The curative lightening; the applications of non-thermal plasma on skin

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Abstract: Non-thermal plasma (NTP) has many beneficial roles on skin. First, the topical application of NTP on skin enhances the absorption of several drugs and cosmetics into the deep skin by modifying cellular junctions. Second, the repeated treatment of NTP on skin stimulates the overall skin rejuvenation and wound healing activity by enhancing proliferative activity of keratinocytes directly. Furthermore, since NTP as strong anti-inflammatory activity, it can be used for treating several types of skin inflammatory diseases including atopic dermatitis. Finally, NTP also can be used for treating melanoma. This presentation will summarize these beneficial effects of NTP and some other medical benefits of NTP those can be used in the field of dermatology.

Keywords: Non-thermal plasma, transdermal drug delivery, skin rejuvenation, wound healing, atopic dermatitis, melanoma

Since 2007, our research group is on the way to long explore searching for new biological and medical functions of non-thermal plasma (NTP). The first and ongoing project of our group was the development of NTP device for dentistry. As a result, the methods for tooth whitening and teeth preservation using NTP had been introduced [1-2]. Furthermore, the new anti-cancer treatment methods using NTP in combination with gold nanoparticles coated with cancer targeting antibodies had been also reported. Recently, our group extended our aim to the NTP-mediated healing of peripheral nerves. In this symposium, we will introduce the summarized recent findings of our group, those can be used in dermatology or cosmetics.

In 2013, we firstly reported that the treatment of NTP on human keratinocytes can enhances the expression of genes related with wound healing and anti-skin aging without thermal or genetic damages (Fig. 1) [3].

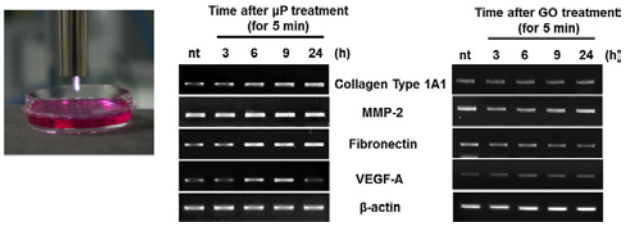

Fig. 1. The effect of microwave-argon plasma jet on expression of anti-skin aging and wound healing promoting genes.

We also suggested the NTP's possible mechanism of action for the plasma-mediated transdermal drug delivery. In our report in 2014, we elucidated the fact that topical application of NTP immediately reduce skin barrier function by inhibiting E-cadherin protein, one of major protein forming cellular junctions in epidermal tissue [4]. By this function, several non-skin penetrating drugs because of its size (larger than 500 Da) can be absorbed (Fig. 2). It is noteworthy that the NTP-mediated disruption of skin barrier function is completely recovered within 3 hours, so that it can be used daily.

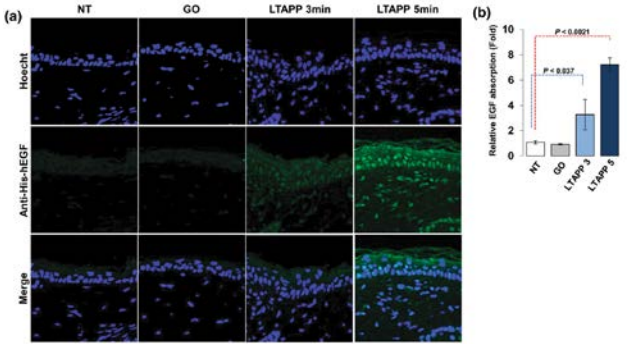

Fig. 2. The topical application of NTP enhances transdermal EGF (epidermal growth factor) effectively.

Interestingly, this NTP-mediated E-cadherin protein inhibition in skin epidermal tissues was directly linked to the proliferation of keratinocytes, which promotes wound healing and skin rejuvenation (Fig. 3) [5].

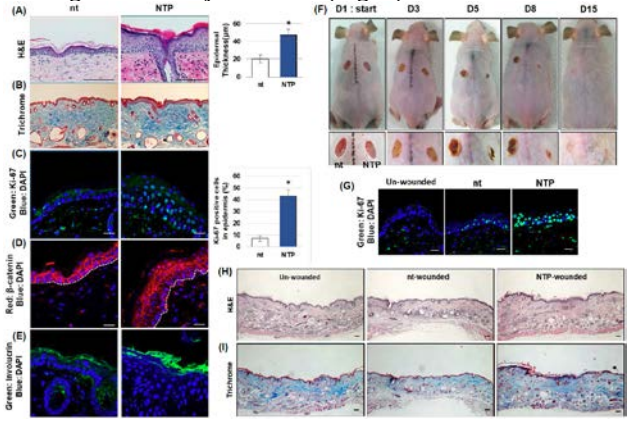

Fig. 3. The repeated treatment of NTP stimulated skin rejuvenation (a-e) and wound healing by stimulating proliferation of epidermal cells.

The NTP-mediated scattering of E-cadherin from cell membrane activated β-catenin, and this activation promoted the cell proliferation. Therefore, the repeated treatment of NTP on mice skin not only stimulated the thickening of skin epidermis, but also stimulated the re-epithelialization process during cutaneous wound healing.

We also reported the possible role of NTP on atopic dermatitis, the most abundant skin inflammatory disease [6]. The topical application of NTP not only blocked the secretion of several inflammatory reaction by inhibiting NF-kB protein activity, but also reduced itching sense by blocking inflammation induced hypersensitization. Furthermore, NTP effectively blocked spongiosis by inhibiting STAT1 protein (Fig. 4).

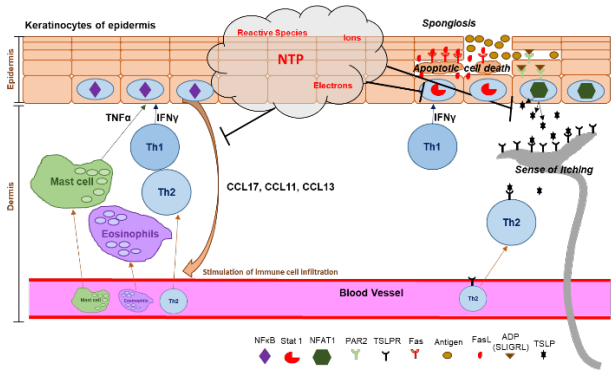

Fig. 4. The schematic diagram elucidating the roles of NTP for treating atopic dermatitis.

In the last part of our presentation, we will address the possible role of NTP on melanoma treatment. One of the main goals of the researchers in the field of plasma cancer treatment is adding selectivity to cancer. For this, we adopted gold nanoparticle (GNP) coated with cancer specific antibodies before the NTP treatment [7-8]. As Fig. 5 shows, this methods killed G361 melanoma cells effectively, but this method has rare effect on HaCaT keratinocytes. Interestingly, this method killed melanocytes immediately after the NTP treatment.

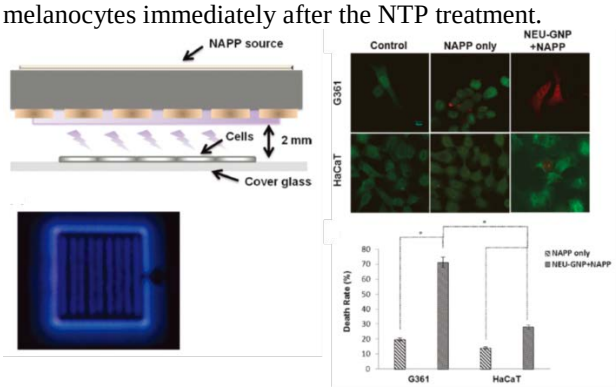

Fig. 5. The experimental set-up and the results of the combinational treatment of NEU-GNP with NTP on G361 melanocytes and HaCaT normal keratinocytes.

Taken together, this presentation will suggest several attractive biological and medical roles of NTP for dermatological and cosmetic uses.

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