ABSTRACT

ROLE OF RESVERATROL IN INDUCTION OF CELLULAR SENESCENCE AND ACTIVATION OF SIRTUINS ON HUMAN DERMAL FIBROBLASTS

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In model organisms resveratrol extends lifespan via activating Sirt1 which is a member of NAD+ dependent histone deacetylase family, sirtuins. On the other hand resveratrol also induces the cell cycle arrest and leads to premature senescence and apoptosis *in vitro* that makes the inhibitory effects of resveratrol on aging controversial. Thus, in this study the potential effects of resveratrol on human normal skin fibroblasts and the relationship between resveratrol and sirtuins were examined. As determined by WST-1 and BrdU tests, starting from 25 μM, resveratrol reduced cell viability. Ki-67 immunostaining results also supported this finding. In addition, utilizing Saβ-Gal staining it was found that resveratrol induced cellular senescence at 25, 50 and 100 μM concentrations. Accordingly, resveratrol caused cell death / apoptosis at high concentratitons such as 300 μM as determined by TUNEL staining. To answer the question whether resveratrol activates sirtuin expression or not, expression of Sirt1, 2, 3, 6 and 7 were examined. As shown by WB analysis at concentrations where resveratrol induced cellular senescence the expression of Sirt1 and 2 were decreased whereas Sirt3, 6 and 7 did not change. Hence, this study shows that resveratrol induced cellular senescence in a time and dose dependent manner and accordingly reduced the expression of Sirt1 and 2.

Key Words: Resveratrol, sirtuins, cellular senescence, human normal dermal fibroblasts (BJ)