药学学报 2008, 43(8) 793-800 DOI: ISSN: CN:

论文

*Shc*相关磷酸化酪氨酸适配蛋白在衰老过程中的调控作用

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摘要:

衰老相关的氧化应激理论和自由基理论能部分地解释衰老过程而被越来越广泛地接受。p66^{Shc}(66-kilodalton isoform of *Shc* gene products)基因编码是一种磷酸化酪氨酸信号适配蛋白，敲除p66^{Shc}基因的小鼠模型寿命可延长30%，并表现出对氧化应激的抗性。氧化应激时，p66^{Shc}的Ser36位点被磷酸化，进而致叉头转录因子(forkhead-type transcription factors,FKHR)失活，而FKHR可调节胞内抗氧化基因的表达。p66^{Shc}信号转导与进化上保守的寿命相关信号转导有直接联系。*Shc*(Src homologue and collagen protein)基本不表达于成人脑和脊髓的成熟神经元中。然而，在神经系统中存在两种*Shc*同源基因，*Sck*/*Shc*B和N-*Shc*/*Shc*C；并有证据表明它们在氧化应激和脑的衰老中发挥作用。*Shc*相关基因的表达在老化过程中受到影响，这可能与衰老时的细胞功能障碍、应激反应和/或认知功能退化有关。

关键词： *Shc* p66 衰老 氧化应激 叉头转录因子

Regulatory effects of *Shc*-related phosphotyrosine adaptor proteins on aging

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Abstract:

Aging-related oxidative stress and free radical theory has become accepted increasingly as explaination, at least in part of the aging process. In murine models of aging, a genetic deficiency of the p66^{Shc} (66-kilodalton isoform of *Shc* gene products) gene, which encodes a phosphotyrosine signal adapter protein, extends life span by 30%, and confers resistance to oxidative stress. Upon oxidative stress, p66^{Shc} is phosphorylated at Ser36, contributing to inactivation of the forkhead-type transcription factors (FKHR/FoxO1), which regulates the gene expression of cellular antioxidants. The p66^{Shc} has a direct connection with the life span related signaling, which is conserved evolutionarily. *Shc* is basically not expressed in mature neurons of the adult brain and spinal cord. Instead, two *Shc* homologues, *Sck*/*Shc*B and N-*Shc*/*Shc*C, which have been proved to be effective on oxidative stress and aging, are expressed in neural system. The expression of *Shc*-related genes is affected in the aging process, which may be relevant to cellular dysfunction, stress response and/or cognitive decline during aging.

Keywords: p66 aging oxidative stress forkhead-type transcription factor *Shc*

收稿日期 2008-03-06 修回日期 网络版发布日期

DOI:

基金项目:

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参考文献:

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