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Interaction of TAGLN and USP1 promotes ZEB1 ubiquitination degradation in UV-induced skin photoaging

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Statement of the Problem: Ultraviolet A (UVA) irradiation can lead to skin damage and premature skin aging known as photoaging. This work found that UVA irradiation caused an imbalance between dermal matrix synthesis and degradation through the aberrant upregulation of transgelin (TAGLN) and studied the underlying molecular mechanism.

Methodology and Theoretical Orientation: A photoaging model was established to preliminarily explore the relationship between TAGLN and photoaging. Then Co-immunoprecipitation (Co-IP) combined with mass spectrometry was implemented to analyze the underlying molecular mechanism of TAGLN regulating photoaging.

Findings: Co-IP and proximal ligation assay results showed that TAGLN can interact with USP1. USP1 can be retained in the cytoplasm by TAGLN in UVAinduced cells, which inhibits the interaction between USP1/zinc finger E-box binding homeobox 1 (ZEB1), promote the ubiquitination degradation of ZEB1, and lead to photoaging. TAGLN knockdown can release USP1 retention and help human skin fibroblasts (HSFs) resist UVA-induced damage. The interactive interface inhibitors of TAGLN/USP1 were screened via virtual docking to search for small molecules that inhibit photoaging. Zerumbone (Zer), a natural product isolated from Zingiber zerumbet (L.) Smith, was screened out. Zer can competitively bind TAGLN to reduce the retention of USP1 in the cytoplasm and the degradation of ZEB1 ubiquitination in UV-induced HSFs. The poor solubility and permeability of Zer can be improved by preparing it as a nanoemulsion, which can effectively prevent skin photoaging caused by UVA in wild-type (WT) mice. Zer cannot effectively resist the photoaging caused by UVA in Tagln-/- mice because of target loss.

Conclusion & Significance: The present results showed that the interaction of TAGLN and USP1 can promote ZEB1 ubiquitination degradation in UV-induced skin photoaging, and Zer can be used as an interactive interface inhibitor of TAGLN/USP1 to prevent photoaging.

Biography

Caibin Zhu is a derma professional at Cheermore Cosmetic Dermatology Laboratory in Shanghai, China. Her researches spread globally and brought an impact in the scientific era.

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