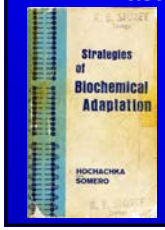
EXPLORING BIOCHEMICAL ADAPTATION:

Synthetic Intuition on a Family Farm

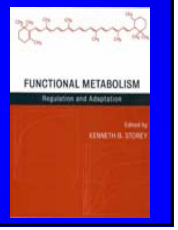
www.carleton.ca/~kbstorey

Biochemical Adaptation - How Animals Work

- Search to identify principles of biochemical regulation across the animal kingdom
- Biochemical unity
- Chemistry bkgd., NO Biology (ever)
- Elastic limits of biochemistry



There are so many songs and only the three cords.
- John Hiatt



A Life of Science Adventure

Mentors

Peter Hochachka

Dave Jones

Knut Schmidt-Neilsen, Ladd Prosser, Kjell Johansen, **Ken Davey**, Hans Krebs, Gene Huber, Les Copley, Geoff Eales, A. Helix

DO YOUR WORK, THEN STEP BACK.
THE ONLY PATH TO SERENITY.
- "Tao Te Ching" by Lao Tzu

Storey Family Farm

SYNTHETIC INTUITION

1) A new mix of ideas leads to a new field:

Chemistry
Mol. Biol.
Biochem.
→ Diverse Techniques → Comparative Experiments

NMR, MRI, DSC, AFM, DSF, UV difference, Protein purification, etc.

2) Models: Zoology, Ecology, Field Trips
3) Any new set of data reorganizes itself through UNRELATED pieces of the puzzle and returns as UNIQUE.
4) Salvage Solutions from Chaos:
   ex. Thesis Ideas, *DATA KNOTS*
5) Time Vampire: "Students Match Projects"

SYNTHETIC INTUITION

Something Old,
Something New,
Something Borrowed,
Some Glue

SYNTHETIC INTUITION

INPUT →
~ Ecology
~ Natural History
~ PHYSIOLOGY
~Chemistry Analytical
~ Biochem methods
~ Mol Biol methods
~ Genes – BioInform.
- NOT Metabolism
~ Equipment Expos
~ Catalogues
~ Tools:
- PHONE (1980)
- EMAIL (1990→)
~ Jan Writing
~ Touring (R&R)

FILTER →
~ Transducer
~ Organizer
~ *Revamp*
~ IDEA LENS
~ Non-sci. Stability
~ Never "Circle the Wagons"
~ COST / BENEFIT

OUTPUT
~ Metabolic Arrangement
~ Reorganization of Metabolism
~ Adaptive Change at Pathway Level
~ Integration: multi-levels of biol. organization
~ Model Organisms as raw material
~ Intracellular: from membrane to Nucleus

BIOCHEMICAL UNITY

Why Am *I* Here

" My lab is full"

>> Said to KBS when turned down by PWH for a spot in his lab.

...15 minutes (discussion) later ...

" Take that desk"

>> Said to KBS when Peter discovered that Ken had a scholarship that paid both salary and research expenses.

And, Students

50 MSc, 36 PhD, 11 PDFs

PDF

J Ballantyne
S Rahman
B Michaelidis
R Ferguson
SPJ Brooks
M Hermes-Lima
C Frank
Q Cai
I Moineau
M Batrukova
E Kotani

PhD

W Plaxton
T Churchill
D Joanisse
Y Su
J Grundy
H Mehrani
C Holden
W Willmore
B Thatcher
K Cowan
J MacDonald
T Bilgen
S-B Wu
T English
A Fahlman
D McNally
K Larade
S Eddy
D Hittel
D McMullen
A de Croos
P Morin
K Abnous
M Hapsatou
C Ramnanan
C Dieni
A Malik
A Krivoruchko
B Lant
K Biggar
J Zhang
C-W Wu
N Dawson
R Bell
A Letourneau
S Tessier

MSc

K Male, D Miller, S Korycan, R Cole, A Chakrabarti, J Duncan, R Whitwam D Kelly, D Schafhauser, C Holden, E Russell, D Douglas, A Muise, T Pannunzio, P Schade, S Greenway, M de la Roche, T English, D Lobsinger, L Jurgensen, S Lautru T Pfister, S Saeedi, M Castellarin, E Sepehr, K Yan, J Ni, L Zhenhong, A Woods, S McFadyen, J Du, J Zhang, J Zhou, L Xie, M Bouffard, J Niles, L-H Yao, J Lama, R Bell, M Mathialagan, O Aguilar, N Dawson, C Brooks, R Roufayel, S Tessier, A Letourneau, M Allan, A Holden, K Sullivan, A Mahmud, J Wu

+ 105 Undergrads

WHY I PERSISTED

- Synthetic Intuition
- JANET
- Talented Team (PhD, MSc, UG)
- Strategy (Student Wrangling)
- PDF (Few but Key) + Luck
- Constant NSERC funding
- Occasional Equipment grants
- Big Scores (timely) CFI-OIT, NIH
- Cardboard Enemies / Big Talent Support

NSERC CRSNG

Canada Research Chairs / Chaires de recherche du Canada

My Presentation : R&R ? Or Comedy ?

- At Rock Shows, you want the group to play the OLD songs just like on the album
- At Comedy Shows, if you hear an OLD joke, you boo. You want the NEW, fresh material.

Answer: Science talks are about tomorrow

Greatest Hits: (Vol 1)
"High Tides & Green Grass"
The early days

- Comparative regulation of glycolysis
- Methods in Enzymology (purification)
- Exercise muscle metabolism: insects & cephalopods
- Octopine (**Storey cycle**), alanopine & strombine
- Glycolytic Enzyme Complex
- Bound water in metabolism
- Reversible phosphorylation control of metabolic enzymes (Novel)
- Phosphagen effects on enzymes
- PFK polymers & $F2,6P_2$

Greatest Hits: (Vol 2)
Anoxia Tolerance

- Anti-Pasteur Effect (Anti-Temperature !)
- Coordinated Metabolic Rate Depression (MRD)
- Anabolism follows Catabolism in MRD
- Reversible phosphorylation of glycolytic enzymes: Gly phos, PFK, PK, etc.
- Protein kinases: PKA, PKG, MAPKs, AMPK, etc.
- Anoxia-induced gene expression
- Antioxidants – adaptation to variable oxygen

Greatest Hits: (Vol. 3)
Cold & Freezing Survival

- Deep supercooling by cold-hardy insects
- Freeze tolerance:
  - insects & molluscs
  - frogs, turtles, lizards, snakes
- Biochemistry of cryoprotectants
- Adaptive evolution from underlying anoxia & dehydration tolerances
- Freeze responsive gene expression
- Novel proteins

Unique Animal Stress Model

Vertebrate whole-body freeze tolerance

Tissue cryopreservation

Tolerance of extreme ischemia and hyperglycemia

Greatest Hits: (Vol. 4) Hibernation

- Regulated MRD drives body temperature down
- Reversible enzyme control in torpor-arousal cycles
- Cold adaptation of mammalian enzymes
- Polysome dissociation, mRNA storage
- Micro RNA
- Gene screening, epigenetic controls
- Antioxidant defense (Tf)
- Atrophy resistance

Greatest Hits: (Vol. 5) Estivation

- MRD parallels
  estivation = low oxygen / anoxia
- Phosphorylation also controls
  - ion motive ATPases (NaK, Ca)
  - novel enzymes
  - protein synthesis flux generators
  - transcription factors
- Involvement of protein kinases – Akt, AMPK, MAPKs, PKA/PKG
- Role of FOXO transcription factors
- Urea effects on enzymes

Greatest Hits: Full Collection

- Animal stories
- Publications
- Research Interests
- Students & projects
- Media
- Textbook with former students

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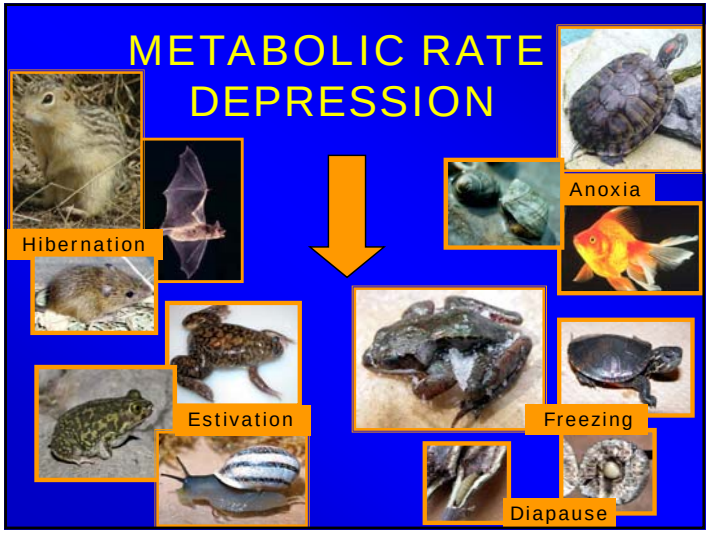
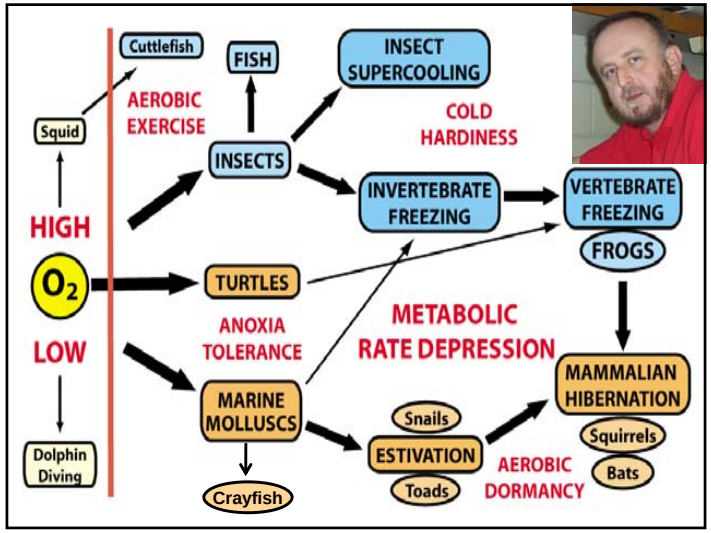
Best Experiment EVER !

CSZ
U. Ottawa
1983



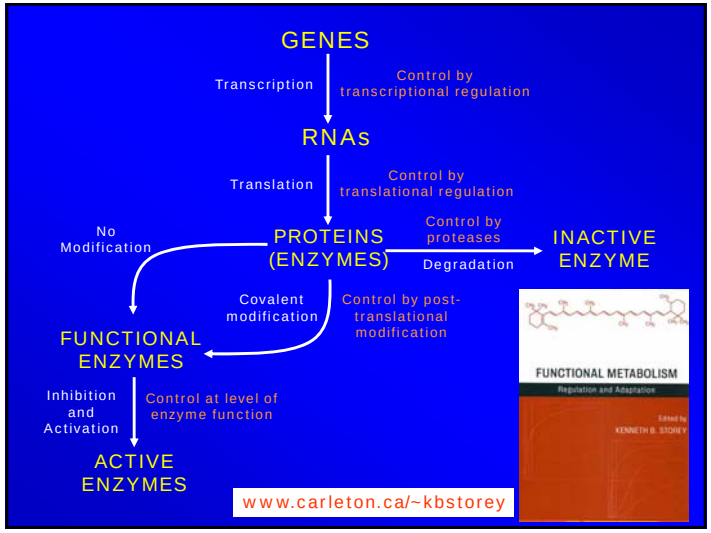


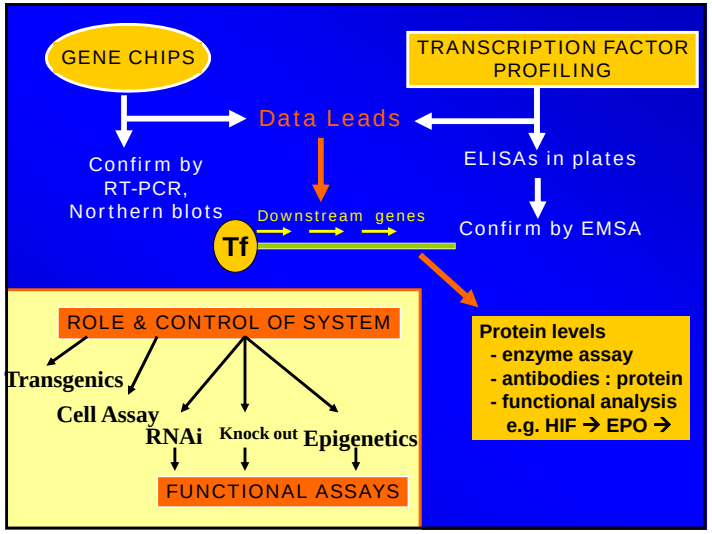
Principles of Metabolic Rate Depression

- Transcriptional + translational + PTM
- Anabolism <u>follows</u> Catabolism in MR
- Coordinated suppression: gene expression, protein synthesis, biosynthesis, cell cycle, etc.
- Reversible phosphorylation of key enyzmes, ion channels, transcription factors, etc.
- Stress-activated protein kinases

Cell preservation in hypometabolism

- Antioxidant defenses, iron sequestered
- Chaperone proteins





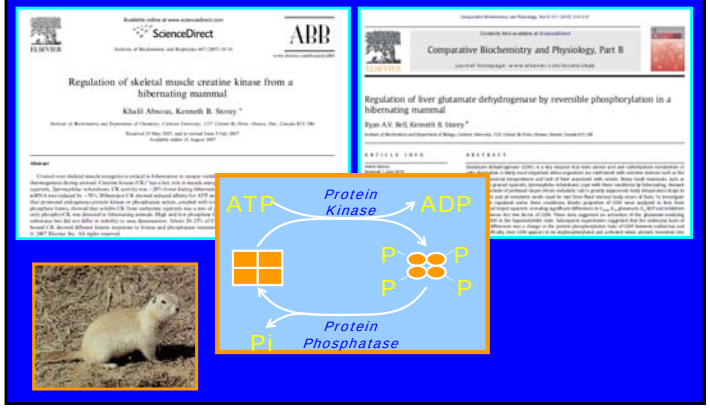
Where do we go from here?

- Human applications of MRD research
- Novel phosphorylations
- Atrophy, hypertrophy
  -- autophagy for survival
- Turning it all off -- microRNA
- Epigenetics & adaptation
- Life span extension
- Antioxidant defense
- Cell cycle suppression
- Unity through evolution

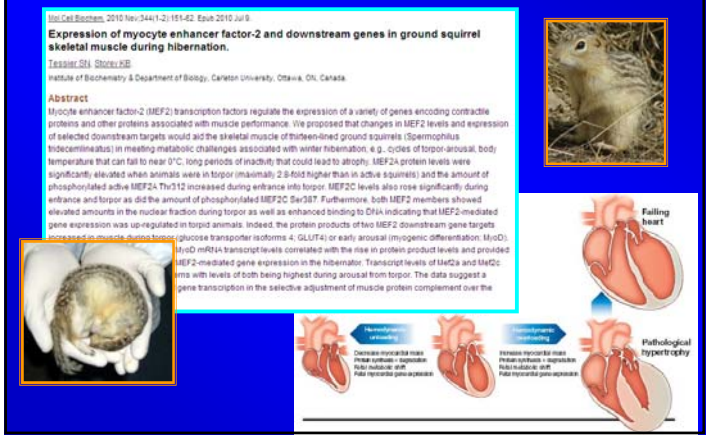
NOW: finally !!! NEW DIRECTIONS

Hibernation and medicine

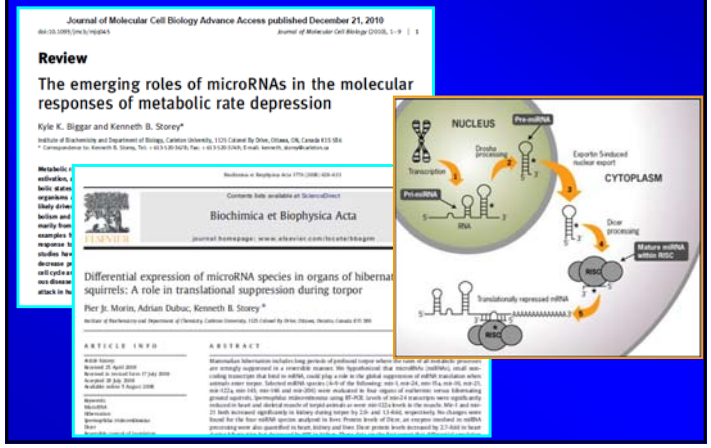
Novel phosphorylations



Atrophy – Hypertrophy

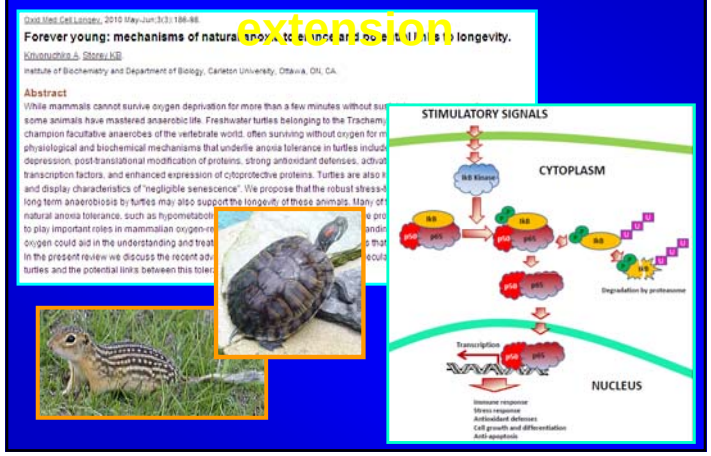


Turning it all off

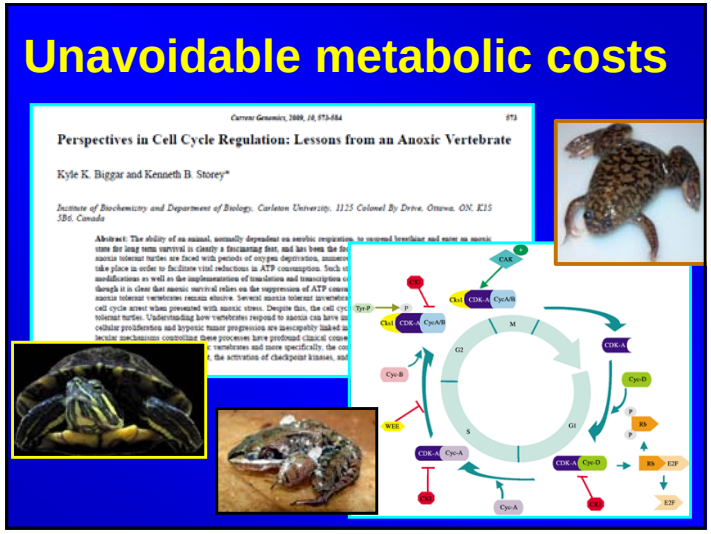


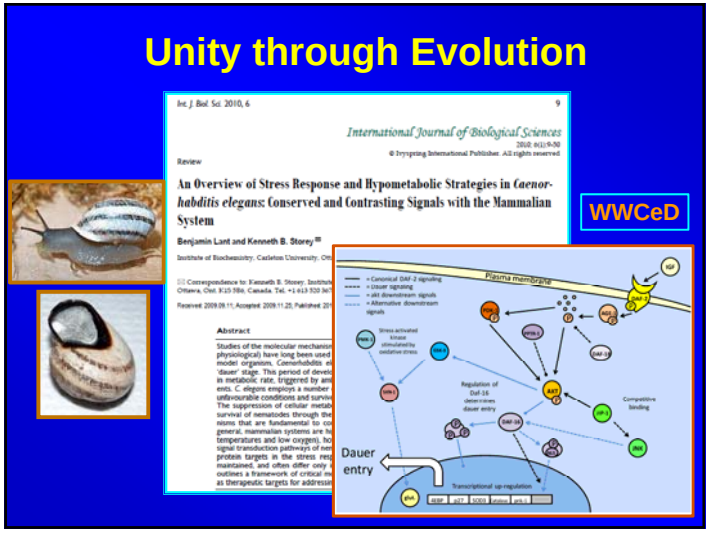
Epigenetics in Adaptation

Life span extension




Ukrainian connection
- Metal & herbicide effects on fish
- Antioxidant defense
Chemosphere
Cytotoxicity of chromium ions may be connected with induction of oxidative stress
Low toxic herbicide Roundup induces mild oxidative stress in goldfish tissues


Unavoidable metabolic costs
Perspectives in Cell Cycle Regulation: Lessons from an Anoxic Vertebrate
Kyle K. Biggar and Kenneth B. Storey


Unity through Evolution
International Journal of Biological Sciences
An Overview of Stress Response and Hypometabolic Strategies in Caenorhabditis elegans: Conserved and Contrasting Signals with the Mammalian System
Benjamin Lant and Kenneth B. Storey
WWCeD
Plasma membrane
Dauer entry


ONWARDS !
MW low → high
pH low → high
Temperature Adaptation in a Changing Climate
WELCOME TO FABULOUS LAS VEGAS NEVADA