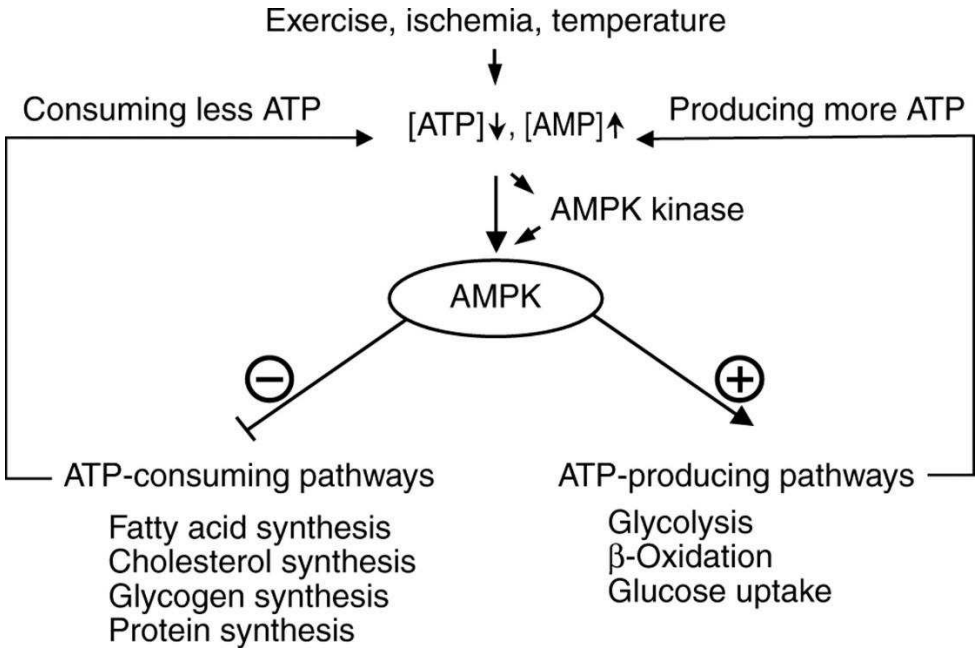
Chronic Fatigue Syndrome – Biology of Muscle and Therapies Suggested

Clinical Discussion and Literature Review: © PS Anderson – www.ConsultDrA.com 2017

Reference: Brown AE, Jones DE, Walker M, Newton JL. (2015) Abnormalities of AMPK Activation and Glucose Uptake in Cultured Skeletal Muscle Cells from Individuals with Chronic Fatigue Syndrome. PLoS ONE 10(4): e0122982. doi:10.1371/journal.pone.0122982

Key Findings: The researchers found four main differences in cultured skeletal muscle cells from subjects with CFS; increased myogenin expression in the basal state, impaired activation of AMPK, impaired stimulation of glucose uptake and diminished release of IL6. The retention of these differences in cultured muscle cells from CFS subjects points to a genetic/epigenetic mechanism, and provides potential to identify novel therapeutic targets.

Clinical Discussion: AMPK (5'-adenosine monophosphate-activated protein kinase) is an enzyme controller in cells throughout the body (highest in hypothalamus, liver, muscle, adipose tissue and pancreas). The graphic and description from Frederich et.al. does an excellent job of a basic overview of the function of AMPK:



Model of the AMP-activated protein kinase (AMPK) cascade. Stressors such as hypoxia, exercise or temperature lead to a decrease in cellular ATP and an increase in cellular AMP. This activates AMPK either directly, or indirectly through an upstream AMPK kinase. Once AMPK is activated, it phosphorylates multiple downstream targets, mainly rate-limiting enzymes of all energy metabolism pathways. The effect of this phosphorylation, in summary, leads to an acceleration of all ATP-producing

pathways and a deceleration of all ATP-consuming pathways. Therefore, AMPK activation preserves the cellular ATP concentration. [Graphic and explanation from: Frederich M, et.al. AMP-activated protein kinase (AMPK) in the rock crab, Cancer irroratus: an early indicator of temperature stress. J Exp Biol. March 2009. vol. 212 no. 5 722-730]

Another way of viewing its "master role" in metabolism is "It is switched on in response to metabolic stresses such as muscle contraction or hypoxia, and modulated by hormones and cytokines affecting whole-body energy balance such as leptin, adiponectin, resistin, ghrelin and cannabinoids. Once activated, it switches on catabolic pathways that generate adenosine triphosphate (ATP), while switching off ATP-consuming anabolic processes." [From PMID: 18719601].

If the cell lines from the ten CFS patients are representative of the overall CFS population, this finding may not only further enlighten a broader understanding of the pathogeneses of CFS but also potential therapeutics as well. One simple way to see this finding is that (just as one sees in a patient with CFS) the cell regulatory mechanisms which should help cell function and regeneration (response to stress, hypoxia, glucose, and low ATP to name a few) are confused. Therefore when the patient with CFS has any demand for new energy production and regeneration in their high energy cell types they cannot efficiently meet those demands. The outcome of this confusion is a long progressive slide into cellular dysfunction.

Although this is undoubtedly not the only cellular dysfunction in CFS it is certainly a central cell regulatory system which can greatly affect cell and organism function over time. A potential for a "chicken or egg" conundrum does exist here in that we do not know if this is a cause of ultimate dysfunction or an effect of earlier dysfunctions that build up to start this response. The answer may be a bit of both (some genetic factors, epigenetic stressors on one side and some cumulative cell stress on the other). Certainly our earlier work [1] looking at the association of MTHFR genetic SNP's and CFS as well as treatment of those SNP variants showed not only an increase in genetic issues but also a very positive treatment response. Whichever it is the ultimate concern is what one does with the information to attempt to undo the problem.

Although not encyclopedic, my personal experience in the past twenty years care of those with CFS would generally match approaches that slowly undo cell regulatory issues such as this AMPK finding. The major areas of help I have seen (but are not limited to) are in the following areas:

- ReDox re-balancing and regulation

    - Supply fat and water soluble nutrients in therapeutic doses
    - Utilize parenteral nutrients and co-factors
    - Use synergistically timed hyperbaric oxygen therapies
- Removal of impediments to nutrient uptake
    - Repair GI function
    - Supply extra nutrition
- Assessment and appropriate treatment of genomic factors
    - Methyl cycle, Mitochondrial
    - Immune, GI etc…
- Removal of immune stressors
    - Deal with autoimmune overlay if present
    - Remove pathogens if present
- Rest, rehabilitation and restoration of high energy tissues
    - Slowly increased graded exercise tolerance
    - Nutrition and Hormonal supply (thyroid, corticoid, iron, mitochondrial support)…to the cells
    - Improve sleep and rest phases
    - Mental emotional repair
- And many others

I am certain that as we learn more about cytokine signaling, cell biology, genetics and other factors, our understanding of chronic fatigue syndrome / systemic exertion intolerance disease will only deepen. To date studies such as this one help us in that they add basis to the physiologic therapies employed in natural medicine and validate the therapies we have clinically seen useful over time. Hopefully future data will not only deepen the understanding but also improve our integrated knowledge of this multi-factorial illness.

References:

1. Anderson, PS (2012, August). Active comparator trial of addition of MTHFR specific support versus standard integrative naturopathic therapy for treating patients with diagnosed Fibromyalgia (FMS) and Chronic Fatigue Syndrome (CFS). Poster Presentation, presented at the American Association of Naturopathic Physicians annual convention, Bellevue, WA.