AUTOPHAGY REDUCES THE ACCUMULATION OF ADVANCED GLYCATION END-PRODUCTS IN SKIN

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Introduction: Accumulation of advanced glycation end-products (AGEs) is etiologically implicated in numerous age- and health-related conditions including yellow, dull appearance via impacting cellular homeostasis and integrity of structural proteins.

Objective: (a) Investigate the role of autophagy on the accumulation of AGEs in skin cells (b) assess the effect of autophagy-enhancing skin-care compounds on AGEs

Materials and Methods: Human keratinocyte or fibroblast were pre-treated for 24 hours with glyceraldehyde (GLA) to quickly generate AGEs in the cells. The impact of autophagy on accumulated AGEs and cell viability was assessed by treating the GLA pre-treated cells with various autophagy activators and inhibitors. A representative AGE, carboxymethyl lysine (CML), was quantified by using LC-MS/MS analysis and normalized to its precursor, lysine in molar ratio. Separately, skin-care compounds were identified to activate autophagy in skin cells by using LC3-II as a marker. The effect of activators on reducing AGEs were evaluated as well.

Results: Pre-treatment of GLA significantly elevated the level of CML in keratinocytes or fibroblasts. Post-treatment of autophagy activators (rapamycin and smcr28) reduced accumulated AGEs effectively, suggesting autophagy plays a role in eliminating AGEs to maintain cellular homeostasis, especially in keratinocytes. An autophagy inhibitor (3-methyladenine) did not affect CML amount. Rapamycin inhibits mTOR (canonical autophagy) whereas smcr28 activates non-canonical autophagy indicating that multiple routes to autophagy help remove AGEs in keratinocytes. We observe cell-specific effects highlighting the complexity of autophagy and AGEs removal. Screening of autophagy activators identified sucrose dilaurate and Galactomyces Ferment Filtrate which also reduced accumulated AGEs in keratinocyte.

Conclusions: The activation of autophagy can reduce accumulated AGEs and maintain cell viability in keratinocytes. Autophagy-activating skin-care compounds can also reduce AGEs in keratinocyte. These data may implicate autophagy plays a crucial role to maintain cellular homeostasis by removing the accumulated AGEs in skin.