EPIGENETIC MECHANISM LINKED TO PIGMENTED SPOTS EXPLORED BY *IN SILICO*, *IN VITRO* AND *IN VIVO* METHODS

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INTRODUCTION

Pigmentation is a natural tanning process resulting in the production of melanin, within melanosomes by melanocytes, and their distribution throughout the epidermis. Tyrosinase is a key enzyme of the melanin synthesis. With aging, some pigmentary disorders appeared because of an over-production of tyrosinase in photo-exposed skin areas, triggering the appearance of pigmented spots. However, some new environmental assaults such as traffic-related air pollution were revealed as new contributors of pigmented spot formation, which opened new perspectives. Because melanin synthesis could be controlled through epigenetic mechanisms, we investigated if specific miRNA modulation could be responsible for melanin regulation.

RESULTS

We demonstrated that miR-490-3p could be a pigmentation regulator for skin pigmented spot improvement

We evidenced in vitro that miR-490-3p controls TYR proteins involved in melanin synthesis

IN VIVO

DISCUSSION

- Based on computational algorithms from Targetscan and Diana microT, we used a new network-based method to analyze miRNA function to create functional relationship between miRNAs⁴. miR-490-3p showed few connections with other miRNA able to compensate its function, suggesting a low redundancy potential. Its modulation may have a high effect on dependent cellular functions such as tyrosinase regulation.
- By targeting the upregulation of this TYR regulator miR-490-3p, we aimed to reduce the skin over-pigmentation. We selected a 100% natural extract of *lansium domesticum* leaves, to increase the TYR regulator miR-490-3p production in melanocytes. The miR-490-3p upregulation by this ingredient at 0.07% consequently decreased in 2 days the tyrosinase synthesis and in 4 days the melanin production respectively in Asian melanocytes and co-culture with keratinocytes.
- Finally we demonstrated the ability of this ingredient to improve the appearance of pigmented spots versus placebo over 56 days in a clinical study on Chinese adult volunteers living in a daily air-traffic pollution and sun exposed area in China. This ingredient show better effect than AA2G (benchmark).

CONCLUSION

By stimulating the pigmented spot-related miR-490-3p which is under environmental influence, *Lansium domesticum* leaf extract controls the skin's epigenetic pattern for reducing the pigmented spot due to daily air-traffic pollutant and sun exposed area.

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