投稿

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是否申請論文獎:■ 是□ 否

Altered miR-21-5p and miR-23a-3p expressions in obstructive sleep apnea modulates cell apoptosis by targeting pro-inflammatory genes

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Background: The purpose of this study is to explore the anti-inflammatory role of microRNAs (miR)-21/23/146a/150/155 targeting the toll-like receptor pathway in response to chronic intermittent hypoxia with re-oxygenation (IHR) injury in patients with obstructive sleep apnea (OSA).

Methods: Gene expression levels of the five miRs, TLR2/4/6, and their down-stream mediators were assessed by quantitative RT-PCR method in peripheral blood mononuclear cells from 40 severe OSA patients, and 20 matched subjects with primary snoring (PS). Human monocytic THP-1 cell lines were induced to undergo apoptosis with IHR exposures, and transfected with miR-21-5p mimic.

Results: Gene expression levels of miR-21-5p (adjusted p=0.024) and miR-23a-3p (adjusted p=0.028) were decreased in treatment-naïve OSA patients as compared with that in PS subjects, while TNF-α gene expression (adjusted p=0.04) was increased. Gene expression levels of both miR-21-5p, and miR-23-3p were negatively correlated with apnea hypopnea index (r=-0.478, p<0.001; r=-0.446, p=0.001) and oxygen desaturation index (r=-0.45, p=0.001; r=-0.421, p=0.001), while TNF-α gene expression positively correlated with apnea hypopnea index (r=0.388, p=0.003). Both miR-21 5p and miR-23-3p gene expressions were negatively correlated with their predicted target gene expressions, including TLR4, TLR6, TNF-α, NFAT5, ELF2, SP1, PDCD4, and HIF-2α. In vitro IHR treatment resulted in increased apoptosis and decreased cell viability along with decreased miR-21-5p, miR-23-3p, and miR-155-5p gene expressions, but increased miR-146a-5p (all p values <0.05). The percentage of cytotoxicity and gene expressions of TNF-α, ELF2, NFAT5, HIF-2α, IL6, IL6R, EDNRB, and TLR4 were increased with IHR as compared with that in normoxic condition, while decreased with miR-21-5p mimic transfection under IHR condition as compared with that in IHR alone condition.

Conclusions: MiR-21-5p and miR-23-3p were down-regulated both in severe OSA patients and with in vitro IHR stimuli, while several predicted pro-inflammatory target genes were up-regulated. The findings provide biological insight into mechanisms by which IHR- suppressed miRs protect cell apoptosis via inhibit inflammation, and indicate that over-expression of the miR-21-5p may be a new therapy for OSA.

中文題目：阻塞性睡眠呼吸中止症異常的第 21 和 23a 型微小核醣核酸表現會經由抑制促進發炎基因來降低細胞凋亡

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