A collective of health practitioners mentoring one another in topics related to nutrition.
Anyone who wishes to join – You select yourself
Second Monday each Month 1 - 2pm
To share and build understanding of the common and uncommon knowledge of the practice of nutrition in the care and treatment of ourselves and the patients under our care.
Share your knowledge with each other.

Competition and knowledge hoarding only supports lost knowledge. This group endeavors to share knowledge and clinical experience to serve not only ourselves, but all people.
"If you want to learn something, read about it.
If you want to understand something, write about it.
If you want to Master something, teach it."
Yogi Bhajan
At some point we ask you to present a topic for presentation to the group. This presentation need only be 35-40 minutes in length with a power point or notes available in Word for the group. You should be able to do a Q&A with the group to follow.

Everyone will be encouraged to participate in the Q&A and it is asked that this become a roundtable type Q&A.

If you chose not to present, that is your decision and you will not be ousted from the group.
Push *6 now to mute your line. When the speaker is finished or asks for open input, or if you have a question or wish to add to the discussion, press *6 to unmute your line.
Hormesis, Heat Shock Proteins, and Sirtuin Upregulation

James Parish, DC
Wolff’s Law

- The structure of a bone will change depending on the forces put on that bone.
- Increased force or stress will cause the remodeling of the trabecular structure of the bone such that the bone can handle those stresses.
- In other words, what doesn’t break the bone makes it stronger.
Just like bone, cells have their own way of making themselves stronger.

Hormesis is the concept that a body will mount a positive physiologic response to small amounts of negative stimuli that could be harmful in larger quantities.

Negative stimuli can range from exercise to phytochemicals to small amounts of radiation.
Hormesis

- 3 forms of hormetic stimuli
  - Lifestyle-Exercise, phytochemical, calorie restriction
  - Environmental-Heat/cold, toxins, radiation
  - Endogenous-Oxidative stress, ischemia, neurochemical

- Factors that disrupt cellular homeostasis activate pathways of cellular compensation with the goal of stabilizing the cell and increasing resistance of future disruptions
The goal is increase your cells ability to deal with any stresses that occur. We know this happens when we exercise, increase our body temperature, calorie restriction, etc.
The pathway by which this occurs is through the upregulation of heat shock factor, heat shock proteins, and sirtuins.
What the heck is a heat shock protein?

- Originally found in bacteria that survived high temperatures when exposed to it in smaller increments rather than all at once.
- Proteins within the bacterial cell performed activities that allowed the cell to adapt.
Heat shock proteins regulate the folding and unfolding of other proteins within the cell, particularly in the nucleus of that cell. Additionally, they chaperone proteins around within the cell for destruction or reassembly when they are damaged. They shift denatured, aggregated proteins toward orderly, functional proteins to allow the cell to perform its necessary functions.
Despite the name, heat shock proteins are really up-regulated in the cell during any type of cellular stress

- Oxidative stress
- Infection
- Oxygen deprivation
- Toxic bombardment

This is an attempt for the cell to maintain homeostasis
Non Stress Conditions

- HSP also occur within the cell on a everyday basis and are an integral part of the cells everyday maintenance.
- Sheparding malformed proteins to disposal sites within the cell, and taking proteins from one area to another to ensure proper folding and implementation within the cell.
Sirtuins are a group of protein enzymes called histone deacetylases.

Regulation of
- Function of cell during low calorie times
- Transcription of cellular components, including heat shock proteins
- Apoptosis
Answering the call

- There is a cascade that occurs for the proliferation of heat shock proteins.
- Sirtuin, particularly SIRT1 binds to Heat Shock Factor and does not allow for the acetylation of HSF, thereby signaling for the increased production of Heat Shock Proteins.
Sirtuin 1 is up-regulated in the cell and binds to heat shock factor.

- Prevents the deacetylation of HSF thereby increasing the heat shock response pathway.

- Resveratrol, silymarin, rhodiola, eleuthro, and schisandra are all sirtuin up-regulators.
Pillar #2-Glycemic Management

- Insulin and cortisol dysregulation are at the heart of this pillar.
- The consequence of sustained insulin up-regulation is the adaptation mechanism of insulin resistance.
Sirtuin 1 (SIRT1), the mammalian homolog of SIR2, was originally identified as a NAD-dependent histone deacetylase, the activity of which is closely associated with lifespan under calorie restriction. Growing evidence suggests that SIRT1 regulates glucose or lipid metabolism through its deacetylase activity for over two dozen known substrates, and has a positive role in the metabolic pathway through its direct or indirect involvement in insulin signaling. SIRT1 stimulates a glucose-dependent insulin secretion from pancreatic beta cells, and directly stimulates insulin signaling pathways in insulin-sensitive organs. Furthermore, SIRT1 regulates adiponectin secretion, inflammatory responses, gluconeogenesis, and levels of reactive oxygen species, which together contribute to the development of insulin resistance. Moreover, overexpression of SIRT1 and several SIRT1 activators has beneficial effects on glucose homeostasis and insulin sensitivity in obese mice models. These findings suggest that SIRT1 might be a new therapeutic target for the prevention of disease related to insulin resistance, such as metabolic syndrome and diabetes mellitus, although direct evidence from clinical studies in humans is needed to prove this possibility. In this Review, we discuss the potential role and therapeutic promise of SIRT1 in insulin resistance on the basis of the latest experimental studies.

**SIRT1 and insulin resistance.**
Pillar #2-Glycemic Management

- Sirtuin overexpression had positive effects on insulin sensitivity and glucose metabolism in obese mice models
- Resveratrol is a potent sirtuin activator
- Should this be a consideration for our insulin resistant patients?
SIRT1, one of the seven mammalian proteins of the sirtuin family of NAD\(^+\)-dependent deacetylases, has recently been shown to attenuate amyloidogenic processing of amyloid-β protein precursor (APP) in cell culture studies in vitro and in transgenic mouse models of Alzheimer’s disease. Mechanistically, SIRT1 increases α-secretase production and activity through activation of the α-secretase gene ADAM10. Because α-secretase is the enzyme responsible for the non-amyloidogenic cleavage of APP, upregulation of α-secretase shifts APP processing to reduce the pathological accumulation of the presumptive toxic Aβ species that results from β-secretase and γ-secretase activity. Interestingly, the spatial patterns of Aβ deposition in the brain might correlate with increased aerobic glycolysis in those regions. Because aerobic glycolysis depletes cellular levels of NAD\(^+\) (through a decreased NAD\(^+\)/NADH ratio), it is possible that a corresponding downregulation of the NAD\(^+\)-dependent sirtuin pathway contributes to the amyloidogenic processing of APP.

The sirtuin pathway in ageing and Alzheimer disease: mechanistic and therapeutic considerations

David J Bonda, BA\(^a\), Hyoung-gon Lee, PhD\(^a\), Antoni Camins, PhD\(^c, d\), Mercè Pallàs, PhD\(^c, d\), Gemma Casadesus, PhD\(^b\), Prof Mark A Smith, PhD\(^a, *\), Xiongwei Zhu, PhD\(^a\).

The upshot of this is that upregulation of sirtuin and heat shock proteins provide a way for us to restore cellular integrity and order, increase cellular vitality, decrease insulin resistance, reduce risk of Alzheimer’s and perhaps increase lifespan.
As we mentioned earlier, introducing phytochemicals can induce this same hormetric response that will allow our cells to be prepared for what comes their way.

Proactionary vs. Reactionary
By invoking this heat shock protein pathway we can mimic:
- Calorie restriction
- Exercise
- Oxidative Stress

This is an overall cellular survivability strategy
Herbavital provides a means for us to influence this hormetic pathway.

- It contains 36 mg of resveratrol, 48 mg of silybin from milk thistle, as well as Korean Ginseng, Masson Pine Bark Extract and Ginkgo.
- 4 tablets provide 150mg of resveratrol
- Lee Carroll states this as the hormetic dose
Introduction of resveratrol increased survivability of mice that were genetically modeled for amyotrophic lateral sclerosis.

The number of surviving motor neurons increased in the resveratrol injected mice.

Acetylation of HSF1 decreased allowing for the subsequent upregulation of HSPs in these mice.

Resveratrol upregulated heat shock proteins and extended the survival of G93A-SOD1 mice. 

Soyoung Han, Jong-Ryoul Choi, Ki Soon Shin, Shin Jung Kang. Brain Research Volume 1483, 5 November 2012, Pages 112–117
Rhodiola and Ginseng

- Rhodiola has been shown to increase serum heat shock protein levels in mice.
- When mice were forced to swim and were given a combination of rhodiola, eluethero, and schisandra there was a multiplicative effect.
- Exhaustion times were also greatly prolonged.
Other considerations

- Nrf2 pathway promotion
  - Vitanox, Cruciferous complete, Garlic
- Antioxidant burden reduction
  - Cellular vitality
- Raw materials for the cell
  - Protefood, RNA
- Maintaining cellular communication
  - Organically Bound Minerals, Calcium Lactate
Thank you for your Time