Metabolic Disequilibrium and Aging: Modifying Favourably with Calorie Restriction and Calorie Restriction Mimetics

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ABSTRACT

METABOLIC DISEASE AND AGING: There is increasing evidence that metabolic disequilibrium and disorders influence the aging process and survival including the quality of life (QOL). The adipose tissue mediates various age-associated metabolic disorders such as insulin resistance (IR), metabolic syndrome (MetS), dyslipidemia and type 2 diabetes mellitus (T2DM), altogether which can negatively affect the lifespan and sends signals to modify the aging process in various tissues and organs. The role of master-switch and genomic guardian, p53 is important in this context.

CALORIE RESTRICTION (CR): The energy needs are determined by the body composition, especially the fat free lean mass and level of physical activity, and there is a change in nutritional needs during the middle age and later. The diet-gene interaction is a major determinant of health and illness, and the amount and type of food ingestion and caloric intake, in general, influence the health and life span. An excess calorie intake causes overnutrition and nutritional overload leading to increased adipose stores culminating as weight gain and obesity, which lead to IR, MetS, T2DM and other metabolic alterations. At the subcellular and cellular level there is increased potentially damaging exposure to reactive oxygen species (ROS).

CR MECHANISMS AND PATHWAYS: There have been identified several metabolic and genetic pathways that govern food ingestion, metabolism and life span. Experimentally, the CR has been shown to achieve increased lifespan in a broad spectrum of life forms from yeast, nematode, fruit fly, rodents and primates, including Homo sapiens, endosing that a diet adequately fulfilling nutritional needs, but low in calories may improve health, prevent many late-onset diseases and extend the life span. But, the benefits of CR are not a passive result of lower caloric intake but the consequence of an active regulatory intervention mimicking the food scarcity and activating certain genetic and metabolic programs that result in various vital beneficial effects. The genetic and molecular studies in model organisms, in fact, suggest that CR is a regulated process, in which the SIRT (Silent Information Regulator 2) gene plays an important role.

IMPACT OF CR ON QOL AND DISEASE: CR has long been recognized for its ability to extend life span and mitigate aging and stall disease processes in various organs. The data from animal and human studies indicate that the CR affects favourably several metabolic and molecular factors that modulate cardiovascular age-related alterations including Cardiac and arterial stiffness, hypertension and heart rate variability. These effects, in combination with various other benefits, such as protection against adiposity, IR and T2DM, neurodegenerative diseases and cancer, suggest that the CR may have a major beneficial effect on health status, quality of life and life span in humans.

IMAGE

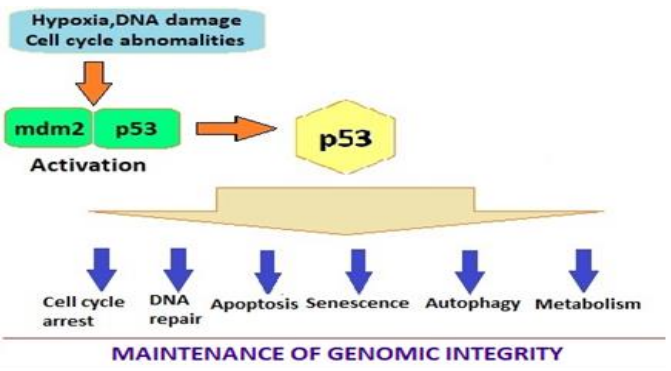


Fig. The stress factors activate p53 by dissociating the mdm2-p53 complex, which influences cell cycle, DNA repair, apoptosis, senescence and aging process (Modified from - Nikhra V. 2014. 'ERDOMA: The Entangled Relationship Between Diabetes, Obesity, Metabolic Syndrome and Aging'. Cardiology Today ISSN 0971-9172 Vol XVIII No. 4, 157-166 (3).

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KEYWORDS: Calorie restriction, Calorie Restriction Mimetics, Cardiovascular disease, Metabolic syndrome, Neuro-degenerative disorders, p53, Reactive oxygen species, SIRT gene, Type 2 diabetes mellitus.



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