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## 口腔鳞状细胞癌中SOCS3 及其DNA 甲基化的表达及生物学意义\*

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### Expression and Biological Significance of SOCS3 and SOCS3 DNA Methylation in Oral Squamous Cell Carcinoma (OSCC)

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摘要

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**摘要** 目的: 研究口腔鳞状细胞癌(OSCC)组织中细胞因子信号转导抑制因子3(SOCS3)的DNA甲基化及蛋白表达水平,探讨其在OSCC发生、发展、浸润和转移中的作用。方法:采用甲基化特异性焦磷酸测序技术(Pyrosequencing)和Western blot法分别检测100例口腔鳞状细胞癌组织中SOCS3的DNA甲基化及蛋白表达水平,并与20例正常口腔黏膜组织进行对照研究,分析其与OSCC临床病理参数的关系。结果:1)OSCC组织SOCS3 DNA甲基化的阳性率为85%,显著高于正常口腔黏膜组织的20%( $P<0.05$ );2)OSCC组织中SOCS3蛋白表达( $1.76\pm 0.12$ )明显低于正常口腔黏膜组织( $1.93\pm 0.25$ ),差异有统计学意义( $P<0.01$ )。口腔鳞状细胞癌组织中甲基化组SOCS3蛋白表达( $1.72\pm 0.21$ )显著低于非甲基化组( $1.92\pm 0.23$ ),差异有统计学意义( $P<0.01$ );3)在TNM分期中III期组表达均低于I~II期组( $P<0.05$ ),伴有淋巴结转移组表达也低于无淋巴结转移组( $P<0.05$ );4)口腔鳞状细胞癌组织中SOCS3蛋白表达水平与肿瘤分化级别呈正相关( $r=0.416$ ,  $P<0.05$ ),与TNM分期、淋巴结转移呈负相关( $r=-0.357$ ,  $P<0.05$ )。结论:口腔鳞状细胞癌组织中SOCS3 DNA甲基化阳性率高,导致SOCS3基因表达下调,与口腔鳞状细胞癌的分化、浸润和转移密切相关。

**关键词:** 口腔鳞状细胞癌 细胞因子信号转导负调控因子3 DNA甲基化

**Abstract:** Abstract Objective: This work aims to study the DNA methylation and protein levels of the suppressor of cytokine signaling 3 (SOCS3) in oral squamous cell carcinoma (OSCC) tissue, and to explore its function in the development, invasion, and metastasis of OSCC. Methods: A total of 20 cases with normal oral mucosa were used as the case-control group. The expression of SOCS3 DNA methylation and SOCS3 protein in 100 cases with OSCC is determined and analyzed using methylation pyrosequencing and Western blot to determine its correlation with clinico-pathological parameters. Results: The positive rate of SOCS3 DNA methylation is significantly higher in OSCC (85%) than that in the normal oral mucosa tissues (20%,  $P < 0.05$ ); ii. The SOCS3 protein expression was also overtly lower in OSCC ( $1.76 \pm 0.12$ ) than in the normal oral mucosa ( $1.93 \pm 0.25$ ,  $P < 0.01$ ). In OSCC, the SOCS3 expression was notably lower in the group with methylation ( $1.72 \pm 0.21$ ) than in the group without ( $1.92 \pm 0.23$ ,  $P < 0.01$ ); iii. Tumor, Node and Metastasis classification revealed that the protein expression in the group with stage III OSCC is lower than in the groups with both stage I and II lesions ( $P < 0.05$ ), and lower in the group with lymph node metastasis compared with the group without metastasis ( $P < 0.05$ ); iv. The expression of SOCS3 protein in OSCC is positively correlated with the differentiation degree ( $0.203 < r < 1$ ,  $P < 0.05$ ), but had a negative correlation with TNM staging and nodal metastasis ( $-1 < r < -0.203$ ,  $P < 0.05$ ). Conclusion: The high positive rate of SOCS3 DNA methylation in OSCC leads to the down-regulation of the SOCS3 gene, which is closely related to the differentiation, invasion, and metastasis in OSCC.

**Key words:** Oral squamous cell carcinoma Negative suppressor of cytokine signaling 3 DNA methylation

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