A Role For Autophagy In Skin Aging
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INTRODUCTION
Facial skin aging is a cumulative result of intrinsic changes, in combination with external factors. During chronological aging, many physiological processes in skin cells are affected. Autophagy is an important cellular process responsible for optimal cellular functions and homeostasis. During autophagy, damaged, unnecessary, dysfunctional macromolecules and organelles are broken down and are recycled for building essential cellular components. Reduced autophagy, which results in the accumulation of damaged cellular components, has been implicated in a number of aging diseases. We led us to hypothesize that autophagy could play a role in skin aging. Here, we show that basal autophagy declines with age and is associated with decreased expression of key regulatory structural proteins in the epidermis and dermis. Interestingly, we have observed that UV-irradiation and free radical inducers also suppress autophagy activity, suggesting autophagy as a common denominator for intrinsic and extrinsic skin aging. Furthermore, we have also observed that an extract of Tiliacora triandra, a climbing vine, which is traditionally used in Southeast Asia, can stimulate autophagy activity, enhance differentiation and stimulate collagen synthesis in skin cells in vitro.

Methods & Materials
Cell culture and treatment: Normal Human dermal Fibroblasts (HDF) were grown in DMEM (Mediatech; cat. #: 15-153-CV) containing 10% Fetal Bovine Serum (Perbio, SH00720.03), Penicillin/Streptomycin (Mediatech, 30-051-C) and L-Glutamine (Mediatech, 25-005-C) and Normal Human Epidermal Keratinocytes (HEK) were grown in Epilife (Cascade Biologics Inc.; CEP-REV06-001A) supplemented with HGSK (Cascade Biologics Inc.; CEP-REV06-001A). Cells were treated with 3-Methyladenine (2-MA) (Sigma, M8371), Chloroquine (Sigma, C6658) and Tiliacora triandra as indicated.  

RESULTS

Suppression of Autophagy Activity Leads to a Reduction in Pro-collagen Production

Human skin fibroblasts (avg age 23yrs) were treated with 2-MA (10µM) or Chloroquine (50µM); 48 hours later cells were harvested for Western blotting analysis of autophagy activity. (a) and tissue culture medium was collected for pro-collagen levels by ELISA. (b) Data represent an average of 3 independent experiments; all values are statistically significant at p<0.05.

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DISCUSSION
Our data demonstrate that Autophagy declines with age in human keratinocytes. We also observe that Autophagy declines upon UV exposure in both skin Fibroblasts and Keratinocytes. These data indicate that Autophagy is a common cellular process that is affected by both intrinsic and extrinsic aging.

Moreover, suppression of autophagy leads to a decrease in collagen production in skin fibroblasts, a delay in epithelial differentiation, and retardation of key differentiation markers in skin keratinocytes. Conversely, we show that stimulation of Autophagy results in an increase in collagen production and an increase expression of epithelial differentiation markers.

We have examined an Avon Patented extract, from Tiliacora triandra, a flowering vine indigenous to Southeast Asia, which has been used traditionally as a nutritional energy drink for detoxifying the body. Our results demonstrate that Tiliacora triandra has autophagy activity, enhance epithelial differentiation and stimulate collagen synthesis in skin cells.

As autophagy activity declines with age and UV exposure in skin cells, this can lead to a decline in collagen production and a retardation of epithelial differentiation and thereby contribute to the appearance of aging signs such as lines, wrinkles, loss of firmness, thinning of the skin, etc. These studies suggest that stimulation of autophagy can positively influence the aging phenotype of the dermis and epidermis and contribute to regeneration of aging skin.