Novel Roles of a DNA Repair Protein, DNA-PKcs, in Obesity, Neurological Function, and Aging

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Technology description

Summary

The catalytic subunit of the DNA-dependent protein kinase complex (DNA-PKcs) has been shown to be important in DNA repair and VDJ recombination in lymphocytes. The inventors have discovered that DNA-PKcs also plays novel, important roles in energy regulation and neurological function. The inventors observed that mature DNA-PKcs-deficient mice (also known as SCID mice) have a lower proportion of fat, resist obesity, and have significantly greater physical endurance than wild-type control mice, particularly with increasing age. The inventors also observed that DNA-PKcs-deficient mice have better memory and less anxiety. One potential explanation for this is that they express higher levels of brain-derived neurotrophic factor (BDNF), which is associated with neurogenesis, memory formation and suppression of anxiety and depression. Moreover, DNA-PKcs-deficient cells produce less oxidative stress. Thus, inhibition of DNA-PKcs may have unexpected utility in the treatment of a wide range of diseases and conditions.

The invention discloses methods of inhibiting DNA-PKcs activity to decrease adiposity, improve physical endurance and increase insulin sensitivity and the number of mitochondria. Also claimed are methods directed to improved neurological function, such as methods for protection from neurodegenerative disease, improving memory and learning ability, and for reducing depression and anxiety. Additionally, the invention discloses methods for reducing inflammation and for treating heart disease.

Market:

Obesity is a large and growing therapeutic market; over thirty percent of Americans are obese, and over sixty percent are overweight.

Similarly, the market for therapeutics directed to insulin-resistant, or Type 2, diabetes is rapidly expanding; the market for such drugs is expected to top $12 billion in 2012.

Loss of endurance and muscle mass is common in the elderly; the average adult loses thirty percent of his muscle mass between the ages of 20 and 70.

Development Status:

Application area

Development of therapeutics targeting obesity, insulin-resistant diabetes, and age-related loss of physical endurance.
Development of therapeutics to treat neurological disorders such as depression and memory loss.

Institution

NIH - National Institutes of Health

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