Global histone H3K23/H3K36 hypoacetylation and HDAC1 up-regulation are associated with disease severity and adverse consequences in obstructive sleep apnea patients

Kaohsiung Chang Gung Memorial Hospital

Yung-Che Chen[1,2], Meng-Chih Lin[1,2], Mao-Chang Su[1,2], Chien-Hung Chin[1,2], Kuo-Tung Huang[1,2], Chia-Wei Liou[3], Chin-Chou Wang[1,2], Wen-Feng Fang[1,2], *Shu-Jun Kong[1,2], Lian-Rong Liu[1,2], Wei-Zhe Liu[1,2], Yi-Jing Li[1,2]*

Objective: The aim of this study is to determine the roles of global histone acetylation (Ac)/methylation (me), their modifying enzymes, and gene-specific histone enrichment in obstructive sleep apnea (OSA).

Methods: Global histone H3K9Ac, H3K14Ac, H3K23Ac, H3K36Ac, H3K56Ac, H4K16Ac, H3K4me3, H3K9me3, H3K27me3, H3K36me3, and H3K79me3 expressions, and their modifying enzyme expressions, including KDM1A, KDM4B, KDM4C, KDM5A-D, KDM6B, and HDAC1-7, were assessed in peripheral blood mononuclear cells from 56 patients with OSA and 16 matched subjects with primary snoring (PS). HIF-1α/2α specific histone modification was measured by ChIP.

Results: Both global histone H3K23Ac and H3K36 Ac expressions were decreased in OSA patients as compared with that in PS subjects. The former was further decreased in OSA patients with prevalent hypertension as compared with that in those without prevalent hypertension. H3K79me3 expression was increased in OSA patients with high serum hsCRP levels as compared with either that in those with low serum hsCRP levels or that in PS subjects. Both HDAC1 gene and protein expressions were higher in OSA patients than that in PS subjects, while HDAC1 gene expression was reduced after > 6-month CPAP treatment in 8 selected OSA patients. HDAC1 gene expression was increased in OSA patients with severe EDS as compared with that in those without severe EDS. HIF-1α gene promoter specific H3K36Ac enrichment was deceased in OSA patients as compared with that in PS subjects.

Conclusions: H3K23/H3K36 hypoacetylation play a role in the development of OSA or its clinical phenotypes, probably through up-regulation of HDAC1.

中文題目：阻塞性睡眠呼吸中止症病患之組蛋白離胺酸乙醯化低下和第一型組蛋白去乙醯酶激活與其疾病嚴重度和臨床表現型相關

作　　者：陳永哲[1] 林孟志[1] 蘇茂昌[1] 秦建弘[1] 黃國棟[1] 孔淑君[2] 劉蓮榮[2] 劉瑋哲[2] 李怡靜[2]

服務單位：高雄長庚醫院 [1]胸腔內科 [2]睡眠醫學中心