AESTHETIC AND COSMETIC DERMATOLOGY (LASERS SEPARATE CATEGORY)

UVA-INDUCED PHOTOAGING INHIBITS AUTOPHAGIC DEGRADATION BY IMPAIRING LYSOSOMAL FUNCTION AND CATHEPSINS EXPRESSION IN DERMAL FIBROBLASTS

Qingfang Xu [(1)] - Yuying Li [(2)] - Yunfen Huang [(1)] - Xinya Xu [(3)] - Yue Zheng [(1)] - Wei Lai [(4)]

The Third Affiliated Hospital Of Sun Yat-sen University, Department Of Dermato-venereology,the Third Affiliated Hospital Of Sun Yat-sen University, Guangzhou, China [(1)] - The Third Affiliated Hospital Of Sun Yat-sen University,, Department Of Dermato-venereology,the Third Affiliated Hospital Of Sun Yat-sen University, Guangzhou, China [(2)] - The Third Affiliated Hospital Of Sun Yat-sen University, Department Of Dermato-venereology,the Third Affiliated Hospital Of Sun Yat-sen University,, Guangzhou, China [(3)] - The Third Affiliated Hospital Of Sun Yat-sen University, The Department Of Dermato-venereology, The Third Affiliated Hospital Of Sun Yat-sen University, Guangzhou, China [(4)]

Background: Autophagy has been associated with a variety of diseases especially aging. Although autophagy has been reported to be decreased in photoaged fibroblasts, the underlying mechanism and its relevance to photoaging remain elusive.

Objective: This study aims to investigate the mechanism that contributes to deficient autophagy in UVA-induced photoaged dermal fibroblasts in vitro and in photoaged skin in vivo.

Methods: Repetitive UVA irradiation was used to induce primary HDFs photoaging in vitro. Effect of photoaging on autophagic flux was assessed through measuring LC3, Beclin 1 and p62 expression in fibroblasts, which was further confirmed with chloroquine (CQ) or rapamycin (RAP) treatment. Lysosomal degradative capacity was compared between photoaged and non-photoaged fibroblasts by detecting the degradation of formed autophagosomes, endogenous LC3 and DQ-Green BSA. Also, lysosomal acidification was examined by LysoSensor yellow/blue DND 160 staining and flow cytometry. Further, the activity and expression of cathepsin D, B and L were investigated. Finally, LC3, beclin1 and p62 expression in sun-exposed and sun-protected skin was studied with immunostaining.

Results: UVA-induced photoaging significantly increased GFP-LC3 puncta per cell, LC3I/II conversion and p62 expression, whereas didn't alter beclin1expression in fibroblasts. Moreover, autophagic flux was not significantly affected by CQ treatment, while was remarkably induced by RAP treatment in photoaged fibroblasts. Both lysosomal degradative capacity and acidification were dramatically decreased in photoaged fibroblasts compared

with non-photoaged cells. Also, photoaging obviously attenuated expression and activity of cathepsin B, L and D. Further, LC3 and P62 expression was significantly increased in photoaged skin, whereas Beclin-1 expression was not altered.

Conclusion: Photoaging inhibits autophagy in the degradation stage both in vitro and in vivo. Lowered lysosomal acidity, and decreased expression and activity of cathepsin B, L and D might contribute to the inhibition of autophagic degradation in UVA-induced photoaged fibroblasts, which might be crucial in the development of photoaging.