

CONTRIBUTION OF GSK3 TO METABOLIC ALTERATION IN CELL SENESCENCE

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Metabolic alteration is one of the characteristic phenotypes of senescent cells. However, it is not clear how this feature is developed in the process of senescence. In the present study, we evaluated the potential roles of glycogen synthase kinase 3 (GSK3), a multifunctional kinase that plays a role in diverse cellular functions, as the key modulator for those apparent features and also for the persistent oxidative stress in senescence. GSK3 inactivation via phosphorylation is commonly observed in diverse cellular senescence models and the liver tissues of aging F344 rats. Interestingly, subcytotoxic concentrations of GSK3 inhibitors (SB415286 and LiCl) were sufficient to induce cellular senescence along with mitochondrial respiratory dysfunction, enhanced glycogenesis, and increased lipogenesis and protein synthesis. Acquisition of senescent phenotypes by GSK3 inactivation was further confirmed by employing GSK3 knockdown using siRNA and/or ectopic expression of dominant negative GSK3 β mutant (K85A). Taken together, our results suggest that GSK3 inactivation is one of the key modulators for metabolic alteration, thereby destining the cells to senescence.

Key words:

cellular senescence, GSK3, oxidative stress, senescent phenotypes

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