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Circulating Soluble-Klotho and IGF-I Responses to Different Exercise Modalities in Young, Elderly and CAD Patients

Saghiv M*

Exercise Physiology Department, University of Mary, USA

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***Corresponding author:** Moran S Saghiv, Associate Professor, Exercise Physiology Department, Casey Center, Room 141B, University of Mary, 7500 University Drive, Bismarck, ND 58504, USA, Fax: 701-255-7687; Tel: 702-908-2390; Email: mssaghiv@umary.edu

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Introduction

Klotho gene expression in positively influenced by different exercise modalities acting as an epigenetic influencer [1], resulting in increased work capacity, performance, and lifespan, and decreased aging in healthy and diseased populations [2-4]. As is the case with exercise, positive adaptations decrease and diminish with time if exercise training is not maintained.

S-Klotho

Klotho is a transmembrane protein that provides some control over the sensitivity of the organism to Insulin and appears to be involved in aging [5]. Age-related declines are manifest by a decreased ability for aged skeletal muscle to respond to physiological stimuli such as muscle loading or acute injury, and disease related effects [6-10].

IGF-I

IGF-I is critical for normal body growth, development and maintenance, and has important roles in multiple biological systems [11,12]. A variety of cellular responses are induced by IGF-I, including cell proliferation, differentiation, migration and survival [13,14]. These cellular responses have implicated IGF-I in several conditions such as the pathophysiology of several cancers [15], or the mitogenic and myogenic processes during muscle development, regeneration or hypertrophy, since, unlike other growth factors, IGF-I acts as both a mitogen and a differentiation factor [16].

Deficiency of IGF-I in skeletal muscle may contribute to Sarcopenia by severely impacting protein synthesis. IGF-I has anabolic effects on muscle protein content by inhibiting protein degradation and promoting Myogenesis. Indirect data have supported the concept that IGF-I may be atherogenetic because it can induce vascular smooth muscle cell proliferation in vitro [17]. Thus, IGF-I has been considered a promoter of arterial obstructive lesions [18].

The Influence of Exercise Modalities on S-Klotho and IGF-I

Regular aerobic exercise participation promotes health and disease prevention [19]. Endurance exercise like biking, walking, swimming and running, appear to benefit longer life expectancy than anaerobic exercise like power lifting [20]. It has been suggested that circulating Klotho levels are up regulated in response to an acute exercise bout, but that the response may be dependent on fitness level [21-24].

Compared to sedentary young and old subjects, in the elite well aerobic trained young runners and master athletes s-Klotho levels are markedly elevated while, IGF-I levels were decreased [25]. IGF-I is generally thought to be associated with anabolism and wellbeing [26], yet, signaling through IGF-I and Insulin receptors is negatively related to adults [27]. A meta-analysis study indicated that increased circulating concentrations of IGF-I are associated with increased risks for colorectal, prostate, and premenopausal breast cancers [28].

Several clinical studies have suggested that Klotho gene exerts strong cardio-protective effects. S-Klotho has been proposed as a key regulator of the development of cardiovascular disease. Associations between low levels of

s-Klotho and the occurrence and severity of cardiovascular disease have been reported, as well as a reduction of cardiovascular risk when levels were high [28]. This protein is related to the attenuation of vascular calcification as well as prevention of cardiac hypertrophy.

Conclusion

Inflection of Klotho expression through aerobic exercise training represents an interesting relationship that may contribute to the explanation of the anti-aging and anti-CAD effects of long lasting aerobic activity. Accordingly, being a long lasting aerobically trained individual, is associated with decreased risk factors, increased s-Klotho that, clearly counteracts the action of IGF-I.

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