

ENHANCED GLYCOGENESIS IS INVOLVED IN CELLULAR SENESCENCE

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Glycogen biogenesis and its response to physiological stimuli have often been implicated in age-related diseases. However, their direct relationships to cell senescence and aging have not been clearly elucidated. Here, we report the central involvement of enhanced glycogenesis in cellular senescence. Glycogen accumulation, glycogen synthase (GS) activation, glycogenin1 induction and glycogen synthase kinase 3 (GSK3) inactivation commonly occurred in diverse cellular senescence models, including the liver tissues of aging F344 rats. Inhibition of GSK3 activity using SB415286, GSK3 knock-down using siRNA and inactive form of GSK3 mutation (K85A) were sufficient to induce cellular senescence with increased glycogenesis. In addition, over-expression of GS and GYG1 induced cellular senescence whereas GS and GYG1 knockdown using siRNA significantly attenuated stress-induced senescence phenotypes. Taken together, these results clearly demonstrate that augmented glycogenesis is not only common, but also directly linked to cellular senescence and aging, suggesting GSK3, GS and GYG1 are novel modulators of senescence, and providing new insight into the metabolic backgrounds of aging and aging-related pathogenesis.

Key words :

GSK3, GS, GYG1, senescence, glycogen biogenesis.