No. 624

Autophagy Alleviates UVA-Induced DNA Damage in Fibrocyte by Activating the Nrf2-dependent Nucleotide Excision Repair Pathway

Yuanmin He[1], Xiaoqi Tan[1], Jiajun He[1], Yongqiong Deng, Xia Xiong[1]*

[1] Department of Dermatology, the Affiliated Hospital of Southwest Medical University, Luzhou, 646000, Sichuan, China

INTRODUCTION

Ultraviolet(UV)-induced DNA damage is a vital risk factor for the development of skin disorders including photoaging and cancers, which is primarily repaired by nucleotide excision repair (NER) pathway. Recent study has indicated that autophagy of keratinocytes can be enhanced following UV exposure. However, the implication of autophagy in UV-induced DNA damage is largely unknown.

To address this, normal human fibrocytes (HFF) were disposed to UVA irradiation and their autophagy state was monitored by western blot and immunofluorescence. We confirmed that UVA exposure amplified the production of DNA damage, as well as autophagy in HFF. In addition, we demonstrated that activation of autophagy by rapamycin(RAP) attenuated the production of DNA damage, whereas inhibition of autophagy by siRNA-ATG5 augmented it. Furthermore, we showed that DDB2, which plays critical role in the process of NER, changed its expression parallelly with autophagy alteration in HFF. Finally, Knockdown of Nrf2 prominently upregulated the production of DNA damage, as well as downregulated DDB2 expression in HFF with UVA exposure.

These findings provide first evidence for the important role of autophagy in alleviating UVA-induced DNA damage in human fibrocytes through Nrf2-dependent NER pathway.

METHODS

Cell culture,
MTT
comet assay
Determination of cell apoptosis in flow cytometer,
Western blot analysis,
Statistical analysis (One way ANOVA)

RESULTS

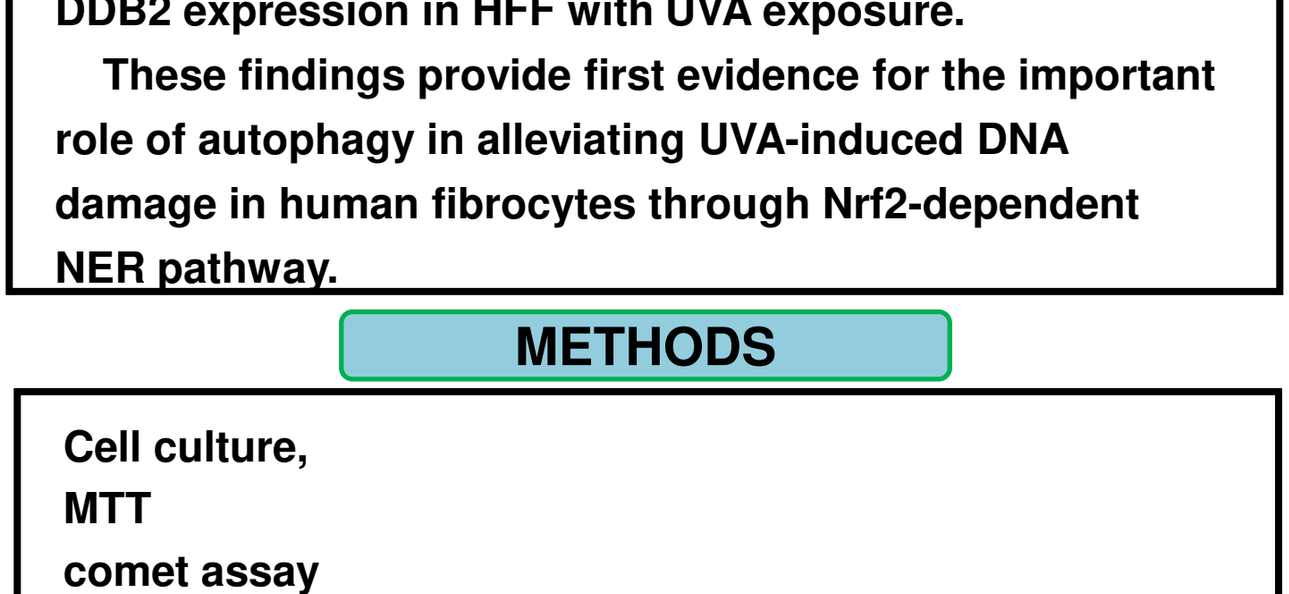

Fig. 1. High levels UVA irradiation induced cell death, DNA damage, NER and autophagy in fibrocyte.

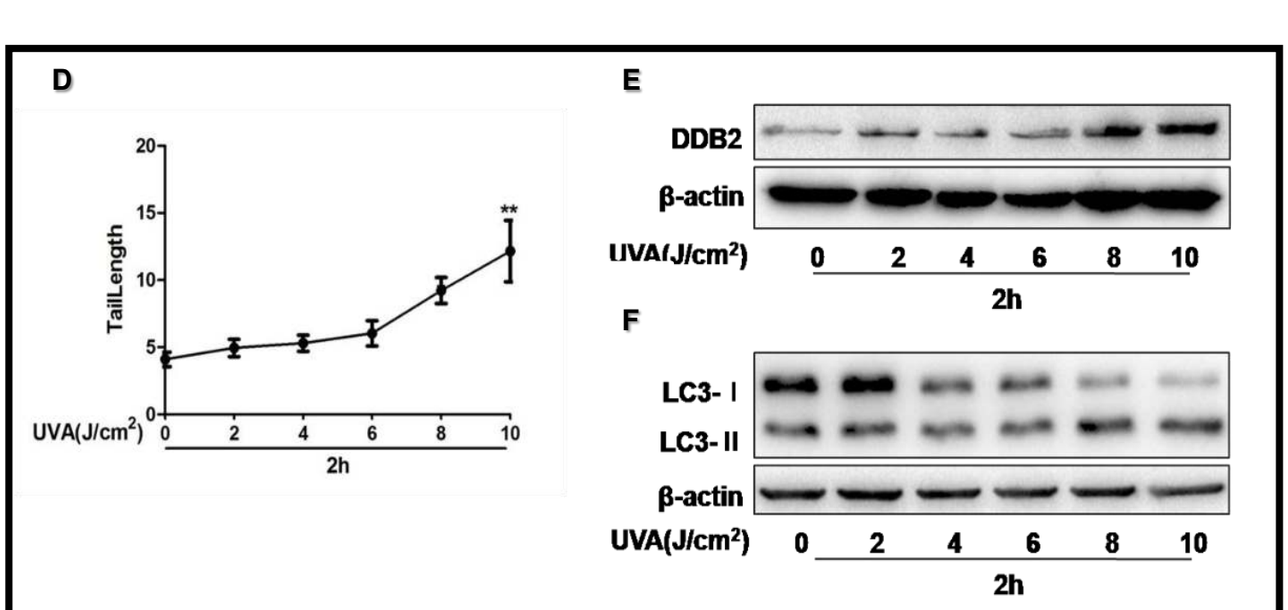

Fig. 2. Autophagy protected fibrocyte from UVA-induced DNA damage.

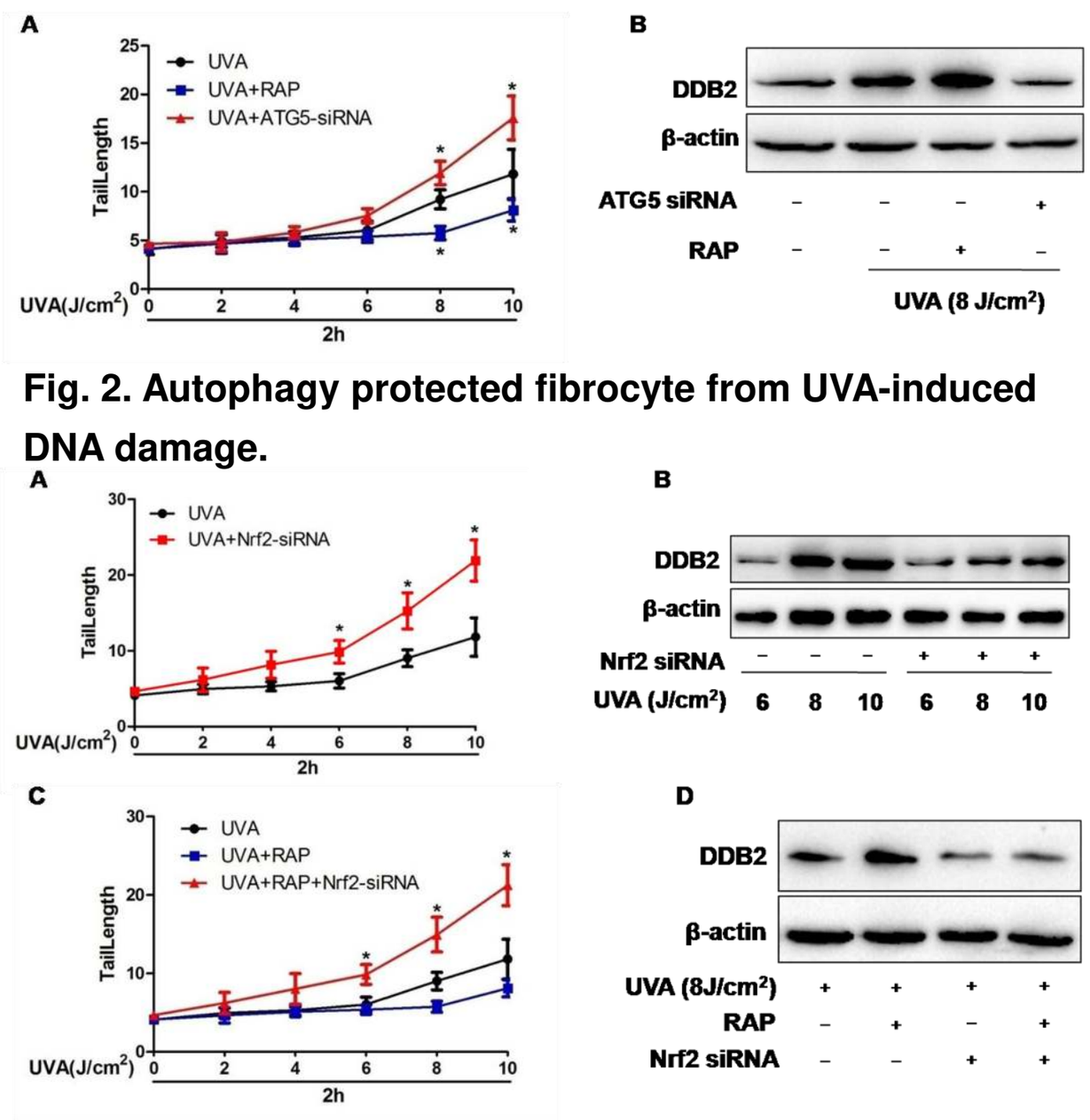

Fig. 3. Autophagy protected fibrocyte from UVA-induced DNA damage.

CONCLUSION

In this study, we firstly found that high levels UVA irradiation induced DNA damage and NER in fibrocyte, and then established that Autophagy protected fibrocyte from UVA-induced DNA damage. Moreover, we confirmed that Autophagy alleviates UVA-Induced DNA Damage in fibrocyte by activating the Nrf2-dependent nucleotide excision repair pathway. our data pointed that modification of autophagy may provide a promising therapy for skin disease related to UVA irradiation.