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Decreases in G0-G1 Switch 2 Expression and Increases in Lipid Peroxidation Impaired Wound Healing in Aging Normal Human Fibroblasts

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and a weak negative correlation with age, but no transition point during the change in the serum scavenging activity was observed ($R2=0.287$, $p<0.001$ for alkoxyl radical, and $R2=0.215$, $p<0.01$ for alkylperoxyl radical). In children, the serum hydroxyl radical scavenging activity was higher in younger age groups, and it exhibited a significant negative correlation with age ($R2=0.257$, $p<0.001$), which was reversed and found to be increased in adults after the age of 15 years. In adults, no significant age-related changes were observed. Singlet oxygen scavenging activity of the serum exhibited a significant but very weak positive correlation with age in children, but no such correlation was observed in adults. These results indicate that the antioxidant profile changes in a multidimensional and complex manner, which undergoes

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An inverse correlation between hypoxia inducible factor-1α expression and lipid droplets associated with a decline in the proliferative index of aging normal human fibroblasts

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Aging is a critical risk factor for numerous chronic diseases, and it presents a rising clinical problem as approximately 19 percent of the US population is predicted to be 65 y and older by 2030 (U.S. Census Bureau). However, the mechanisms that regulate the process of aging are still not well understood. Results from RNA sequencing and bioinformatics analysis showed a significant difference in global gene expression between old (58 - 70 y) compared to young (3 d – 12 y) Normal Human Fibroblasts (NHFs). Gene set enrichment analysis ranked lipid metabolism as the top pathway that is altered in older NHFs. Significant changes in the expression of more than 40 genes related to lipid metabolism including Hypoxia inducible Factor 1 alpha (HIF-1α) and its target gene G0-G1 Switch 2 (G0S2; negative regulator of lipolysis) were observed. Results from RT-qPCR and immunoblotting analysis showed a significant decrease in HIF-1α expression in older (>50 y) compared to young (<50 y) NHFs that correlated with decreases in its target gene, G0S2 expression. Live cell imaging of NHFs using BODIPY 493/503 fluorescent probe showed approximately 100% increase in lipid droplets in older NHFs. Results from live cell imaging of proliferation of NHFs showed a significant decrease in the cell growth index of NHFs from donors of older (>50 y) compared to young (<50 y) healthy donors. Whereas the involvement of HIF-1α in carbohydrate metabolism and switching to anaerobic glycolysis under hypoxia is well established, to the best of our knowledge, we were the first to report a novel role of HIF-1α in lipid metabolism and proliferative capacity of NHFs during aging.

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Decreases in G0-G1 Switch 2 expression and increases in lipid peroxidation impaired wound healing in aging Normal Human Fibroblasts

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Human longevity is increasing; in fact, the United States Census Bureau predicts that there will be a 10% increase in individuals 65 y of age and older by 2050. Unfortunately, increases in longevity is also associated with increased risk factors for numerous health issues, and decreased effectiveness of medical interventions. Aging cells lose their ability to renew and repair damage. RNA sequencing and bioinformatics analysis of primary cultures of Normal Human Fibroblasts (NHFs) from healthy donors of different ages (3 d – 70 y) ranked lipid metabolism as the number one metabolic process that is significantly altered during aging. Using BODIPY C11 fluorescent probes to measure ratio of lipid peroxides (LOO•) to neutral lipids, our results showed an age associated increase (up to 100%) in lipid peroxidation in 20 different NHFs aged from 17 y up to 79 y. Results from Immune blot analysis showed significant decreases (greater than 50%) in the expression of G0-G1 Switch 2 (G0S2), a negative regulator of the lipolytic enzyme, Adipose triglyceride lipase (ATGL) in older NHFs, whereas no significant difference was observed in the protein levels of fatty acid synthase (FASN) and ATGL or its co-activator Comparative Gene Identification-58 (CGI-58). Using Platypus cell migration and wound healing assay, results showed that NHFs from older individuals have slower wound closing ability when compared to NHFs from younger individuals. Over all these results indicate that a G0S2 dependent lipolytic signaling contributes to age-related impairment in wound healing via lipid peroxides. Intervention of the G0S2-ATGL lipid signaling pathway is an attractive and novel avenue to mitigate age-associated decline in the regenerative efficacy of tissues.

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Investigation of a thiol antioxidant and a novel nanodelivery platform for the prevention of cataract in whole lens cultures

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