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Expression of Cold-Inducible RNA-Binding Protein in Normal Skin, Actinic Keratosis and Squamous Cell Carcinoma

Bo Mi Park, Jae Hyuk Lee[1], Seong Jin Kim

Departments of Dermatology and [1]Pathology, Chonnam National University Medical School, Gwangju, Korea

Dear Editor:

Cold-inducible RNA-binding proteins (CIRP) are a kind of RNA binding protein associated with diverse cellular responses including cell growth, proliferation, and apoptosis[1]. CIRP are induced by various cellular stresses in addition to cold exposure such as ultraviolet (UV) radiation and hypoxia[1,2]. Recently, their proto-oncogenic functions have been suggested, but a detailed expression pattern in skin tumor has not been reported[3-5]. Therefore, we aimed to simply observe the expression pattern of CIRP in photodamaged epidermis of actinic keratosis (AK), squamous cell carcinoma (SCC) and normal skin by immunohistochemical staining.

Five samples of normal skin were obtained from 5 healthy individuals undergoing cosmetic surgery. Among them, 3 were taken from the back and 2 from the face. Specimens of AK and SCC were obtained from the faces of 5 patients who underwent excisional surgery. SCC samples were confined to that which developed after long-standing AK. Clinically and pathologically active lesions were taken as the samples. In all cases, informed consent was obtained from patients according to the ethics committee of the Chonnam National University Hospital. Serial paraffin sections of each specimen were stained with monoclonal antibodies specific for CIRP (Proteintech Group, Chicago, IL, USA) at a dilution of 1 : 100 according to the manufacturers' protocols. The expression of CIRP in epidermal keratinocytes was scored semi-quantitatively by two dermatologists. Nuclear and cytoplasmic staining were assessed separately. We considered both staining intensity and the ratio of positively stained cells in comparison with adjacent stromal cells, lymphocytes, and sebaceous and eccrine glands. No staining was cited as 0, weaker staining than stromal cells as 1, similar to stromal cells as 2, and stronger as 3. Statistical analysis was performed using the chi-square test and Wilcoxon's rank sum test to compare the expression pattern (SPSS ver. 17.0; SPSS Inc., Chicago, IL, USA).

In normal skin specimens, CIRP expression was more evident in nuclei than in cytoplasm throughout the epidermal keratinocytes (Fig. 1). However, in specimens from the face, the most sun exposed area, cytoplasmic CIRP staining intensity was increased compared to that in specimens from the back, a less-sun exposed area. In the case of AK, nuclear CIRP expression was decreased while cyto-

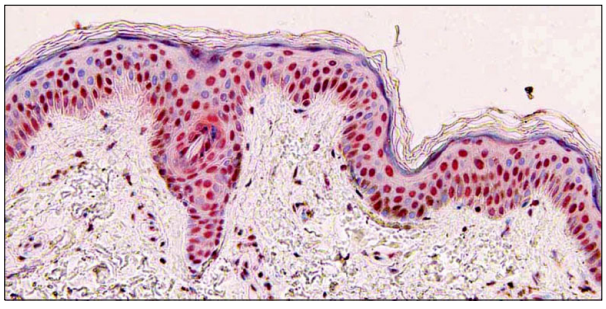

Fig. 1. Cold-inducible RNA-binding protein (CIRP) expression is evident in the nuclei of epidermal keratinocytes in normal skin from back (CIRP immunohistochemical stain, ×200).

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Corresponding author: Seong Jin Kim, Department of Dermatology, Chonnam National University Medical School, 160 Baekseo-ro, Dong-gu, Gwangju 501-746, Korea. Tel: 82-62-220-6683, Fax: 82-62-222-4058, E-mail: seongkim@jnu.ac.kr

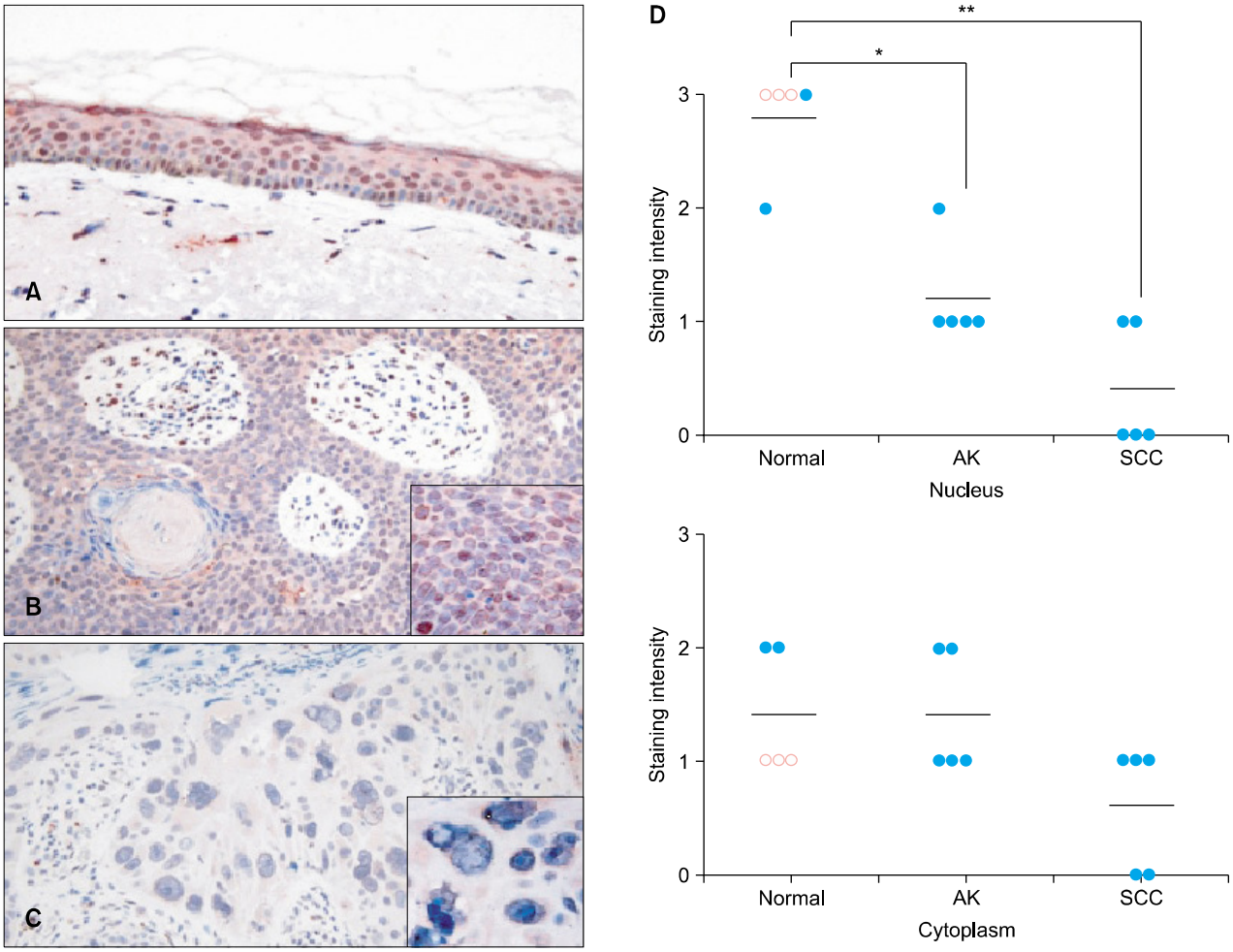

Fig. 2. Expression patterns of Cold-inducible RNA-binding protein (CIRP). Representative pictures of five cases in each normal skin from face (A), actinic keratosis (AK) (B), and squamous cell carcinoma (SCC) (C) (A~C: CIRP immunohistochemical stain, ×200). Inset: higher magnification of the hot spot of the specimen (CIRP immunohistochemical stain, ×400). (D) Statistical analysis of staining intensity shows significantly decreased nuclear CIRP expression in actinic keratosis and squamous cell carcinoma compared with normal skin specimens. Open circles: tissue sample from back. Closed circle: tissue sample from face. Open circle indicates a normal skin specimen from the back. *$p<0.05$, **$p<0.01$, Wilcoxon's rank sum test.

plasmic expression was maintained or rather increased. And in the most pathologic spots of SCC, CIRP expression was significantly decreased both in the nuclei and cytoplasm. Statistical analysis revealed significantly decreased expression of CIRP in nuclei of AK and consequent SCC compared with normal skin. There was no statistically significant difference in cytoplasmic staining intensity among them (Fig. 2).

In previous studies of human cancer, the majority of endometrial carcinoma showed decreased staining intensity[4]. However, staining intensity was increased in several other human tumors, such as colon and prostate cancer[5]. These conflicting results may come from the early inducing mechanism of CIRP. CIRP regulates gene expression at the level of translation[1,3]. Therefore, the exact cellular function of CIRP remains unknown at the moment and the expression pattern in cancer cells could vary according to the state of the tumor. The increased cytoplasmic CIRP expression we observed in sun-exposed areas might be explained by relocalization of CIRP that was triggered by UV exposure[2].

We observed a significant decrease of nuclear CIRP expression in AK and SCC compared with normal skin. Further studies are needed to elucidate the relationship between CIRP and UV radiation and consequent tumorigenesis in the skin.

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Pemphigus Vulgaris in Pregnancy Associated with Herpes Virus Type 1 Infection

Jiwon Gye, Chan Hee Nam, Ji Seok Kim, Jee Young Kim, Byung Cheol Park, Myung Hwa Kim, Seung Phil Hong

Department of Dermatology, Dankook University Hospital, Cheonan, Korea

Dear Editor:

Pemphigus vulgaris (PV) rarely occurs during pregnancy. We report a case of PV associated with herpes simplex type 1 virus (HSV-1) which occurred in the third trimester of pregnancy.

A 32-year-old second gravida at 37 weeks' gestation was admitted for multiple bullous skin lesions that persisted for over a month.

These vesicular and erosive lesions initiated from the periumbilical region and spread to the oral mucosa and the skin of the back (Fig. 1A, B). The diagnosis of PV was confirmed by biopsy (Fig. 1C), and direct immufluorescence detected anti-immunoglobulin G and C3 antibodies. Anti-desmoglein 1 and anti-desmoglein 3 antibodies were elevated at 82.1 U/ml (normal, <14 U/ml) and 184.9 U/ml (normal, <7 U/ml) in peripheral blood. Tzanck smear and viral polymerase chain reaction (Seeplex STD B41 Detedtion; Seegene, Seoul, Korea) were done on the base of a vesicular lesion on the trunk. Tzanck smear was negative, but, viral polymerase chain reaction (PCR) was positive for HSV-1 (Fig. 2).

Prednisolone at a dose of 20 mg/d was initiated. Foll-

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Corresponding author: Seung Phil Hong, Department of Dermatology, Dankook University Medical College, 119 Dandae-ro, Dongnam-gu, Cheonan 330-714, Korea. Tel: 82-41-550-6485, Fax: 82-41-552-7541, E-mail: zamoo97@naver.com