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Topic: Structural Insight and Biophysical Characterization of Irisin: A Mechanistic Approach for Elucidation of its role in Metabolism and Neurodegenerative Disorders

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Findings

PhD title: Structural Insight and Biophysical Characterization of Irisin: A Mechanistic Approach for Elucidation of its role in Metabolism and Neurodegenerative Disorders

In my PhD, I have cloned, expressed, and purified the recombinant irisin. Irisin is a recently identified myokine which is also considered to be a molecular mimic of exercise as it imparts the beneficial effects of exercise on human health. At first, irisin was biophysically characterized and the molecular basis of structural stability of irisin has been measured under the stress of urea. In the next section, we investigated the glycation in irisin and characterized the irisin-AGE adducts formed due to glycation through various biophysical spectroscopic as well as microscopic approaches. We have also identified N-acetyl aspartate (a brain osmolyte) as a novel inhibitor of irisin glycation in subsequent study. Further, we have also determined the heat-induced aggregation profile of irisin and the inhibition of aggregation by using trehalose as a co-solute through various spectroscopic and microscopic approaches. It was observed that trehalose prevents the aggregation of irisin in a concentration-dependent manner. Further, we have determined the Microtubule Affinity Regulating Kinase 4 (MARK4) inhibitory potential of irisin. Our results demonstrated that irisin binds to MARK4 with a good affinity subsequently inhibiting its enzymatic activity indicating that enhancing the levels of irisin either pharmacologically or through exercise induction can be a therapeutic strategy for the treatment of MARK4–associated disorders. Further, an *in-vitro* model of hypoxia was made by incubating the SH-SY5Y cells in glucose-deficient and oxygen-deprived conditions. The mRNA expression level of different inflammatory cytokines (TNF-α, IL6) was investigated with the help of RT-PCR. It was found that in hypoxic conditions, the expression of pro-inflammatory cytokines was downregulated by irisin. So, it can be inferred that irisin is having neuroprotective role against ischemic injury. At last, co-immunoprecipitation study showed that irisin is having close interaction with few important proteins implicated in physiological processes.