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Therapeutic Effects of a Light Emitting Diode at a Variety of Wavelengths on Atopic Dermatitis-Like Skin Lesions in NC/Nga Mice

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Dear Editor:

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disorder with severe itching and relapsing eczematous lesions[1]. The main principles of AD management are epidermal barrier repair, identification and elimination of trigger factors, anti-inflammatory therapy with topical steroid or calcineurin inhibitors, and phototherapy or systemic immunosuppressants in severe cases[2-4]. With regard to phototherapy, ultraviolet (UV) A1 (in the acute phase) and narrowband UVB (in the chronic phase) have been reported as the most suitable phototherapy modalities for AD treatment[4]. However, these conventional phototherapies have limitations, especially in pediatrics, because of a potentially increased cumulative risk of skin cancer[5].

Recently, the therapeutic effects of low-level laser therapy (LLLT) with a light-emitting diode (LED) have been demonstrated. LEDs cover a wide spectrum ranging from UV to visible to near infra-red (NIR) bandwidth (247 to 1,300 nm)[6]. The energy level of an LED is low, and it is much more economical and safe than conventional laser sources[7]. In addition, it allows production of an efficient wavelength combination optimal for a variety of purposes, and can be prepared in all sizes for the treatment of small or large areas[7]. Therefore, LED phototherapy has become a treatment for various dermatological conditions, particularly because of its healing and anti-inflammatory properties[6].

Despite the potential effects of LED or LLLT in AD treatment, there have been only two experimental trials[8,9]. The effects of LED phototherapy on AD as it correlates with wavelength remain largely unproven. Thus, this study aimed to investigate the therapeutic effects of LED irradiation with variable wavelengths and its immunomodulatory effects on AD-like skin lesions in a NC/Nga mouse model.

As an animal model of AD, four-week-old NC/Nga male mice, purchased from SLC Japan (Tokyo, Japan), were divided into six groups (n=5 per each group). Animal care, handling and experimental procedures were performed in accordance with a protocol approved by the Animal Care and Use Committee of the Catholic University of Korea (CUMC-2015-0124-01). Induction of AD using 2,4-dinitrochlorobenzene (DNCB) was performed as previously described[10]. After induction, the ear skin and back skin of mice was irradiated by an LED device, with 10 J/cm^2 twice a week for 2 weeks (on days 1, 4, 8, and 11). The LED irradiation device (Korea Electronics Technology Institute, Seongnam, Korea) used in this study emitted 415 (4.23 mW/cm^2), 525 (3.85 mW/cm^2), 660 (2.42 mW/cm^2), and 830 nm (24.72 mW/cm^2), respectively. The results were evaluated on the last day of the experiment (day 11). Ear thickness was measured using a dial caliper (KoriSeiki MFG, Tokyo, Japan). Ear skin samples were obtained on day 11, fixed in 4% paraformaldehyde, embedded in paraffin, and sectioned at a thickness of 5 μm. Tissue sections were stained with hematoxylin and eosin (H&E) and toluidine blue for counting the number of mast cells in five high power fields (×400). Interleukin (IL)-4 and interferon (IFN)-γ in the ear skin and serum, and serum immunoglobulin (Ig)E levels were measured by a quantitative reverse tran-

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scription-polymerase chain reaction and enzyme-linked immunosorbent assay, respectively, as previously described[10]. Statistical analysis was performed using the Kruskal-Wallis test followed by the Mann-Whitney test with Bonferroni correction. All data were expressed in box-and-whisker plots that represented the median, the lower and upper quartiles, and the minimum to the maximum value. A p-value less than 0.05 was considered significant.

The representative clinical features of NC/Nga mice are shown in Fig. 1A. Compared with the non-irradiated group (DNCB only), the ear thickness of the 830-nm-irradiated group was significantly decreased ($p<0.05$), and that of the 660-nm-irradiated group was also decreased, although there was no significant difference (Fig. 1A). In ear skin, epidermal hyperplasia and inflammatory cell infiltrations, including eosinophils and mast cells in the dermis, were commonly decreased in all LED-irradiated groups, compared with the non-irradiated group (data not shown), and the number of mast cells was significantly decreased in the 660-nm and 830-nm-irradiated groups ($p<0.05$) (Fig. 1B).

The mRNA expression of IL-4 and IFN-r in ear skin was significantly decreased in all LED-irradiated groups compared with the non-irradiated group ($p<0.05$). Compared with the non-irradiated group, the protein production of IFN-r in serum was also significantly decreased in all LED-irradiated groups ($p<0.05$), but there was no difference in serum IL-4 levels (Fig. 2A). Total serum IgE levels also showed decreased production in all LED-irradiated groups, compared with the non-irradiated group, although this difference was not significant, except in the 525-nm-irradiated group (Fig. 2B).

In this study, we analyzed the therapeutic effect of LED phototherapy with variable wavelengths on AD-like skin lesions induced by DNCB in NC/Nga mice. Clinical and histological analysis showed LED phototherapy with longer wavelengths (red and NIR) had significant therapeutic effects on AD-like skin lesions. In previous studies, LED phototherapy with exclusively NIR wavelengths (830 and 850 nm) also led to improvement in AD[8,9].

The suppression of both IL-4 (Th2 subset) and IFN-r (Th1 subset) mRNA expression in this study implies that LED

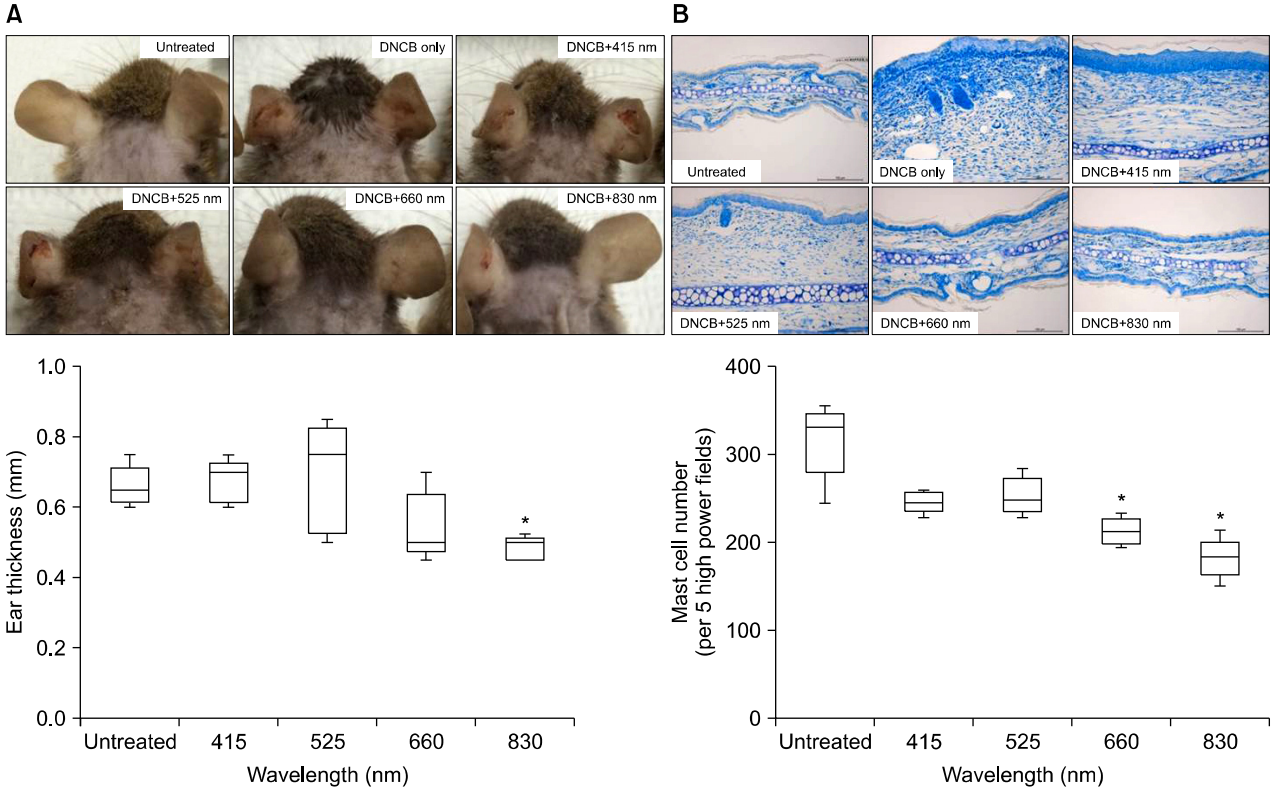

Fig. 1. Clinical and histologic features of DNCB-induced AD-like lesions in NC/Nga mice. (A) Representative images of the ear lesions and ear thickness taken from each group on day 11. (B) Histological features of ear skin (toluidine blue stain, ×200) and number of mast cells in 5 randomly chosen visual fields at ×400 magnification. Data are expressed in box-and-whisker plots that represent the median, the lower and upper quartile and the minimum to the maximum values. DNCB: 2,4-dinitrochlorobenzene, AD: atopic dermatitis. *$p<0.05$ compared with the non-irradiated group (DNCB only).

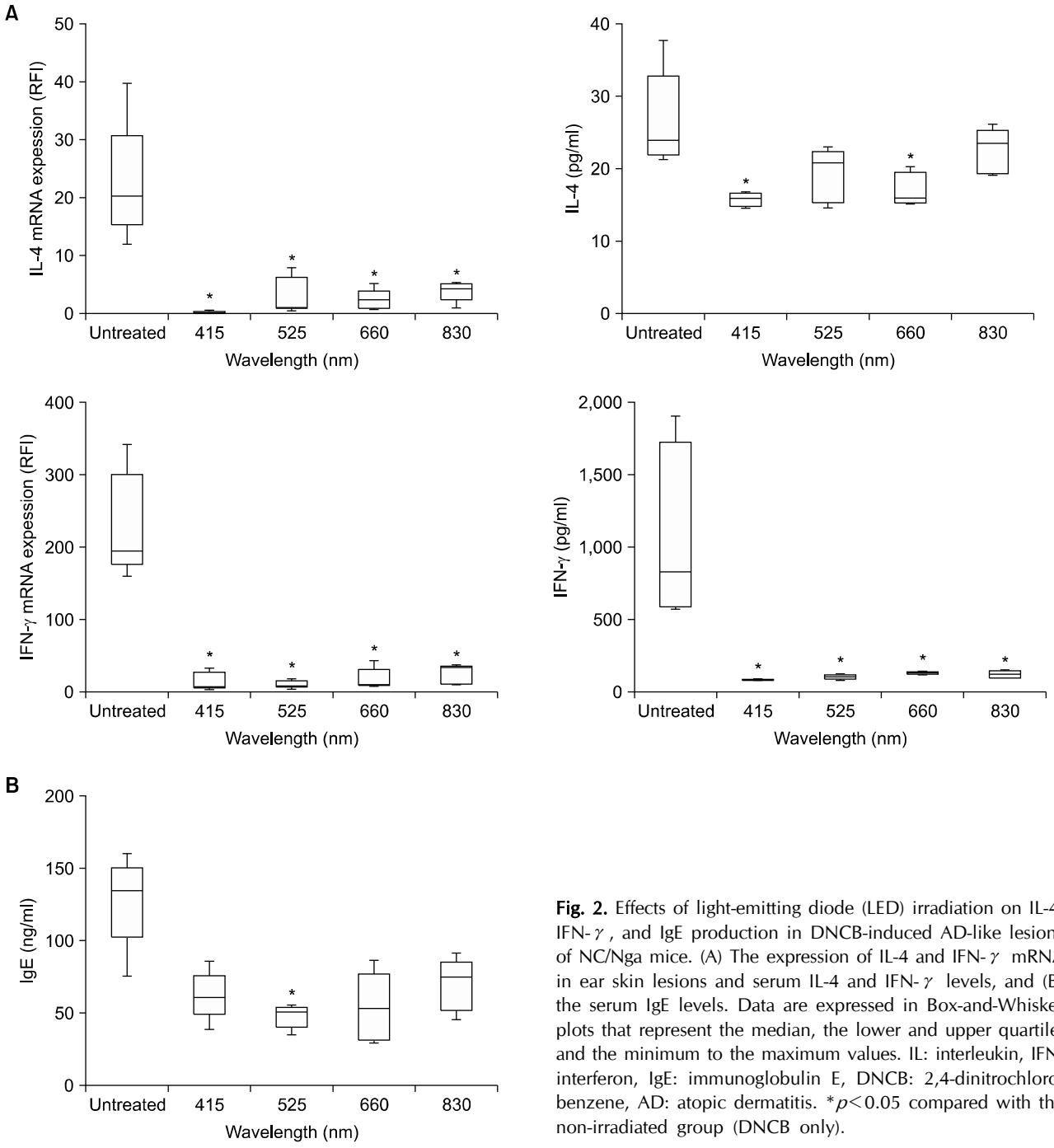

Fig. 2. Effects of light-emitting diode (LED) irradiation on IL-4, IFN-γ, and IgE production in DNCB-induced AD-like lesions of NC/Nga mice. (A) The expression of IL-4 and IFN-γ mRNA in ear skin lesions and serum IL-4 and IFN-γ levels, and (B) the serum IgE levels. Data are expressed in Box-and-Whisker plots that represent the median, the lower and upper quartile, and the minimum to the maximum values. IL: interleukin, IFN: interferon, IgE: immunoglobulin E, DNCB: 2,4-dinitrochlorobenzene, AD: atopic dermatitis. *$p<0.05$ compared with the non-irradiated group (DNCB only).

phototherapy might have therapeutic effects on both acute and chronic AD. Moreover, the decrease of IL-4 and IFN-γ production in serum suggested that LED phototherapy might exert systemic as well as local immunomodulatory effects on AD. These findings were also supported by decreases in serum IgE levels in all LED-irradiated groups. To elucidate the therapeutic mechanisms of LED phototherapy with variable wavelengths, further studies are needed.

In conclusion, our study demonstrates that LED phototherapy with longer wavelengths can improve AD-like skin lesions in NC/Nga mice, probably through regulation of both Th1 and Th2 responses. Thus, LED phototherapy with red and NIR wavelengths could be a potential phototherapeutic modality for AD management.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Seven Cases of Senile Gluteal Dermatoses Developed with Ulcer

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Dear Editor:

Senile gluteal dermatoses (SGD) is the hyperkeratotic lichenified skin lesions around of the gluteal cleft which was first reported in Japan[1]. Distinctive skin lesions of SGD are brownish scaly plaques on the gluteal cleft and both sides of the buttocks assuming a pattern of "three cor-

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