The Editor's Choice

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Androgens modulate keratinocyte differentiation indirectly through enhancing growth factor production from dermal fibroblasts

The main pathogenesis of acne vulgaris is increase in sebum production and abnormal keratinization of the hair infundibulum. However, the molecular mechanisms of abnormal keratinization of the hair infundibulum are not fully elucidated. Kumtornrut C et al hypothesized that the androgens affect the dermal fibroblasts, another androgen receptor-positive cells in the skin, resulting in abnormal keratinization through keratinocyte-fibroblast interaction. In vitro, androgens but not estrogens significantly increased fibroblast growth factor (FGF) 10 mRNA and protein expressions in human fibroblasts but not in keratinocytes. In vivo, FGF10 was more abundant in acne lesion compared to normal facial skin. FGF10 suppressed cytokeratin 1 and cytokeratin 10 expression, which was along with the decreased ratio of cytokeratin 10 against cytokeratin 14 in acne lesions compared to normal facial skin. These observations suggested that androgens enhance growth factors production from dermal fibroblasts, and growth factors from fibroblasts alter keratinocyte differentiation in acne lesion.

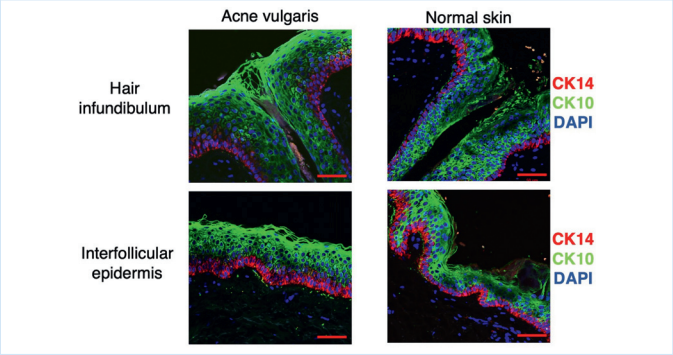

Fig. 3 (B–E). Altered expression of cytokeratins in AV hair infundibulum.
(b–e) Representative images of CK14 (**red**) and CK10 (**green**)-positive layers in hair infundibular area and interfollicular epidermis in acne vulgaris and normal skin are shown. Scale bars are 50μm.

Extracellular vesicles derived from Malassezia furfur stimulate IL-6 production in keratinocytes as demonstrated in in vitro and in vivo models

Malassezia is one of the commensal microorganisms colonized on human skin and has been shown to be related to several inflammatory cutaneous disorders. Previous studies indicated that Malassezia. sympodialis (M. sympodialis) can produce extracellular vesicles, however, the immunoregulatory function of Malassezia extracellular vesicles on keratinocytes has not been studied. Zhang YJ et al investigated the extracellular vesicular production capability of Malassezia. furfur (M. furfur) and their immunoregulatory effects both in vitro and in vivo. M. furfur produced ovoid-shaped nanoparticles, which could be then internalized into HaCaT cells, as well as mice epidermal keratinocytes. IL-6 expression was significantly enhanced in response to extracellular vesicular stimulation both in vitro and in vivo, in which process the activation of NF-kB was involved. M. furfur has the ability to release extracellular vesicles, which can be internalized into keratinocytes and promote the production of IL-6 with the involvement of NF-kB dependent pathway. These findings reveal important new insights into Malassezia pathogenesis and therapy.

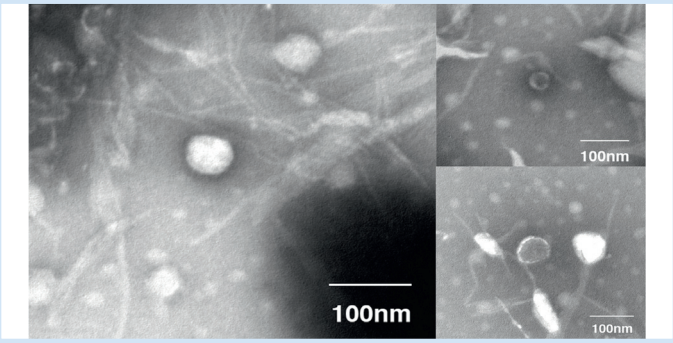

Fig. 1 (B). M. furfur produces extracellular vesicles.
TEM. *M. furfur* extracellular vesicles isolated by ultracentrifugation and visualized with use of TEM.

Exosomal miRNA derived from keratinocytes regulates pigmentation in melanocytes

Pigmentation is controlled by complex mechanisms. Evidence suggests that miRNAs can regulate pigmentation. However, the mechanism has not been fully elucidated. In this study, we revealed a novel mechanism that regulates pigmentation involving exosomes, miRNAs and the crosstalk between keratinocytes and melanocytes. Liu Y et al used miR-330-5p in keratinocytes to verify the effect of keratinocyte derived exosome on melanocyte pigmentation. Keratinocytes secrete exosomes carrying miR-330-5p; moreover, greater miR-330-5p expression was found in exosomes derived from keratinocytes that overexpressed miR-330-5p. Second, exosomes derived from keratinocytes with overexpression of miR-330-5p caused a significant increase in miR-330-5p in melanocytes. Finally, exosomes derived from keratinocytes that overexpressed miR-330-5p induced a significant decrease in the production of melanin and expression of TYR in melanocytes. Meanwhile, overexpression of miR-330-5p in melanocytes also proved the inhibitory effect of miR-330-5p on pigmentation. These findings suggest that keratinocytes crosstalk with melanocytes in the epidermal melanin unit via exosomal miRNAs, indicating a new pathway of melanogenesis.

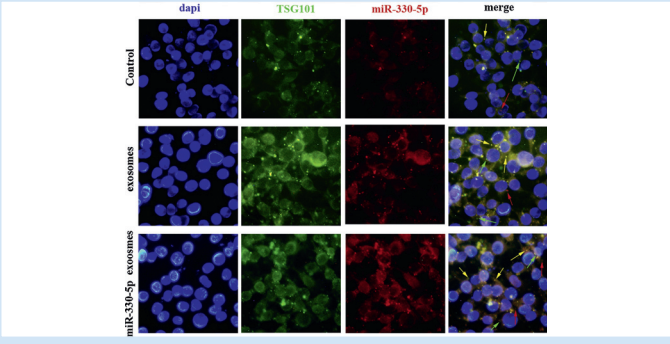

Fig. 2 (A). The interaction between the exosomes derived from keratinocytes with melanocytes. (a) TSG101 (green), miR-330-5p (red) and DAPI (blue) fluorescence in situ hybridization of melanocytes after incubating with exosomes derived from keratinocytes. The results were observed as punctate structures in contact with melanocytes. In the merged column, the green dots indicate that the exosomes are not loaded with miR-330-5p, the orange dots represent the exosomes carrying miR-330-5p, and the red dots represent miR-330-5p.