Long non-coding RNA FKSG29 over-expression in patients with obstructive sleep apnea modulates intermittent hypoxia-induced oxidative stress and endothelial dysfunction via sponging miR-23a-3p-IL6R signaling

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Objective: We hypothesized that long non-coding (lnc) RNAs may contribute to the development of adverse consequences of obstructive sleep apnea (OSA).

Methods: Affymetrix Human Transcriptome Array (HTA 2.0) was used to identify differentially expressed non-coding RNAs in peripheral blood mononuclear cell samples from 12 OSA patients and 6 healthy non-snorers. Candidate lncRNAs were validated in 12 subjects with primary snoring (PS) and 48 OSA patients.

Results: A total of 101 differentially expressed non-coding RNAs associated with OSA, including 39 lncRNAs (31 up-regulated and 8 down-regulated), were identified. In the validation cohort, TC13001253.hg.1 (FKSG29) lncRNA, NOX2, NOX5, and VEGF-A gene expressions were increased in OSA patients versus PS subjects, while SOD2 and VEGF-B gene expressions were decreased. MiR-23a-3p gene expression was decreased in patients with hypertension versus those without hypertension, and GPX1 gene expression was decreased in patients with depression versus those without depression. In vitro intermittent hypoxia with re-oxygenation (IHR) experiment in THP-1 and HUVEC cell lines showed that FKSG29 knock-down by small interfering RNA transfection reversed IHR-induced reactive oxygen species over-production, early apoptosis, and aberrant gene expressions of the pro-oxidants and vasoactive genes through miR-23a-3p-IL6R signaling. Dual-luciferase reporter assays confirmed that FKSG29 was a sponge of miR-23a-3p, which regulated IL6R directly. Either FKSG29 knock-down or miR-23a-3p over-expression decreased up-take of oxidized LDL in HUVEC, and reversed IHR-induced ICAM1/VCAM1 up-regulations.

Conclusions: The findings provide biological insight into mechanisms by which IHR-activated lncRNA FKSG29 in OSA may augment oxidative stress and endothelial dysfunction via miR-23a-IL6R-ICAM1/VCAM1 signaling, and indicate that combined lncRNA FKSG29 knock-down and miR-23a-3p over-expression may be a new therapy for OSA-related hypertension.

中文題目：阻塞性睡眠呼吸中止症的長鏈非記錄型核醣核酸 FKSG29 過度表現

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