

## EXPRESSION ANALYSIS OF NOVEL MOLECULES ASSOCIATED WITH SKIN DISEASES

### Abstract

The skin is constantly exposed to various environmental factors, which increase the risk of developing skin diseases such as skin cancer and intractable diseases<sup>1,2</sup>. Skin diseases not only reduce the quality of life of patients but can also cause death. However, the pathogenesis of these diseases remains unclear, and there are many diseases for which no treatment has been established to cure them completely. Since it is important to elucidate the unknown pathogenesis of these diseases in order to develop novel therapies to solve them, we searched for and analyzed the expression of novel molecules associated with various skin diseases. We analyzed the expression levels of X, a candidate molecule associated with skin diseases, by immunohistochemistry of human skin tissue sections, and found that the expression levels tended to be lower in UV-exposed skin and pathological specimens than in UV-unexposed skin. This suggests a correlation between the expression level of Molecule X and the skin condition changes caused by UV exposure, and a functional relationship was inferred. In the future, we plan to increase the number of specimens and make comparisons by age group. In addition, we plan to verify the trend observed in human tissue sections in mice and cultured cells, where individual differences are smaller than in humans. Furthermore, we plan to analyze the interaction of skin disease-related molecules with other proteins and their intracellular functions to further our analysis. The elucidation of the pathogenic mechanism of skin diseases through this research is expected to contribute to the development of new therapeutic strategies targeting novel molecules in the future.

### Introduction

- Skin is at risk of developing various diseases such as skin cancer\* and intractable diseases due to daily exposure to environmental factors such as ultraviolet radiation.
- The pathogenesis of many skin diseases is still unknown, and although temporary symptomatic treatments exist, there are many diseases for which no causative therapy has been established to achieve a complete cure.
- In order to develop novel therapies to cure diseases completely, it is extremely important to elucidate the unknown pathogenic mechanisms.
- From previous studies in this laboratory, it is predicted that a certain protein X is involved in other skin diseases.
- Protein X was the first target for expression analysis as a candidate for novel molecules related to skin diseases to elucidate the pathogenic mechanism.

#### \* Skin cancer favorably affected by ultraviolet rays

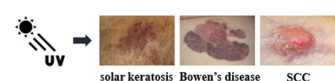
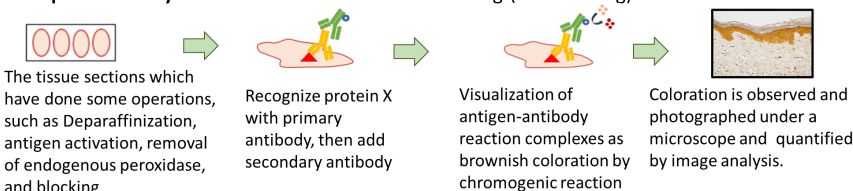


Image:  
① Mochida Pharmaceutical Co. "Symptoms of Sunlight Keratosis".  
<https://www.mochida.co.jp/nikko-kakusho/about/symptom.html>  
② Keio University Hospital KCMFAS. "Bowen's disease".  
<https://kompas.hosp.keio.ac.jp/content/000676.html>  
③ Saiseikai. "What is spinous cell carcinoma?".  
[https://www.saiseikai.or.jp/medical/disease/squamous\\_cell\\_carcinoma/](https://www.saiseikai.or.jp/medical/disease/squamous_cell_carcinoma/)

- **solar keratosis** : It is caused by long-term exposure to ultraviolet light and can be cured by early detection, but if left untreated, it can develop into squamous cell carcinoma, which is a highly malignant form of cancer.
- **Bowen's disease**: Early-stage cancer in which cancer cell growth is confined to the epidermis; if left untreated, cancer cells invade the dermis, resulting in a condition like squamous cell carcinoma.
- **squamous cell carcinoma** : Malignant tumors that often arise over prior lesions such as scars, solar keratosis, and Bowen's disease, and may metastasize to nearby lymph nodes or other organs.

### Methods and Materials

- **Skin tissue** : Human skin tissue sections provided by the Department of Dermatology, Aichi Medical University  
(UV unexposed normal skin, UV exposed normal skin and skin pathology specimen sections)  
※Approval No: 20-039 (Shibaura Institute of Technology), 2020-419 (Aichi Medical University)
- **Experimental system** : Immunohistochemical staining (DAB staining)



### Results

**Figure1.** In UV-exposed skin (D, E), a decrease in the level of protein X staining in the epithelium was observed compared to UV-unexposed skin (A, B). A decrease in protein X staining was also observed in each pathological specimen (G, H, J, K, M, N) compared to UV-unexposed skin (A, B). In squamous cell carcinoma (I, J), weak expression of protein X was also observed in tumor cells that had invaded into the dermis by infiltration. The bottom row of each sample shows an overall view of the cellular and histological structures in the HE-stained images (C, F, I, L, O).

Scale bar: low magnification 200  $\mu$ m, high magnification 50  $\mu$ m

**Figure2.** As with the staining level findings in microscopy, quantitative analysis of coloration showed a trend toward lower levels of protein X staining in the epithelium in UV-exposed areas and in each pathological specimen compared to UV-unexposed skin. In particular, there was a greater tendency for staining levels to decrease in sunlight keratosis and squamous cell carcinoma compared to non-UV-exposed skin. (Statistics: n = 3, Steel-Dwass test)

These results suggest a correlation between changes in skin condition induced by UV exposure and the expression level of protein X, and a functional relationship is inferred. Since protein X is also known as a regulator of cell apoptosis-promoting properties, it is possible that suppression of protein X expression inhibits UV-induced apoptosis, leading to the development of various skin diseases, including cancer.

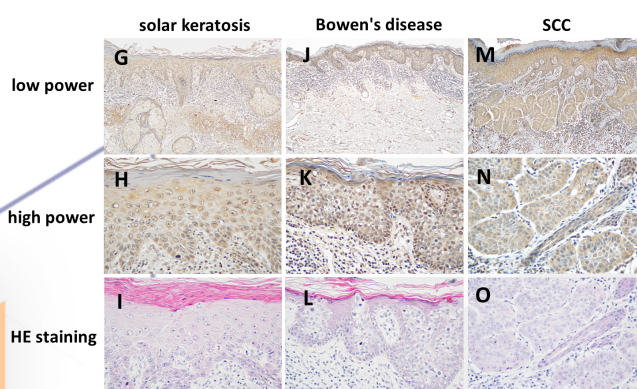
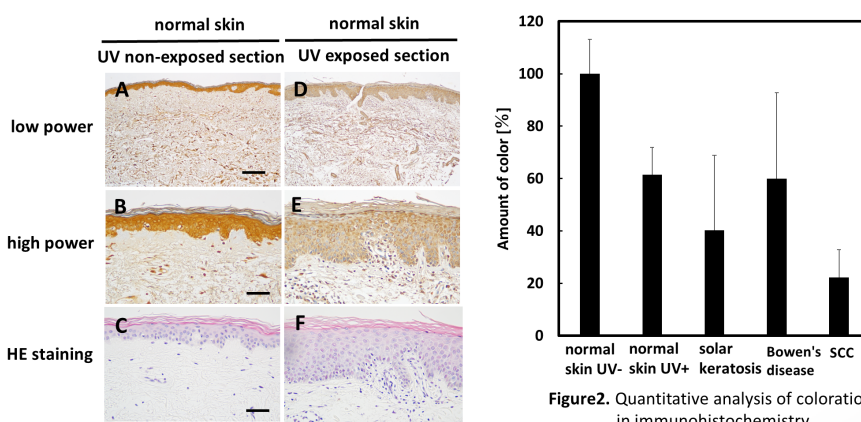


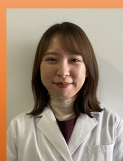
Figure1. Immunohistochemistry image of human skin tissue section

### Discussion / Conclusions

- This study suggests that the expression level of protein X is involved in the pathogenesis of skin diseases. However, since there are large individual differences in human skin tissue sections due to differences in the duration of UV exposure, living environment, etc., it is necessary to verify the trends observed in human skin tissue sections in mice, cultured cells, etc. in the future.
- In the next step, we will increase the number of samples for more detailed analysis, and also conduct comparisons between age groups. We will also conduct comparisons between age groups.
- As part of the functional analysis of skin disease-related molecules, further analysis of their interactions with other proteins and We will further analyze the interactions with other proteins and their intracellular functions as part of our functional analysis of molecules related to skin diseases.

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2. Ministry of the Environment UV Environmental Health Manual 2015.