SKIN CANCER (OTHER THAN MELANOMA)

ALA-PDT ENHANCES THE ANTITUMOR EFFECT DURING SQUAMOUS CELL CARCINOMA BY INDUCING CXCL13 CHEMOKINE PRODUCTION IN CAF

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Background: The infiltration of a large number of inflammatory cells into tumor tissue is the key process of photodynamic therapy (PDT) treating cutaneous squamous cell carcinoma of the skin (cSCC). And the PDT treatment efficacy increases with the severity of the infiltration. Moreover, studies have shown that chemokines play an essential role in the recruitment of inflammatory cells. Therefore, a scientific question is provided that whether PDT induces upregulation of certain chemokines, which in turn leads to the infiltration of a large number of inflammatory cells and contributes to the efficacy of PDT.

Methods: Differential gene expression analysis of RNA isolated from cSCC before and after ALA-PDT were performed using Affymetrix GeneChip® Mouse Gene 1.0 ST Array. The expression and transcriptional activity of CXCL13 were determined by immuno-histochemical staining, and reverse-transcription quantitative real-time PCR (RT-PCR). Also, RT-PCR was used to compared the changes of CXCL13 in the supernatant of three cell lines (fibroblasts, squamous carcinoma cells and macrophages) stimulated by mouse cSCC homogenate. In addition, the role of CXCL13 on effect of ALA-PDT was also assessed in vitro.

Results: Based on the analysis of gene chip before and after ALA-PDT, chemokines and receptors transcript screening identifies that CXCL13 expression displayed the most significant difference. Moreover, RT-PCR indicated that CXCL13 expression in human and mouse local tumor tissues were significantly up-regulated after treatment with ALA-PDT, In vitro, the expression of CXCL13 was increased in fibroblasts and decreased in macrophages. In vivo, the mouse tumor volume was the largest in the CXCL13 antibody group, and smallest in the CXCL13 protein group compared to the blank control.

Conclusion: ALA-PDT treatment of cSCC induced tumor-associated fibroblasts to up-regulate the expression of CXCL13 and enhance its anti-tumor effect.