Pharmaceutical Companies Behind the Eight Ball in Treatment of Mitochondrial Dysfunction

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Intro

As mitochondrial dysfunction has become better recognized as a factor in disease, research is starting to focus on targeted treatment. Pathology in chronic disease is repeatedly showing damage to the mitochondria. Oxidative stress from the environment causes harm to the mtDNA, proteins, and lipids of the mitochondria leading to decreased energy production. If the mitochondria are less efficient, more free radicals are produced. This creates an ongoing cycle of progressive mitochondrial dysfunction.

Currently there are no FDA approved treatments for mitochondrial disease[1]. Multiple pharmaceutical companies have ongoing early clinical trials targeting mitochondria. Upon looking at the mechanisms of these medicines, it is apparent they are targeting specific areas of mitochondrial dysfunction. Although energy production through the mitochondria involves multiple steps, these new medicines are focusing in on one specific function.

Targeting oxidative stress

One pharmaceutical medicine currently in clinical trials is MTP-131[1]. The medicine is administered by IV or topically for ophthalmic use. The medicine MTP-131 was created to enter the mitochondria to reduce oxidative stress. The target of the medicine is a lipid called cardiolipin which is critical for the inner mitochondrial cell membrane. The electron transport chain forms ATP exclusively on this inner membrane. If the membrane is altered causing damage to the cardiolipin, it releases cytochrome C into the cytosol of the cell beginning the process of apoptosis or self-destruction of the mitochondria. Often an increase in free radicals causing oxidative stress will damage cardiolipin.

Targeting activation of Nrf-2

Activating the Nrf-2-Keap 1 pathway begins a cascade of events that decrease inflammation and increase anti-oxidants. It initiates the production of the anti-oxidant enzymes catalase, superoxide dismutase, and glutathione peroxidase. Activation of Nrf-2 also decreases the release of pro-inflammatory cytokines such as TNF-alpha. Mitochondrial efficiency and ATP production is also enhanced by this pathway. Targeting these cellular processes through the nrf-2 pathway has been an aim of pharmaceutical companies. A medicine called RTA 408 was developed to activate nrf-2. Clinical pre-phase 3 trials are currently underway.

Targeting production of glutathione

An investigational medicine called RP 103, a form of cysteamine is in ongoing clinical trials[1]. The molecule helps convert cystine into cysteine needed for formation of glutathione. Glutathione is the main antioxidant in cells. Cysteine is the rate limiting amino acid in glutathione production. The medicine by increasing levels of glutathione in the cells will be predicted to decrease oxidative stress damage to the mitochondria. Ongoing open label clinical trials are determining dosing levels, safety, and efficacy of the new medicine.

Natural alternatives

From an integrative perspective, it is more important to look at the underlying cause of the disease than the disease itself. Understanding the cellular mechanisms will help guide treatment more than a diagnosis. If there is mitochondrial dysfunction or oxidative stress, this needs to be treated. It does not matter if the disease is Autism or Alzheimer's.

Targeting mitochondrial function involves supporting the mitochondrial membrane and supplementing the key nutrients needed for the formation of ATP[2,3]. It also requires increasing antioxidant reserves in the body and decreasing oxidative stress. A comprehensive treatment approach requires supporting these functions simultaneously instead of one targeted treatment as in the pharmaceutical approach.

While the pharmaceutical companies are studying precursors for glutathione, liposomal glutathione is already available. Research on absorption has shown increases in glutathione levels with oral use[4]. In addition, studies have shown clinical improvements in chronic disease with oral liposomal glutathione[5]. Since glutathione is a critical anti-oxidant in the body, being able to safely and effectively restore levels is critical for healing.

Many natural treatments have shown to activate nrf-2 receptors. Curcumin, one of the active ingredients in turmeric has multiple studies showing its ability to bind to the nrf-2 receptor and decrease pro-inflammatory cytokines[6,7,8]. Resveratrol, EGCG in green and black tea extract have been also shown to be effective. Polyphenols, which include curcumin, resveratrol, EGCG among others all appear to be able to activate nrf-2 to increase anti-oxidants and decrease inflammation[9-13].

A unique anti-oxidant, molecular hydrogen has research supporting its ability to activate nrf-2 receptors also[14-16]. In addition, molecular hydrogen has the capability to scavenge the dangerous hydroxy free radical[14-16]. This free radical is more reactive with cellular tissues resulting in more oxidative stress. Molecular hydrogen does not affect the free radicals needed for mitochondrial function or the activation of the antioxidant enzyme cascade including superoxide dismutase and catalase[14-16].

Finally, awareness of the importance of mitochondria dysfunction and oxidative stress are being recognized for their role in chronic disease. Integrative medicine has been treating these issues for years. With an integrative and holistic mind set, we are well aware of the importance of a multi-modal approach. The pharmaceutical industry is trying to target the correct pathways but is still focusing on one part of a complex puzzle. Luckily, we have many natural treatments to implement simultaneously to promote recovery from chronic illness.

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