

ENHANCED LIPOGENESIS IS INVOLVED IN CELLULAR SENESCENCE

You-Mie Kim¹, Yong-Hak Seo^{1,2}, Gyesoon Yoon^{1,2,3}

¹*Dept. of Biochemistry and Molecular Biology, School of Medicine,*

²*Dept. of Molecular Science & Technology, The Graduate School (BK21),*

Research Institute of Pharmaceutical Science & Technology

Ajou University, Suwon 443-721, Korea

Flattened and enlarged cellular morphology is one of the characteristics of senescent cells. We previously observed highly elongated mitochondria with their increased masses in diverse cellular senescences of human hepatocyte-derived Chang cells. We here observed that the masses of most cellular organelles compartmented by phospholipids membranes are obviously increased during the senescent progresses. In this study, we examined whether enhanced lipogenesis is involved in cellular senescence. Thin layer chromatographic analysis proved apparent increments in total lipids, including phospholipids, in the senescent cells. We found that the expression levels of lipogenic enzymes, such as fatty acid synthase (FAS), ATP citrate lyase (ACLY), and the level of active sterol regulatory-element binding protein (SREBP) 1, a key regulator of many lipogenic genes, were clearly augmented. Blocking glycogen synthase kinase 3 (GSK3) activity using specific inhibitor or siRNA induced cellular senescence accompanied by increased amounts of total lipids, SREBP1 activity and levels of lipogenic enzymes. We observed that overexpression of SREBP1 effectively induced cellular senescence in Chang cells. SREBP1 or ACLY knockdown using siRNA and FAS inhibitors significantly attenuated the senescence phenotype induced by stresses. Taken together, our results demonstrate that augmented lipogenesis is directly involved in cellular senescence. [KRF-2007-313-C00575]

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senescence, lipogenesis