# Comparison of gene expression profiles of keratinocytes irradiated with narrow-band UVB and excimer light

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## Introduction

Phototherapy, such as narrow-band UVB (NB-UVB) and excimer light, is frequently employed to treat dermatoses, which do not respond to existing treatments. NB-UVB is known to be a good therapeutic option to improve skin lesions and pruritus in atopic dermatitis (AD) patients with no documented serious short-term side effects. Previously, we have found that treatment with excimer light once a week for two months significantly reduced local EASI scores and VAS scores in patients with AD or prurigo. Cumulative evidence has shown that phototherapy for dermatoses would work due to several factors like the suppression of the antigen presenting function of the Langerhans cells, the induction of apoptosis in infiltrating T cells and induction of antimicrobial peptides.
However, the molecules that are induced in keratinocytes after phototherapy and are involved in the improvement of dermatoses are largely unknown. Furthermore, there are few papers in which the difference in the gene expression profiles in keratinocytes between NB-UVB (311nm) treatment and excimer light (308nm) treatment is examined.

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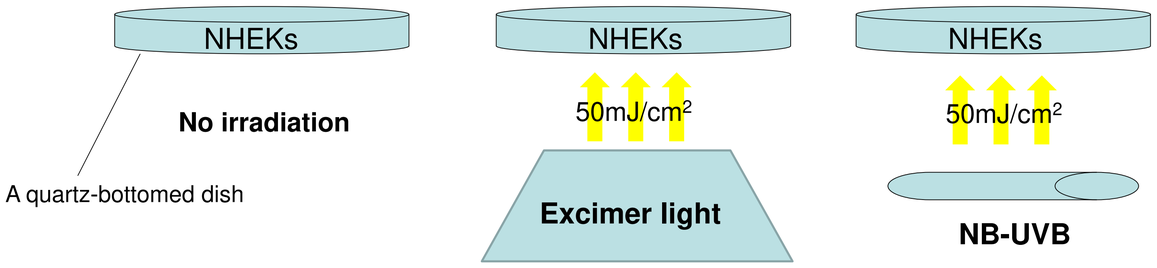
## Aim of Study

The aim of this study is to compare the gene expression profiles in normal human keratinocytes (NHEKs) after irradiation between 311nm NB-UVB and 308nm excimer light .

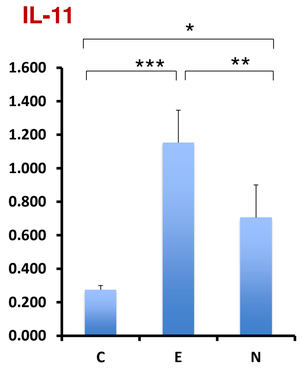
## Results

**Fig.1 Comparison of gene expression profiles of NHEKs after irradiation with NB-UVB and excimer light**



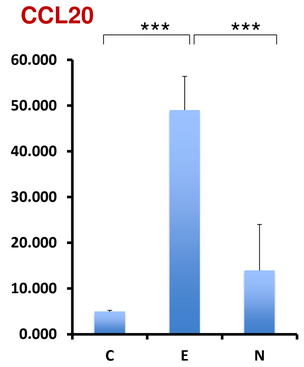

1. NHEKs cultured in a quartz-bottomed dish were irradiated with 50mJ/cm$^2$ NB-UVB or 50mJ/cm$^2$ 308nm excimer light through the bottom surface of the dish.
2. Six hours after irradiation, cells were harvested, and then RNA was collected in each sample.
3. Microarray analysis was performed using the RNA samples and some genes that altered significantly after irradiation were selected.
4. Real-time PCR was used to quantify mRNA levels for selected genes and the results were compared between NB-UVB and excimer light.

**IL-11**



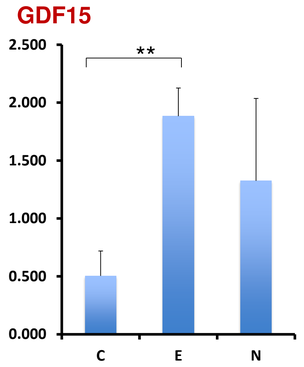

IL-11 is a member of the IL-6 cytokine family.
Previous reports have shown that IL-11 shows anti-inflammatory, immunomodulatory and cytoprotective effects.
IL-11 mRNA expression was increased more in both irradiated cells than in the control cells.

**CCL20**



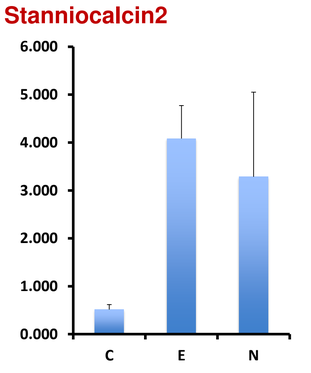

CCL20 is a CC chemokine and an unique functional ligand for CCR6.
CCR6 is expressed by Th17 cells and Treg cells.
It was expressed at higher levels in excimer light treated cells than in NB-UVB treated cells.

**GDF15**



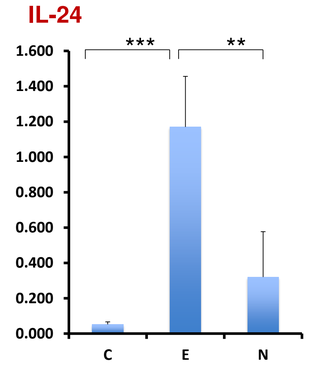

GDF15 is growth differentiation factor 15.
It is a member of the TGFβ superfamily and has a role in regulating inflammatory and apoptosis pathways during tissue injury.
It was expressed at higher levels in both irradiated cells than in the control cells.

**Stanniocalcin2**



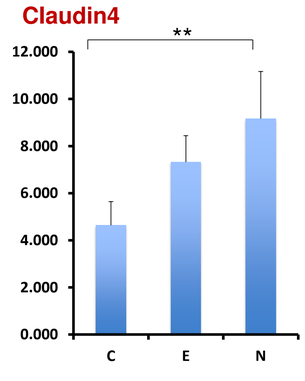

Stanniocalcin2 is a glycoprotein hormone and is involved in calcium and phosphate homeostasis.
Stanniocalcin2 mRNA expression was increased in both irradiated cells than in the control cells.

**IL-24**



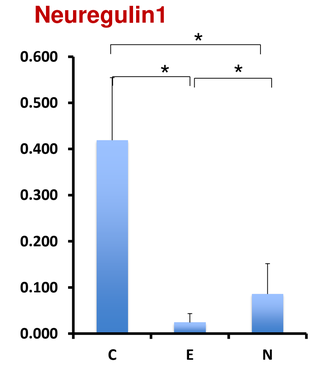

IL-24 is a member of the IL-10 cytokine family.
It is pro-inflammatory cytokine and has an important role in psoriasis.
It was expressed at higher levels in the excimer light treated cells than in the NB-UVB treated cells.

**Claudin4**




Claudin4 is a crucial component in the tight junction which is involved in the organization of cellular barrier.
It was expressed at higher levels in the NB-UVB treated cells than the control cells.

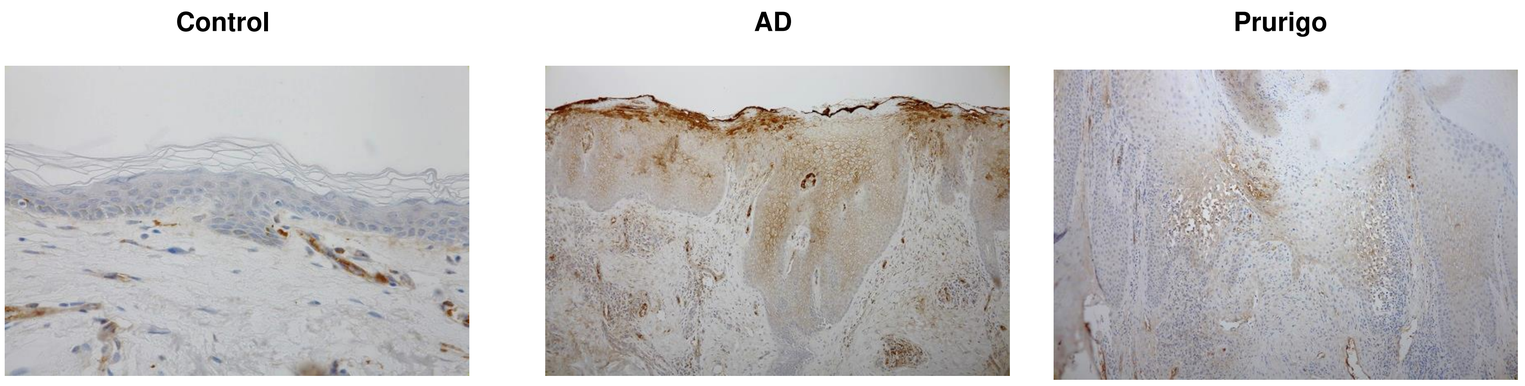
**Neuregulin1**




Neuregulin1 (NRG1) is a trophic factor that contains epidermal growth factor-like domain.
It has several isoforms, most of which are synthesized as membrane-anchored precursors and are secreted after cleavage by ADAM family proteins.
It is known to have a major role in neural, mammary and cardiac development.
However, its function in the keratinocytes is unknown.
NRG1 expression levels were more decreased in the excimer light treated cells than in the NB-UVB treated cells.

**E : Excimer light**
**N : NB-UVB**
**C : Control (No irradiation)**

**Fig.2 NRG1 is highly expressed in the epidermis of AD and prurigo patients**




Skin biopsy specimens from healthy controls, AD and prurigo patients were stained using anti-NRG1 antibody.

## Conclusion

- **We focused on seven genes that have changed significantly after irradiation with NB-UVB and excimer light.**
- **Excimer light irradiation had different effects on gene induction than NB-UVB irradiation because significant difference was found in some genes such as IL-11, CCL20, IL-24 and NRG1.**
- **Only NRG1 showed reduced gene expression after NB-UVB treatment and excimer light treatment.**
- **NRG1 is highly expressed in keratinocytes of AD and prurigo lesions and might be an important molecule for inflammation and pruritus.**