[1]赵宁波,杨凯,陈丹,等.生物钟PER1基因在口腔鳞癌中的昼夜节律变化及与体内肿瘤生长的关系[J].第三军医大学学报,2013,35(14):1489-1492.

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生物钟PER1基因在口腔鳞癌中的昼夜节律变化及与
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Title: Circadian rhythm variations of clock gene PER1 expression in oral squamous cell carcinoma and their relations with tumor growth *in vivo*

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摘要: 目的 探讨生物钟PER1基因在口腔鳞癌中的昼夜节律变化情况和与肿瘤体内生长的关系。 方法 60只裸鼠置于12 h光照和12 h黑暗交替环境中饲养3周后，将人颊鳞癌BcaCD885细胞接种于裸鼠颊部，建立口腔颊鳞癌模型。3周成瘤后，在24 h内按灯亮后4、10、16、22 h （4 HALO、10 HALO、16 HALO、22 HALO）的4个时间点分别处死15只裸鼠，取出肿瘤，称量，常规切片在HE染色下计算各时间点肿瘤的有丝分裂指数(MI)；分别用S-P免疫组化、Western blot和Real-time RT-PCR检测各时间点癌细胞中PER1蛋白和mRNA的表达；分别用方差分析和余弦分析检验各指标在4个时间点的差异性和是否具有昼夜节律性。 结果 颊鳞癌细胞PER1蛋白、PER1 mRNA、肿瘤MI和肿瘤质量在昼夜不同时间点具有显著性差异（$P<0.01$），其变化波动具有昼夜节律性特征（$P<0.05$）；肿瘤MI和肿瘤质量与PER1的表达水平呈反比关系，PER1 mRNA表达的峰值与肿瘤MI和质量的谷值均位于活动相的中期，而PER1 mRNA表达的谷值与肿瘤MI和质量的峰值均位于休息相中期。 结论 口腔鳞癌中PER1的表达、肿瘤MI和质量在昼夜不同时间点的波动具有24 h昼夜节律性规律，PER1在口腔鳞癌中为抑癌基因。

Abstract: Objective To determine the circadian rhythm variations of the expression of clock gene PER1 in oral squamous cell carcinoma (OSCC) and their relations with tumor growth *in vivo*. Methods Sixty nude mice were raised under 12 h light/12 h dark cycles for 3 weeks. Human OSCC cell line BcaCD885 was inoculated in the cheek of nude mice to establish a nude mice model of OSCC. In 3 weeks after the implantation, 15 mice were sacrificed at 4 time points, including 4 h after light onset (HALO), 10 HALO, 16 HALO and 22 HALO, respectively, during a period of 24 h. Tumor tissues were excised and weighed. HE stained sections were prepared and mitotic index (MI) was calculated. The protein and mRNA expression of PER1 in the tumor cells at the 4 time points were determined by immunohistochemical assay (SP method), Western blot analysis and real-time RT-PCR. The differences of its expression in the 4 time points were assessed by ANOVA, and a cosine analysis method was applied to determine whether the expression of PER1 at protein and mRNA levels obeyed a circadian rhythm. Results There were significant differences in PER1 expression at protein and mRNA levels in the OSCC cells, tumor MI, and tumor weight among the 4 time points （P<0.01）, and these changes were in a circadian rhythm（P<0.05）. Tumor MI and tumor weight were negatively correlated with the expression level of PER1. The peak of PER1 mRNA expression and the valley values of tumor MI and weight appeared at the middle of active phase. However, the valley of PER1 mRNA expression and the peaks of tumor MI and weight occurred at the middle of rest phase. Conclusion PER1 expression, tumor MI, and xenografted tumor weight of OSCC cells show circadian rhythm during a period of 24 h. PER1 is an anti-tumor gene in OSCC.

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