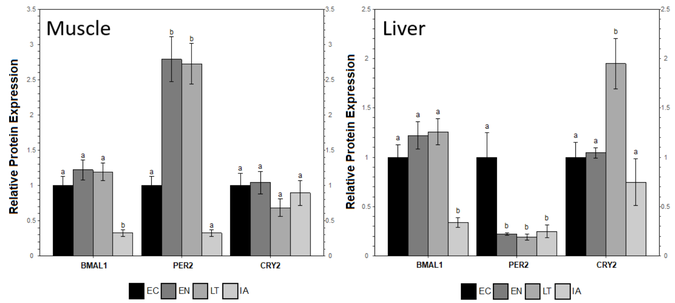


Fig 1. Thirteen-lined ground squirrel CLOCK gene expression levels in Muscle and Liver throughout the hibernation cycle.
EC – Euthermic Control, EN – Entrance into Torpor, LT – Late Torpor, IA – Interbout arousal.