Anti-Aging Gene linked to Appetite Regulation Determines Longevity in Humans and Animals

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EDITORIAL

The process of aging is determined by various genetic and environmental factors. Aging is associated with increased oxidative stress that alters cellular chromatin structure, DNA methylation with histone modifications. These epigenetic alterations lead to nuclear changes associated with mitochondrial apoptosis that is a major defect in the global chronic disease epidemic (1). The variability in longevity between individuals in different communities implicate various nutritional and environmental factors involved in transcriptional dysregulation that lead to cell damage that accumulates with age and contributes to mitophagy, insulin resistance and programmed cell death. The absence or malfunction of a gene (2) necessary for transcriptional regulation of gene expression, DNA repair and telomere maintenance in neurons has become essential with relevance to neurodegeneration that determines aging and lifespan.

Key words: longevity; species; appetite; immune system; human; mitophagy; animals; neurodegneration; Sirtuin 1; nutritional therapy

Major implementations in lifestylestyle changes have been conducted and to introduce calorie restriction that alters cell metabolism by the use of specific nutrients to improve immunity connected to longevity (3). Genes that determine premature lifespan in humans have been identified and include genes (3,4) such as breast cancer genes BRCA1 and BRCA2 and hyperlipidemia genes (the low-density lipoprotein receptor, apolipoprotein B). Four candidate genes (3) have been implicated in longevity such as apolipoprotein E, angiotensin-converting enzyme, histocompatibility locus antigen and plasminogen activator inhibitor 1. These genes have effects on longevity in animals and humans by effects of calorie restriction (5) that determine the function of homeostatic proteins with effects on nutrient metabolism and immunity. A genome-wide scan has identified new loci for exceptional longevity and reveal a genetic overlap between longevity and age-related diseases and traits that include coronary artery disease and Alzheimer's disease (6). In humans and animals (dogs, cats, bears, horses, elephants, livestock/cattle) lifespan can vary between 29-86 years and in man depending on the community human lifespan can reach a maximum of 104 years with average age (70-80 years). Centenarians have very low levels of chromosome abnormalities (7) and indicate the absence of the malfunction in genes associated with DNA repair and DNA methylation that prevent mitochondrial apoptosis linked to various chronic diseases such as diabetes and neurodegenerative diseases. An anti-aging gene (8) that determines longevity and lifespan in various species

(**Figure 1**) has been identified as Sirtuin 1 (Sirt 1). Sirt 1 is a nicotinamide adenine dinucleotide (NAD +) dependent class III histone deacetylase (HDAC) that targets transcription factors (peroxisome proliferator-activated receptor-gamma coactivator, p53, pregnane x receptor) to adapt gene expression to metabolic activity and as a deacetylase is involved in the deacetylation of the nuclear receptors critical to neuron proliferation, insulin resistance and non alcoholic fatty liver disease (1). Sirt 1 is involved in telomere maintenance and DNA repair with its critical involvement chromosome stability and cell proliferation. Sirt 1 is important to the regulation of other anti-aging genes such as klotho, p66shc and Forkhead box protein O1 with relevance to age related diseases (8).
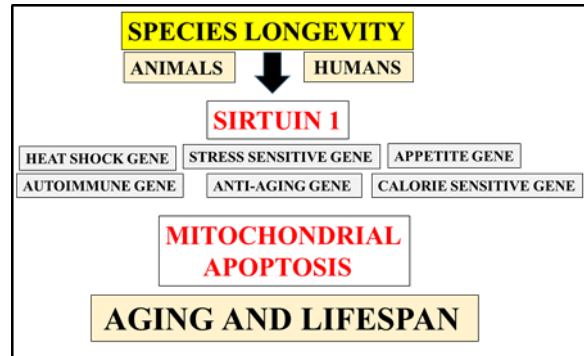

Figure 1. In humans and animals Sirt 1 is the anti-aging/heat shock gene that is sensitive to heat/cold stress with relevance to the induction of mitochondrial apoptosis and autoimmune disease. Sirt 1 regulates food intake and is the calorie sensitive gene that determines species survival linked to diabetes and neurodegenerative diseases.

Major interests in appetite regulation has indicated that appetite control is critical to longevity and lifespan and connected to various chronic diseases (9). Sirt 1 as a heat shock gene is important to the immune system in various species (10) with its repression linked to autoimmune disease (11). Core body temperature dysregulation will inactivate Sirt 1 and induce mitochondrial apoptosis with relevance to autoimmune disease and species longevity (12). Diet, environment and lifestyle (stress) changes incriminate Sirt 1 as the defective gene (**Figure 1**) involved in aging and lifespan and associated with neurodegeneration and chronic disease. In animals food quality (13) is essential to maintain Sirt 1 expression and activity with relevance to regulation of core body temperature and autoimmune disease. The longevity of lifespan in cattle and livestock will be determined by the xenobiotic content (10) and

food end products from bacteria/fungus such as bacterial lipopolysaccharides and mycotoxins (14). Animals may be more sensitive to neurodegeneration and synaptic plasticity with dietary interventions essential to maintain neuron and synapse interactions (14). The role of caffeine and Indian Spices (15,16) in food products has become of interest and may determine longevity in man. Furthermore inactivation of Sirt 1 is associated with senescence and its role in antimicrobial activity and mitophagy (17) may be critical for the survival of animal

Conclusion

In humans the function of the anti-aging gene Sirt 1 is critical to the maintenance of other longevity and anti-aging genes involved with aging and lifespan. Appetite regulation is connected to Sirt 1 function with mitochondrial apoptosis and neurodegeneration linked to various chronic diseases. Food consumption in the cattle and livestock industry should be carefully controlled since Sirt 1 and its dysregulation may be more sensitive to mitochondrial apoptosis in animals with effects on neurodegeneration and synaptic plasticity that determines species longevity.

Acknowledgements

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