

miR-15b-5p protects against obstructive sleep apnea-related systemic inflammation and cardiovascular disease through modulating macrophage polarization via NF- κ B

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Objective: The role of M1/M2 macrophage polarization in obstructive sleep apnea (OSA)-related cardiovascular disease (CVD) is unknown. This study aimed to identify the key microRNA (miRNA) involved in OSA-induced M1 polarization and systemic inflammation, and explore the underlying mechanisms.

Method: Blood monocyte M1/M2 ratios and M1/M2-related gene expressions of peripheral blood mononuclear cells were analyzed in 47 OSA patients with CVD, 39 OSA patients without CVD, and 10 primary snoring (PS) subjects without CVD. THP-1 macrophages were exposed to intermittent hypoxia-reoxygenation (IHR) for 3 days to investigate the regulatory role of miR-15b-5p.

Results: miR-15b-5p and *PPAR- γ* (M2 marker) gene expressions were decreased in OSA patients with CVD versus those without CVD or PS group, whereas the M1/M2 ratio and M1 markers, including *TNF- α* , *STAT1*, and *NF- κ B* genes, were increased. Receiver operating characteristic curves showed that the risks of OSA and CVD were well-captured by blood monocyte M1/M2 ratio at cut-off values of 8.5 (AUC=0.884, p value<0.001) and 15.97 (AUC=0.653, P=0.01), respectively. Continuous positive airway pressure therapy in OSA patients reversed M1polarization markers and miR-15b-5p under-expression. Luciferase assays confirmed that miR-15b-5p directly targeted the *NF- κ B* gene. In THP-1 macrophage, miR-15b-5p overexpression reversed IHR-induced M1 polarization, oxidative stress, apoptosis, NF- κ B activation, aberrant expressions of M1/M2 markers, and atherogenic foam cell transformation.

Conclusions: Chronic IHR in OSA patients with CVD led to M1 polarization and accelerated foam cell transformation via the miR-15b-5p/NF- κ B axis. Modulating this pathway may be a therapeutic strategy for mitigating inflammation and atherosclerosis in OSA-related CVD, which can be early identified by M1/M2 ratio.

中文題目：微核糖核酸 miR-15b-5p 透過 NF- κ B 途徑調節巨噬細胞極化，進而防止阻塞性睡眠呼吸中止症相關的全身性發炎及心血管疾病

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