ISSN (Print) 1225-9918
ISSN (Online) 2287-3406
Journal of Life Science 2015 Vol. 25. No. 6. 686~692 DOI : http://dx.doi.org/10.5352/JLS.2015.25.6.686

The Distribution of CD8- and Foxp3-positive T Cells in Skin Squamous Cell Tumors and Basal Cell Carcinomas

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Received March 24, 2015 /Revised April 21, 2015 /Accepted April 21, 2015

Cancer is subject to dynamic interactions between contrary immune reactions that drive both tumor growth and suppression. Forkhead box p3 positive T cells (Foxp3 positive T cells) might support tumor promotion, while CD8 positive T cells might protect the host. The present study examined the distributions of CD8- and Foxp3-positive T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in skin squamous cell carcinoma (SCC) and its precancerous lesions; it also compared this with data for basal cell carcinoma (BCC). Iimmunohistochemical staining for CD8 and Foxp3 was conducted in 20 cases of SCC, Bowen's disease (BD), actinic keratosis (AK) and BCC. The BD and SCC cases exhibited significantly increased numbers of both CD8- and Foxp3-positive T cells in their advancing regions compared with the AK and BCC cases, and the BD cases exhibited significantly lower CD8 positive T cells / Foxp3 positive T cells ratio in these regions than did the AK and BCC cases. There was no significant difference in both T cells and the ratio between BD and SCC. The degree of both T cells infiltration differed between the advancing and central areas in SCC and BCC. Immune microenvironments differ between cutaneous squamous cell tumors and BCC and differ as well among tumor compartments.

Key words : Basal cell carcinoma, CD8 positive T cell, Foxp3 positive T cell, skin squamous cell carcinoma

Introduction

Ultraviolet radiation is closely implicated in the carcinogenesis of squmaous cell carcinoma (SCC) and basal cell carcinoma (BCC) because it induces DNA mutations and immunosuppression [1, 17]. Both tumors frequently occur in organ transplant recipients (OTR), in which their occurrences are also correlated with the level of immunosuppression [8]. Therefore, the status of immune system is markedly related to the development of both tumors. Cancer cells are able to express immunogenic tumor-associated antigens that are targets for cellular immune responses [2]. Th1 immune responses foster anti-tumor immune reactions through the activation of CD8 positive T cells which kill tumor cells by releasing toxic granules [13, 16]. In contrast, cancer can overcome immunosurveillance through many mechanisms, in which regulatory T cells (Tregs) plays an important role in a variety of cancers [7]. Tregs are CD4 positive CD25 positive T cells, express the forkhead box p3 (Foxp3) transcription factor, and suppress the activation of conventional T cells through direct contact or the release of cytokines [6, 24]. In other words, Foxp3 positive T cells may impair the anti-tumor immune responses of CD8 positive T cells and natural killer cells in a variety of cancers [7, 21]. Combined analysis for both Foxp3 positive T cells and cytotoxic T cells are to be done to evaluate the immune response against tumors. Foxp3 positive T cells have also been observed in SCC and BCC, and their numbers were reported to increase during the development of skin SCC [5, 10, 12]. Recently, the CD8 positive T cells/ Foxp3 positive T cells ratio was shown to be significantly lower in transplant associated SCC compared to otherwise SCC [4, 27]. In these studies, the ratio was suggested as a valuable tool for the prediction of development and aggressive growth of transplant associated SCC. Renal transplant recipients showed more increased incidence for SCC than BCC [17]. Previous studies have shown that MHC class I expression and CD8 positive T cell infiltration were significantly decreased in BCC compared to SCC [3, 23]. Aforementioned findings suggest that the tumor immune microenvironment differs between both tumors. The present study was conducted to examine the distribution of CD8 positive T cells, Foxp3 positive T cells and CD8 positive T

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Table 1. Characteristics of patients

	Number of cases	Age distribution	Gender (male:female)
Squamous cell carcinoma	20	95~50	8:12
Bowen's disease	20	93~55	6:14
Actinic keratosis	20	93~56	8:12
Basal cell carcinoma	20	90~58	8:12

cells/ Foxp3 positive T cells ratio in skin SCC and its precancerous lesions, and compare them to those of BCC.

Materials and Methods

Patients and tissue samples

We used only one representative tissue section in formalin-fixed paraffin-embedded tissues from 80 patients who were diagnosed with actinic keratosis (AK), Bowen's disease (BD), SCC, or BCC at Dongguk University Gyeongju Hospital between 2011 and 2013. The distribution of age and gender in this study subjects are shown in Table 1. Any patients did not receive radiotherapy or chemotherapy before diagnosis.

Immunohistochemistry and assessment

Tissue preparation and immunohistochemical staining were performed in same method done in our previous study [10]. The primary antibodies included anti-CD8 (1:250, Dako, Santa Barbara, CA, USA) and anti-Foxp3 antibody (1:100, Abcam, Cambridge, UK). Rabbit and mouse IgG isotype were used as negative controls, while tonsil tissue was used as a positive control. Lymphocytes with positive signal for CD8 or Foxp3 were assessed in the tumor region and in the stroma at the advancing and central area for SCC and BCC, as well as in the adjacent stroma and tumor region for AK and BD. Their numbers were counted in five randomly selected high-power fields (HPFs) and were averaged. CD8 positive T cells/ Foxp3 positive T cells ratio was calculated based on the number of both T cells.

Statistical analysis

Mean was 71 for CD8 positive T cells, 44 for Foxp3 positive T cells and 2.2 for the CD8 positive T cells/ Foxp3 positive T cells ratio in all the examined cases. The number and ratio were divided into high (mean or more) and low group (less than mean) based on mean. The range of tumor depth in SCC and BCC was from 1 mm to 6 mm and its mean value was 2.98 mm. Therefore, both tumors were divided into two groups based on 3 mm of tumor depth. Fisher's exact test was used. A p-value of less than 0.05 was considered to indicate significance.

Results

Immunohistochemical staining of CD8 and Foxp3 in SCC and BCC

As shown in Fig. 1, CD8 positive T cells and Foxp3 pos-

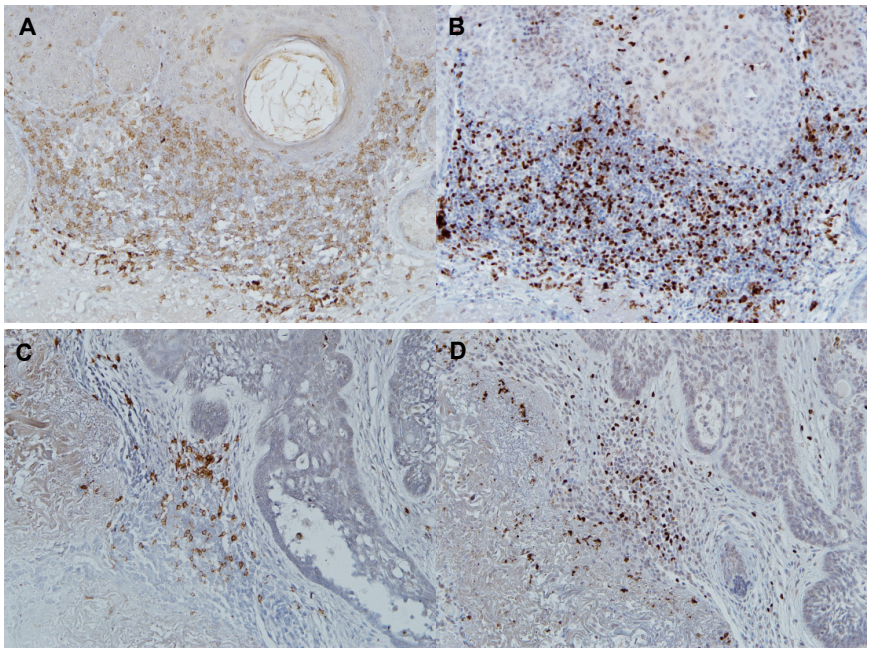

Fig. 1. Immunohistochemical staining of CD8 (A and C) and Foxp3 (B and D) in squamous cell carcinoma (SCC) (A and B) and basal cell carcinoma (BCC) (C and D), (A-D, x200). CD8 positive T cells and Foxp3 positive T cells predominantly infiltrated the tumor stroma versus the tumor epithelial region in SCC and BCC.

itive T cells predominantly infiltrated the tumor stroma versus the tumor epithelial region in SCC and BCC. This finding was also observed in AK and BD.

The rate of high group for both T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in the advancing area of SCC and BCC, and the adjacent stroma and tumor epithelial regions of AK and BD

As shown in Fig. 2, the rate of high group for CD8 positive T cells was 20% (4/20) in AK, 75% (15/20) in BD, 70% (14/20) in SCC and 25% (5/20) in BCC. The rate of high group for Foxp3 positive T cells was observed in 5% (1/19) of AK, 60% (12/20) of BD, 80% (16/20) of SCC and 20% (4/20) of BCC. Therefore, BD and SCC showed significantly high infiltration of CD8 positive T cells and Foxp3 positive T cells compared to AK and BCC (p<0.05). The rate of high group for the ratio was found in 55% (11/20) of AK, 20% (4/20) of BD, 40% (8/20) of SCC and 55% (11/20) of BCC. Therefore, the ratio was significantly lower in BD than in AK and BCC (p=0.045). There was no significant difference in the grade of infiltrating CD8 positive T cells, Foxp3 positive T cells and the ratio between BD and SCC. Therefore, BD and SCC were combined into one, and then both T cells and the ratio were compared to those of AK and BCC. In the combined group, the rate of high group was 73% (29/40) for CD8 positive T cells, 70% (28/40) for Foxp3 positive T cells and 30% (12/40) for the ratio. Both T cells infiltration were significantly higher in the combined group than in AK and BCC (p<0.05), and the ratio was lower in the combined group compared to AK and BCC with no statistical significance.

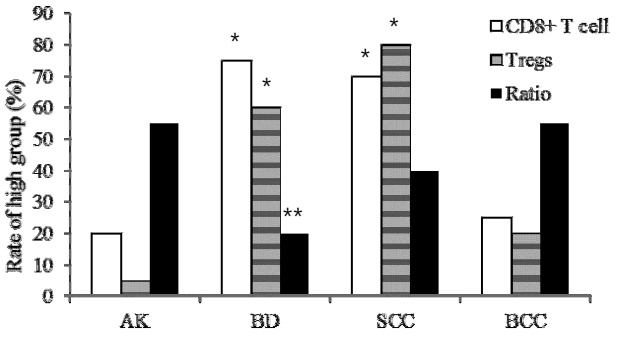

Fig. 2. The rate of high group for CD8 positive T cells, Foxp3 positive T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in actinic keratosis (AK), Bowen's disease (BD) and the advancing area of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The rate of high group for both T cells was significantly higher in BD and SCC than in AK and BCC (an asterisk, p<0.05), and that for the ratio was higher in AK and BCC than in BD (two asterisks, p=0.045). Tregs, regulatory T cells.

The rate of high group for both T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in the central area of SCC and BCC

As shown in Fig. 3, the rate of high group for CD8 positive T cells was observed in 25% (5/20) of SCC and 0% (0/20) of BCC. The rate of high group for Foxp3 positive T cells was 40% (8/20) in SCC and 5% (1/20) in BCC. Therefore, SCC showed significantly high infiltration of CD8 positive T cells and Foxp3 positive T cells compared to BCC (p<0.05). The rate of high group for the ratio was observed in 15% (3/20) of SCC and 30% (6/20) of BCC. The ratio was high in BCC compared to SCC with no statistical significance.

Comparison of both T cells and CD8 positive T cells/ Foxp3 positive T cells ratio between the central area and the advancing area in SCC and BCC

As shown in Fig. 4, in SCC, the rate of high group for CD8 positive T cells was 70% (14/20) in the advancing area and 25% (5/20) in the central area, and that for Foxp3 positive T cells in SCC was 80% (16/20) in the advancing area and 40% (8/20) in the central area. Therefore, both T cell in SCC showed significantly higher infiltration in the advancing area than in the central area (p<0.05). In BCC, the

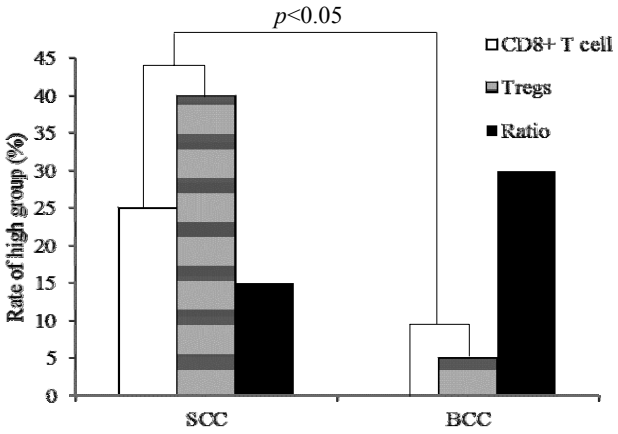

Fig. 3. The rate of high group for CD8 positive T cells, Foxp3 positive T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in the central area of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The rate of high group for both T cells was higher in SCC than in BCC (p<0.05). The ratio was high in BCC compared to SCC with no statistical significance. Tregs, regulatory T cells.

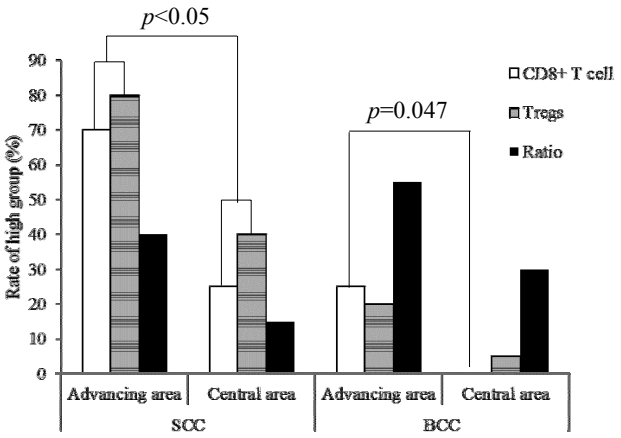

Fig. 4. The rate of high group for CD8 positive T cells, Foxp3 positive T cells and CD8 positive T cells/ Foxp3 positive T cells ratio between the advancing area and central area in squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). The rate of high group for both T cells in SCC was higher in the advancing area than in the central area (p<0.05) and that for CD8 positive T cells in BCC was in the advancing area than in the central area (p=0.047). There was no significant difference in the ratio between the advancing and central area in SCC and BCC. Tregs, regulatory T cells.

rate for high group for CD8 positive T cells was 25% (5/20) in the advancing area and 0% (0/20) in the central area, and that for Foxp3 positive T cells was 20% (4/20) in the advancing area and 5% (1/20) in the central area. Therefore, CD8 positive T cells in BCC showed significantly higher infiltration in the advancing area than in the central area (p=0.047). The rate of high group for the ratio in SCC was 40% (8/20) in the advancing area and 15% (3/20) in the central area, and that in BCC was 55% (11/20) in the advancing area and 30% (6/20) in the central area. There was no significant difference in the ratio between the advancing and central area in SCC and BCC.

Clinicopathological significance of both T cells and CD8 positive T cells/ Foxp3 positive T cells ratio in SCC and BCC

Both T cells and the ratio in the central and advancing area was evaluated according to gender and the differentiation, depth and growth pattern of tumor in SCC and BCC (Table 2). In SCC, the rate of high group for CD8 positive T cells in the advancing area was observed in 38% (3/8) of tumor with infiltrative growth and 92% (11/12) of tumor with expanding growth (p=0.018). In BCC, Any significant difference was not found.

Discussion

Cancer shows a dynamic immune interaction between

Table 2. CD8 positive T cells, Foxp3 positive T cells and CD8 positive T cells/ Foxp3 positive T cells ratio according to clinicopathologic parameters in SCC and BCC

Disease	Variable	Group	No.	Advancing area			Central area		
				CD8 positiveT cell (%)	Foxp3 positiveT cells (%)	Ratio (%)	CD8 positiveT cell (%)	Foxp3 positiveT cells (%)	Ratio (%)
SCC	Gender	Male	8	5(63)	6(75)	2(25)	2(25)	4(50)	2(25)
		Female	12	9(75)	10(83)	6(50)	3(25)	4(33)	1(8)
	Differentiaton	Well	7	4(57)	6(86)	4(57)	3(43)	5(71)	1(14)
		Moderate	13	10(77)	10(77)	4(31)	2(15)	3(23)	2(15)
	Depth	<3 mm	11	8(73)	9(82)	4(36)	2(18)	3(27)	2(18)
		≥3 mm	9	6(67)	7(78)	4(44)	3(33)	5(56)	1(11)
	Growth pattern	Infiltrative	8	3(38)	5(63)	2(25)	1(13)	3(38)	1(13)
		expanding	12	11(92)*	11(92)	6(50)	4(33)	5(42)	2(17)
BCC	Gender	Male	8	2(25)	0(0)	6(75)	0(0)	0(0)	4(50)
		Female	12	3(25)	4(33)	5(42)	0(0)	1(8)	2(17)
	Depth	<3 mm	10	3(30)	3(30)	5(50)	0(0)	0(0)	2(20)
		≥3 mm	10	2(20)	1(10)	6(60)	0(0)	1(10)	4(40)
	Growth pattern	Infiltrative	11	3(27)	3(27)	7(64)	0(0)	1(9)	4(36)
		expanding	9	2(22)	1(11)	49(44)	0(0)	0(0)	2(22)

SCC, squamous cell carcinoma; BCC, basal cell carcinoma.
*p=0.018.

contrary immune reactions driving tumor growth and tumor suppression. Cancer immunoediting is the conceptual basis for this dual opposing function of immune response against tumor, and its process consists of elimination, equilibrium and escape [7]. Immunosurveillance networks eradicate tumor cells during the elimination phase. Less immunogenic tumor cells emerge and are selected for growth during the equilibrium phase. They progressively grow and make detectable mass through immune evasion during the escape phase. Treg cells suppress the function of CD8 positive T cells through causing apoptosis and releasing inhibitory cytokines [6, 22, 24]. This finding is consistent with several clinical studies reporting that the interplay of T cell subsets has been a valuable factor in predicting disease outcome [19, 20, 26]. A previous study showed that the CD8 positive T cells/ Foxp3 positive T cells ratio was significantly lower in transplant associated SCC than in the SCC of immunocompetent patients, suggesting that the ratio may show the level of immunosurveillance against tumors [27]. In the current study, the number of both CD8 positive T cells and Foxp3 positive T cells was significantly increased in BD and SCC compared to AK, and the ratio was significantly lower in BD than in AK. There was no significant difference in both T cells and the ratio between BD and SCC. Although we did not examine these in normal skin, a previous study showed that the number of Foxp3 positive T cells was higher in AK than in normal skin tissue [25]. Taken together, the immune evasion phase begins in AK and worsens in BD and SCC. Our study did not show any difference in the degree of immune evasion between BD and SCC. A recent study analyzing immune phenotype in the SCC and BD of immunocompetent patients reported that SCC showed less infiltration of CD8 positive T cells and higher CD4 positive T cell/CD8+ T cell ratio than BD [9]. This finding suggests that the level of immune evasion is higher in SCC than in BD and further study for CD4 positive T cell subpopulation is necessary.

In the present study, the infiltration of both T cells was more decreased in BCC than in BD and SCC. Previous studies showing that MHC class I expression and CD8 positive T cell infiltration were significantly lower in BCC than in SCC support our current result about the numerical difference of infiltrating CD8 positive T cells among BCC, BD and SCC [3, 23]. Tregs infiltration was previously observed in BCC and SCC [12, 15]. In those studies, the authors found that Tregs infiltration was associated with the TH2 dominant microenvironment. These findings confirm a previous report that IL-10 produced in the tumor cells of BCC and SCC may generate a tumor microenvironment for escaping from the local T cell-mediated anti-tumor response, and support the fact that IL-10 is related to the development of Tregs [14, 18]. In addition, CCL22, chemokine responsible for the chemotaxis of Tregs, was reported to be increased in BCC [12]. However, a previous study showed that Tregs infiltration in SCC did not express CCR4 and suggested that another addressin was necessary for the recruitment of Tregs [5]. Upregulation of cytokines and chemokines responsible for the induction and chemotaxis of Tregs may be the reason for the higher proportion of Tregs in SCC than in BCC. Additionally, our study showed that the CD8 positive T cells/ Foxp3 positive T cells ratio was higher in BCC than in BD, suggesting that the level of immune evasion may be lower in BCC than in BD. Overall, cutaneous squamous cell tumors and BCC show a different immune environment.

The current study showed that the degree of infiltrating both T cells differed between the advancing and central area in SCC and BCC and the ratio was low in the tumor center without statistical significance. Our previous study about the distribution of both T cells in colorectal cancer also showed similar results [11]. It thus appears that tumor compartments show a different immune environment. Further study about mechanical interactions among various cells in the tumor microenvironment of skin tumors may explain these findings, however, this is beyond the scope of our study at this time. In the current study, CD8 positive T cells more frequently infiltrated in expanding SCC compared to infiltrative SCC in the advancing area. This finding can be explained by the previous study suggesting that infiltrating lymphocytes around tumor cells in the invasive front of colorectal cancer were involved in the loss of tumor budding by causing the apoptosis of budding tumor cells [28].

In summary, BD and SCC showed significantly increased number of both CD8 positive T cells and Foxp3 positive T cells in the advancing area compared to AK and BCC, and BD revealed significantly lower CD8 positive T cells / Foxp3 positive T cells ratio in that area than AK and BCC. Any significant difference was not found in both T cells and the ratio between BD and SCC. The degree of both T cells infiltration differed between the advancing and central area in SCC and BCC. Taken together, an immune microenvironment differs between skin squamous cell tumors and BCC and among tumor compartments.

References

1. Beissert, S. and Loser, K. 2008. Molecular and cellular mechanisms of photocarcinogenesis. *Photochem. Photobiol.* **84**, 29-34.
2. Boon, T., Cerottini, J. C., Van den Eynde, B., van der Bruggen, P. and Van Pel, A. 1994. Tumor antigens recognized by T lymphocytes. *Annu. Rev. Immunol.* **12**, 337-365.
3. Cabrera, T., Garrido, V., Concha, A., Martin , J., Esquivias, J., Oliva, M. R., Ruiz-Cabello, F., Serrano, S. and Garrido, F. 1992. HLA molecules in basal cell carcinoma of the skin. *Immunobiology* **185**, 440-452.
4. Carroll, R. P., Segundo, D. S., Hollowood, K., Marafioti, T., Clark, T. G., Harden, P. N. and Wood, K. J. 2010. Immune phenotype predicts risk for posttransplantation squamous cell carcinoma. *J. Am. Soc. Nephrol.* **21**, 713-722.
5. Clark, R. A., Huang, S. J., Murphy, G. F., Mollet, I. G., Hijnen, D., Muthukuru, M., Schanbacher, C. F., Edwards, V., Miller, D. M., Kim, J. E., Lambert, J. and Kupper, T. S. 2008. Human squamous cell carcinomas evade the immune response by down-regulation of vascular E-selectin and recruitment of regulatory T cells. *J. Exp. Med.* **205**, 2221-2234.
6. Deaglio, S., Dwyer, K. M., Gao, W., Friedman, D., Usheva, A., Erat, A., Chen, J. F., Enjyoji, K., Linden, J., Oukka, M., Kuchroo, V. K., Strom, T. B. and Robson, S. C. 2007. Adenosine generation catalyzed by CD39 and CD73 expressed on regulatory T cells mediates immune suppression. *J. Exp. Med.* **204**, 1257-1265.
7. Dunn, G. P., Old, L. J. and Schreiber, R. D. 2004. The three Es of cancer immunoediting. *Annu. Rev. Immunol.* **22**, 329-360.
8. Euvrard, S., Kanitakis, J. and Claudy, A. 2003. Skin cancers after organ transplantation. *N. Engl. J. Med.* **348**, 1681-1691.
9. Freeman, A., Bridge, J. A., Maruthayanar, P., Overgaard, N. H., Jung, J. W., Simpson, F., Prow, T. W., Soyer, H. P., Frazer, I. H., Freeman, M. and Wells, J. W. 2014. Comparative immune phenotypic analysis of cutaneous Squamous Cell Carcinoma and Intraepidermal Carcinoma in immune-competent individuals: proportional representation of CD8+ T-cells but not FoxP3+ Regulatory T-cells is associated with disease stage. *PLoS One* **9(10),** e110928.
10. Jang, T. J. 2008. Prevalence of Foxp3+ T regulatory cells is increased during progression of cutaneous squamous tumors. *Yonsei Med. J.* **49,** 942-948.
11. Jang, T. J. 2013. Progressive increase of regulatory T cells and decrease of CD8+ T cells and CD8+ T cells/regulatory T cells ratio during colorectal cancer development. *Korean J. Pathol.* **47**, 443-451.
12. Kaporis, H. G., Guttman-Yassky, E., Lowes, M. A., Haider, A. S., Fuentes-Duculan, J., Darabi, K., Whynot-Ertelt, J., Khatcherian, A., Cardinale, I., Novitskaya, I., Krueger, J. G. and Carucci, J. A. 2007. Human basal cell carcinoma is associated with Foxp3+ T cells in a Th2 dominant microenvironment. *J. Invest. Dermatol.* **127**, 2391-2398.
13. Keene, J. A. and Forman, J. 1982. Helper activity is required for the *in vivo* generation of cytotoxic T lymphocytes. *J. Exp. Med.* **155**, 768-782.
14. Kim, J., Modlin, R. L., Moy, R. L., Dubinett, S. M., McHugh, T., Nickoloff, B. J. and Uyemura, K. 1995. IL-10 production in cutaneous basal and squamous cell carcinomas. A mechanism for evading the local T cell immune response. *J. Immunol.* **155**, 2240-2247.
15. Kosmidis, M., Dziunycz, P., Suarez-Farinas, M., Muhleisen, B., Scharer, L., Lauchli, S., Hafner, J., French, L. E., Schmidt-Weber, C., Carucci, J. A. and Hofbauer, G. F. 2010. Immunosuppression affects $CD4^+$ mRNA expression and induces Th2 dominance in the microenvironment of cutaneous squamous cell carcinoma in organ transplant recipients. *J. Immunother.* **33**, 538-546.
16. Morishima, N., Owaki, T., Asakawa, M., Kamiya, S., Mizuguchi, J. and Yoshimoto, T. 2005. Augmentation of effector CD8+ T cell generation with enhanced granzyme B expression by IL-27. *J. Immunol.* **175**, 1686-1693.
17. Rangwala, S. and Tsai, K. Y. 2011. Roles of the immune system in skin cancer. *Br. J. Dermatol.* **165**, 953-965.
18. Rutella, S. and Lemoli, R. M. 2004. Regulatory T cells and tolerogenic dendritic cells: from basic *biology* to clinical applications. *Immunol. Lett.* **94**, 11-26.
19. Suzuki, H., Chikazawa, N., Tasaka, T., Wada, J., Yamasaki, A., Kitaura, Y., Sozaki, M., Tanaka, M., Onishi, H., Morisaki, T. and Katano, M. 2010. Intratumoral CD8 (+) T/FOXP3 (+) cell ratio is a predictive marker for survival in patients with colorectal cancer. *Cancer Immunol. Immunother.* **59**, 653-661.
20. Tosolini, M., Kirilovsky, A., Mlecnik, B., Fredriksen, T., Mauger, S., Bindea, G., Berger, A., Bruneval, P., Fridman, W. H., Pagès, F. and Galon, J. 2011. Clinical impact of different classes of infiltrating T cytotoxic and helper cells (Th1, Th2, Treg, Th17) in patients with colorectal cancer. *Cancer Res.* **71**, 1263-1271.
21. Trzonkowski, P., Szmit, E., Mysliwska, J., Dobyszuk, A. and Mysliwski, A. 2004. CD4+ CD25+ T regulatory cells inhibit cytotoxic activity of T CD8+ and NK lymphocytes in the direct cell-to-cell interaction. *Clin. Immunol.* **112**, 258-267.
22. Vignali, D. A., Collison, L. W. and Workman, C. J. 2008. How regulatory T cells work. *Nat. Rev. Immunol.* **8**, 523-532.
23. Walter, A., Barysch, M. J., Behnke, S., Dziunycz, P., Schmid, B., Ritter, E., Gnjatic, S., Kristiansen, G., Moch, H., Knuth, A., Dummer, R. and van den Broek, M. 2010. Cancer-testis antigens and immunosurveillance in human cutaneous squamous cell and basal cell carcinomas. *Clin. Cancer Res.* **16**, 3562-3570.
24. Wing, K., Onishi, Y., Prieto-Martin, P., Yamaguchi, T., Miyara, M., Fehervari, Z., Nomura, T. and Sakaguchi, S. 2008. CTLA-4 control over Foxp3+ regulatory T cell function. *Science* **322**, 271-275.
25. Yanjing, X. U. and Shulan, G. U. O. 2010. Expression and significance of FOXP3 in normal skin and epidermis neoplasm. *J. Shandong Univ.* **48,** 149-151.
26. Yoon, H. H., Orrock, J. M., Foster, N. R., Sargent, D. J., Smyrk, T. C. and Sinicrope, F. A. 2012. Prognostic impact of FoxP3+ regulatory T cells in relation to CD8+T lymphocyte density in human colon carcinomas. *PLoS One* **7**,

e42274.
27. Zhang, S., Fujita, H., Mitsui, H., Yanofsky, V. R., Fuentes-Duculan, J., Pettersen, J. S., Suárez-Fariñas, M., Gonzalez, J., Wang, C. Q., Krueger, J. G., Felsen, D. and Carucci, J. A. 2013. Increased Tc22 and Treg/CD8 ratio contribute to aggressive growth of transplant associated squamous cell carcinoma. *PLoS One* **8**, e62154.
28. Zlobec, I., Lugli, A., Baker, K., Roth, S., Minoo, P., Hayashi, S., Terracciano, L. and Jass, J. R. 2007. Role of APAF-1, E-cadherin and peritumoral lymphocytic infiltration in tumour budding in colorectal cancer. *J. Pathol.* **212**, 260-268.

초록 : 피부에 발생하는 편평세포종양 및 기저세포암종 조직에서 CD8 양성 T 림프구와 Foxp3 양성 T 림프구의 분포에 관한 연구

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암조직에 대한 면역반응은 종양의 성장을 억제하거나 유도한다. Foxp3 양성 T 림프구는 종양에 대한 면역억제 반응을 유도하여 종양의 성장을 유도하는 반면 CD8 양성 T 림프구는 종양의 성장을 억제한다. 본 연구에서는 피부에서 발생한 편평세포암종, 편평세포 암종의 전암병변인 광선각화증과 보웬병 그리고 기저세포암종 조직에 면역조직화학염색을 시행하여 CD8 양성 T 림프구 및 Foxp3 양성 T 림프구의 분포 그리고 두 종류의 림프구의 비(CD8/Foxp3)를 조사하여 다음과 같은 결과를 얻었다. CD8 양성 T 림프구와 Foxp3 양성 T 림프구는 보웬병과 평평세포암종의 침습부위에서 광선각화증과 기저세포암종의 침습부위에 비하여 더 많이 침윤하였으며 CD8/Foxp3는 보웬병에서 광선각화증과 기저세포암종의 침습부위에 비하여 낮았다. CD8 양성 T 림프구와 Foxp3 양성 T 림프구의 침윤 정도 및 CD8/Foxp3는 보웬병과 편평세포암종의 침습부위에서 유의한 차이가 없었다. 기저세포암종과 편평세포암종에서 CD8 양성 T 림프구와 Foxp3 양성 T 림프구는 침습부위에서 종양의 중심부위에 비하여 더 많이 침윤하였다. 이러한 결과로 보아 편평세포종양과 기저세포암종은 서로 다른 면역반응을 보이며 종양내에서도 부위에 따라 상이한 면역반응을 보인다고 생각된다.