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Expressions of oncogenes *c-fos* and *c-myc* in skin lesion of cutaneous squamous cell carcinoma

Yan Zheng, Guo-Rong Wang, Jin-Jing Jia, Su-Ju Luo, Hao Wang, Sheng-Xiang Xiao*

Department of Dermatology, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China

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ABSTRACT

Objective: To explore the expressions of *c-fos* and *c-myc* in skin lesion of cutaneous squamous cell carcinoma (CSCC). **Methods:** Using retrospective analysis, 73 cases of CSCC were selected from Department of Dermatology, the Second Affiliated Hospital of Xi'an Jiaotong University, which were removed between January 2000 and January 2012. It was considered as experimental group. Meanwhile, 11 cases of normal skin specimens of non tumor patients were selected as control group. The expression level of *c-fos* and *c-myc* was compared in the two groups. **Results:** The expressions of *c-fos* [72.60% (53/73)] and *c-myc* [83.56% (61/73)] in experimental group were statistically significant ($P \leqslant 0.05$) compared with control group (0%). Expression of *c-myc* protein was negatively related to differentiation of CSCC. The difference was statistically significant ($\chi^2=7.26$, $P=0.001<0.05$). While expression of *c-fos* protein was positively related to differentiation of CSCC, which was statistically significant ($\chi^2=7.47$, $P=0.0012<0.025$). **Conclusions:** The expression level of *c-fos* and *c-myc* can be used as an important indicator of CSCC differentiation, and it has closely connection with the differentiated degree, which can guide clinical prognosis.

1. Introduction

Cutaneous squamous cell carcinoma (CSCC) is also called dermoid cancer. Starting from the squamous epithelium of the skin, it is most found in palpebral margin, the junction of skin and conjunctiva[1]. CSCC develops fast and has destructive effect. According to the existing data, the incidence rate of CSCC accounts for 82.10% of malignant skin tumors, posing a serious threat to human body health. The present study aimed to explore the expressions of oncogene *c-fos* and *c-myc* protein in skin lesion of CSCC. A total of 73 cases of CSCC specimens and 11 cases of normal skin specimens were selected as the object of this study.

*Corresponding author: Sheng-Xiang Xiao, Department of Dermatology, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710004, Shaanxi Province, China.
Tel: 13227701303
E-mail: xiao_sx@163.com
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2. Materials and methods

2.1. Materials

The study was performed through retrospective analysis. CSCC specimens of 73 cases were selected from Department of Dermatology, the Second Affiliated Hospital of Xi'an Jiaotong University, which were removed between January 2000 and January 2012. It was considered as experimental group. Among them, 51 were male, and 22 were female, aging 28-84 years with the average age of (56.12±12.54) years. Meanwhile, 11 cases of normal skin specimens of normal healthy subjects were selected as control group, including 6 males and 5 females, aging 25-81 years with the average age of (57.85±11.74) years. The baseline information of both groups had no significant difference and was comparable.

2.2. Methods

Paraffin samples were selected. The specimens were fixed with paraffin and prepared into pathological slices. Followed by conventional dewaxing and hydration, they were restored with microwave antigen. The slices were incubated with rabbit anti-human *c-fos* and *c-myc* polyclonal antibody (Beijing Zhong Shan Golden Bridge Biotechnology Co., Ltd) and stained with DAB. Phosphate buffered saline was used for negative control.

2.3. Outcome measures

Standard of positive expression is that positive particles of oncogenes *c-fos* and *c-myc* are located within the nucleus and cytoplasm, and particles are brown to dark brown.

According to the cell pigmentation, the expressions of *c-fos* and *c-myc* are divided into negative (-), positive (+) and positive (++). Standard of negative (-): no brown to dark brown particles are seen in cell nucleus; standard of positive (+): brown particles are less than 50% in cell nucleus; standard of positive (++): brown particles are more than 50% in cell nucleus. The specimens of two groups were placed under high power lens, and 6 views were selected randomly to observe rate of positive particles in total cells.

2.4. Statistical analysis

Data were analyzed using statistical software SPSS13.0. *Chi*-square test was used. $P \leqslant 0.05$ was considered as statistically significant.

3. Results

3.1. Expressions of c-fos and c-myc proteins

Among 73 cases of specimens in experimental group, 53 (72.60%) were the expression of oncogene *c-fos*, and 61 (83.56%) were *c-myc* protein. The two protein expressions were not found among the specimens of 11 cases in control group. The difference was statistically significant ($\chi^2=6.142$, $P=0.001<0.05$, $\chi^2=7.451$, $P=0.012<0.05$) (Figures 1-6).

3.2. The correlation between oncogene proteins and CSCC differentiation

Expression of *c-myc* protein was negatively related to CSCC differentiation. With the decrease of differentiation, the expression increased accordingly. The difference was statistically significant ($\chi^2=7.26$, $P=0.001<0.05$). Expression of *c-fos* protein was positively related to CSCC differentiation. With the decrease of differentiation, the expression decreased as well. The difference was statistically significant ($\chi^2=7.47$, $P=0.0012<0.025$) (Table 1).

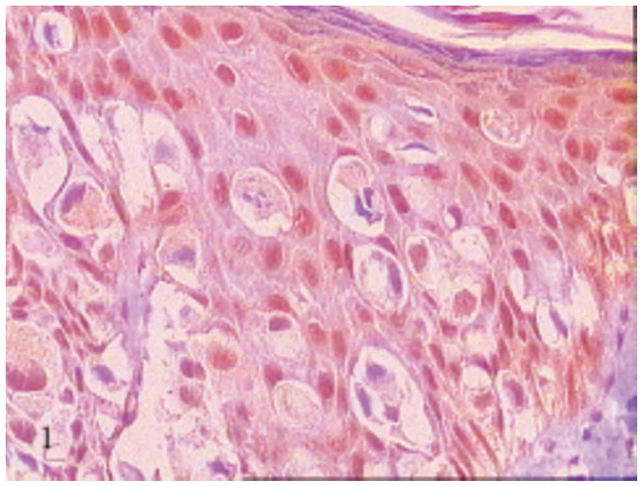

Figure 1. Expression of *c-fos* in CSCC (SP, ×100).

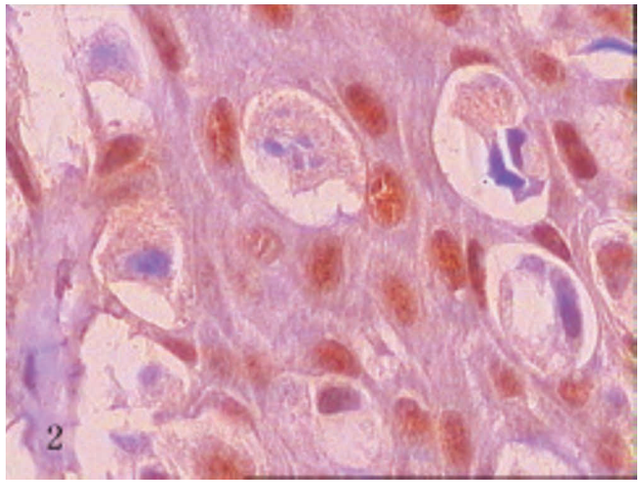

Figure 2. Expression of *c-fos* in CSCC (SP, ×400).

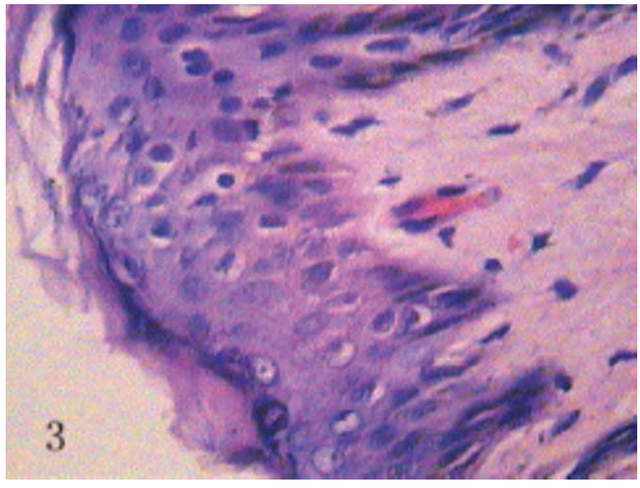

Figure 3. Non expression of *c-fos* in normal skin (SP, ×100).

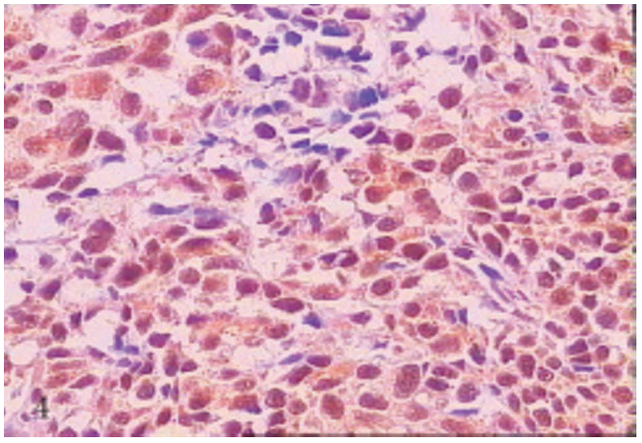

Figure 4. Expression of *c-myc* in CSCC (SP, ×100).

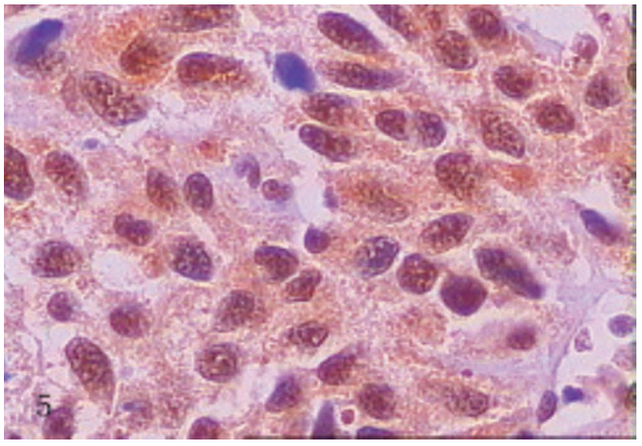

Figure 5. Expression of *c-myc* in CSCC (SP, ×400).

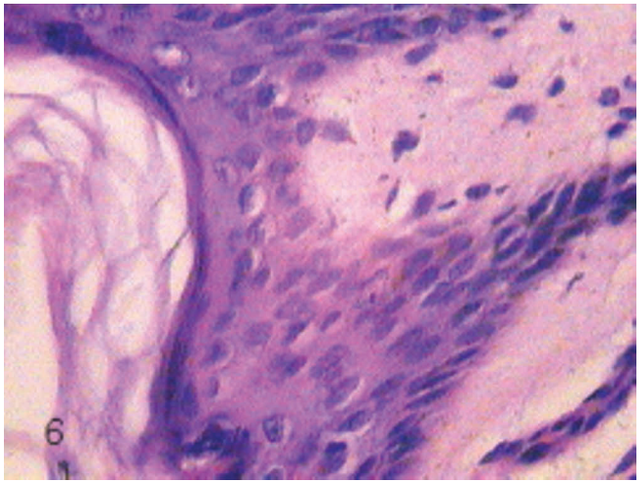

Figure 6. Non expression of *c-myc* in normal skin (SP, ×100).

Table 1
The correlation between the expressions *c-myc* and *c-fos* proteins and CSCC differentiation. (*n*%).

Oncogene	Differentiation	(+) Expression	(−) Expression	Total
C-myc	High	13	4	17
	Moderate	24	7	31
	Low	22	3	25
	Total	59	14	73
C-fos	High	23	3	26
	Moderate	20	5	25
	Low	9	13	22
	Total	52	21	73

4. Discussion

CSCC, belonged to malignancy, develops fast and has serious influence on the patients. Therefore, it is significant to strengthen early diagnosis and treatment[2-6]. Proto-oncogene is a kind of house-keeping gene for regulation of cell proliferation and differentiation in normal cells. Only under the influence of various factors, it will activate and get out of control to cause genetic mutation and transform normal cells into malignant cells. The relationship between proto-oncogene nucleoprotein *c-fos* and *c-myc* of transcription factor in nucleoprotein oncogene and tumour has been hot topics of the medical research[7-11].

C-fos gene, belonged to the oncogene of encoding nucleoprotein, is a member of immediate early genes, which is composed of five exons. When genes are affected by chemistry, biology, physics, *etc*., transcription factors are generated and will make effect on normal cells[12-15]. *C-fos* gene is an important component of *Fos* gene proteins, and its expression product exists in cell nucleus. *C-myc* is a intranuclear transcription factor, consisting of 3 exons and 2 introns. It is almost not expressed at static stage, but the expression will increase accordingly under the influence of various factors. According to relevant studies[16-19], *c-myc* is involved in the initiation of variety of gene expressions and signal transmissions, which belongs to regulatory gene. Researchers reported that *c-myc* gene contributes to cell differentiation in rectum tumor, colon tumor, testis tumor and other malignant tumors[20-25]. But so far, little is known about expression of *c-myc* protein in CSCC. Therefore, the present study is of great significance for expression of *c-myc* and *c-fos* proteins in CSCC.

In the present study, expression levels of *c-myc* and *c-fos* proteins were detected by immunohistochemical method. It was found that *c-myc* and *c-fos* proteins were not expressed in normal skin tissue, but the expression rates in CSCC were 83.56% and 72.60%, respectively. This evidence suggested that the occurrence and development of skin cancer cells are closely correlated with *c-myc* and *c-fos* proteins, which was consistent with the related reports. In addition, our study also found that expression of *c-myc* protein was negatively related to CSCC differentiation; expression of *c-fos* protein was positively related to CSCC differentiation. So *c-myc* and *c-fos* can be regarded as an important indicator of CSCC differentiation for early diagnosis. The present study further illustrated that levels of *c-fos* and *c-myc* proteins can be regarded as an important indicator of CSCC differentiation, which was consistent with related reports.

In conclusion, the expression levels of *c-fos* and *c-myc* can be used as an important indicator of CSCC differentiation, and it has closely connection with the differentiated degree, which can guide clinical prognosis.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

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