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Sirt基因家族及其对细胞寿命的调节

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在酵母、线虫和果蝇中，Sir2（silent information regulator2，沉默信息调节因子）基因家族是寿命调节的关键因子。哺乳动物的Sirt基因家族在进化上与Sir2基因高度同源，共有7个成员。Sir2基因调节酵母寿命的机理已比较清晰。而哺乳动物Sirt基因，特别是Sirt1基因与细胞衰老的关系正在成为新的研究热点。最近的研究表明，在热量限制（caloric restriction）或氧化逆境条件下，SIRT1蛋白主要是通过以下三个途径延长细胞寿命：一是抑制PPAR-γ（peroxisome proliferators activataed receptor－γ）以减少白色脂肪，从而减少脂质过氧化的损伤；二是脱乙酰化PGC-1α（ PPAR－gamma coactiveator-1α），诱导糖异生基因表达和肝糖元的生成；三是激活FOXO3α（Forkhead box class O3α），启动细胞的抗氧化途径。进一步研究Sirt基因家族对揭示哺乳动物寿命之谜具有重要的科学意义

The mammalian SIRT gene family and its role in regulation of cell lifespan

The Sir2 (Silent information regulator2) gene family modulates cell lifespan in Saccharomyces cerevisiae, Caenorhabditis elegans, and Drosophila. The Sir2 homologues in mammalian is called Sirt gene family and it is comprised of seven members. The mechanism of lifespan regulation by Sir2 gene in the Saccharomyces cerevisiae is relatively clear. While, the role of Sirt genes, especially, the Sirt1gene, in protection mammalian cell from senescence become a new area of research interest. Current knowledge shows that SIRT1 participates in three pathways to regulate lifespan during caloric restriction and oxidative stress. First, SIRT1 represses PPAR-γ (peroxisome proliferators activataed receptor－γ) to induce a shedding of body fat from white adipose tissue in order to reduce the toxic effects of LPA (lipid peroxidation). Second, SIRT1 induces gluconeogenic genes and hepatic glucose output through deacetylase PGC-1α (PPAR－gamma coactiveator-1α). In ddtion, SIRT1 modulates the effects of PGC-1a in repression of glycolytic genes in response to asting. Third, SIRT1 increases the ability of FOXO3α (Forkhead box class O3α) to resistent oxidative stress. In this review, we summarize and discuss the latest findings regarding SIRT gene family and their role in regulation of mammalian lifespan.

关键词