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Author(s)	Han, Q; Yeung, SC; Ip, MSM; Mak, JCW
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Modification of serum adiponectin and CINC-1 levels by intermittent hypoxia and/or hyperlipidemia in vivo

Q Han[1], SC Yeung[1], MSM Ip[1,2], JCW Mak[1,2,3]
[1]Department of Medicine, The University of Hong Kong, Hong Kong
[2]Reserach Centre of Heart, Brain, Hormone and Healthy Aging, The University of Hong Kong, Hong Kong
[3]Department of Pharmacology, The University of Hong Kong, Hong Kong

Background: Intermittent hypoxia (IH) is a hallmark feature in obstructive sleep apnoea (OSA), which is closely associated with atherosclerosis. Hyperlipidemia is another risk factor of atherogenesis. Adiponectin is an adipokine that exerts anti-inflammatory and anti-atherogenic properties. This study aimed to explore the effects of IH and hyperlipidemia on circulating levels of adiponectin and cytokine-induced neutrophil chemoattractant (CINC)–1 in the rat model in vivo.

Methods: Male S-D rats were randomly divided into four groups: regular chow diet or high-fat high-cholesterol diet (HFHC)–fed (Research Diets, US) plus intermittent normoxia (IN) or IH. The IH exposure was performed using OxyCycler A84 System (BioSpherix, US) daily, which was composed of cycles of 4 min 10% O_2 followed by 2 min 21% O_2 for 6 hours. After 28 days, rats were sacrificed and serum levels of cholesterol, adiponectin, and CINC-1 were measured by ELISA.

Results: The HFHC-fed groups showed an increase of serum total cholesterol levels. The IH or HFHC/IN group caused a decrease in serum adiponectin levels (6.09±0.37 [IH group] or 4.61±0.54 [HFHC/IN group] vs 8.24 ±0.82 μg/mL [IN group], P<0.05 and P<0.01, respectively). The HFHC/IN group caused an increase in serum CINC-1 levels (259.64±40.87 [HFHC/IN group] vs 105.9±20.95 pg/mL [IN group], P<0.05). The IH group also led to upregulation (179.1±12.62 pg/mL, P<0.05) compared to IN group, and to further elevation of serum CINC-1 levels in HFHC/IH group (330.3±21.99 pg/mL, P<0.01).

Conclusion: These data demonstrated that IH led to suppression of serum adiponectin and elevation of serum CINC-1 in our rat model. IH in combination with diet-induced hyperlipidemia synergised the elevation of serum CINC-1, in support of enhanced inflammatory response in subjects with OSA.

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In-vitro growth inhibitory effects of arsenic trioxide in non–small-cell lung cancer with different epidermal growth factor receptor mutations

F He, YL Kwong, JC Ho
Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Previous studies have demonstrated differential treatment responses of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) in non–small-cell lung cancer (NSCLC) with different EGFR mutation status. In particular, deletions in exon 19 and point mutation in exon 21 (L858R) confer drug sensitivity, while T790M point mutation in exon 20 is commonly associated with resistance. Arsenic trioxide (ATO) has been an established treatment in acute promyelocytic leukaemia in which preliminary data on head and neck cancer suggested its potential regulation of EGFR signallings. Therefore this study aimed at investigating the growth inhibitory effect of ATO treatment in NSCLC with different EGFR mutation status.

Methods: Growth inhibitory effects of ATO and erlotinib (an EGFR TKI) were studied in seven NSCLC cell lines with different EGFR mutation status (wild-type [WT], exon 19 deletion and double mutant [L858R and T790M]) by 3-(4, 5-dimethyl-2-thiazolyl)-2, 5-diphenyl-2H tetrazolium bromide (MTT) assay and Annexin-V/Propidium Iodide assay. Experiments were conducted with varying drug concentrations and time course.

Results: Both ATO and erlotinib work in a time- and dose-dependent manner. When treated with drug concentration of 3 micro molar for 48 h, ATO is more efficient than erlotinib on growth inhibition in the following cell lines NCI-H23 (WT), HCC2935 (del 19), NCI-H1650 (del 19), and NCI-H1975 (L858R/T790M) [mean inhibitory rate ranging from 53.1 to 67.1% for ATO vs –0.5 to 26.53% for erlotinib; P<0.05 for significant difference]. On the other hand, erlotinib demonstrates stronger growth inhibition than ATO in two cell lines with EGFR del 19 (mean inhibitory rate with erlotinib vs ATO in HCC827: 86.7±2.6% vs 45.71±3.0%; in HCC4006: 80.8±2.3% vs 33.31±5.3%; P<0.05). While for NCI-H358 (WT) there is no significant difference between two drugs.

Conclusions: ATO exerts stronger growth inhibition than erlotinib on most of the NSCLC cell lines tested, except two with EGFR exon 19 deletions. However the anti-cancer pathway of ATO seems not relying on EGFR mutation status with an implication on multiple downstream signallings.