

# Serum proteomic changes in adults with obstructive sleep apnoea

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**SUMMARY** To examine whether differentially expressed proteins are present in the serum of patients with obstructive sleep apnoea (OSA), iTRAQ techniques (isobaric tags for relative and absolute quantification) were employed in a prospective study. Individuals were assigned to either a non-OSA control group (apnoea–hypopnoea index, AHI < 5) or an OSA group (AHI ≥ 5). Blood samples were collected, aliquoted and frozen at –80 °C. Protein digestion and tagging with iTRAQ4plex<sup>®</sup> and mass spectrometry analysis was then performed (MALDI TOF/TOF). Ten male subjects were included in the control group (age = 45 ± 9.7 years) and 30 male patients in the OSA group (age = 45 ± 10.7 years), the latter being then subdivided into three severity groups. A total of 103 proteins were identified with differential levels between patients with OSA and controls. Of these, 11 proteins were underexpressed and 19 were overexpressed in patients with OSA. C4BPA and thrombospondin were underexpressed in all three OSA severity groups. Among the overexpressed proteins, 13 were overexpressed in the mild OSA group, seven in the moderate group and five in the severe group. Analysis of interactions between the identified proteins revealed that protein alterations in OSA are primarily associated with derangements in lipid and vascular metabolic pathways. This study provides initial evidence that differential protein expression occurs in adults with OSA, and that such proteins change according to disease severity, and appear to primarily involve lipid and vascular metabolic pathways.

**KEYWORDS** isobaric tags for relative and absolute quantification, mass spectrometry, OSA, protein expression, quantitative proteomics

## INTRODUCTION

Obstructive sleep apnoea (OSA) is a frequent respiratory disorder with an estimated prevalence of 3–6% in the general population, and reaching much higher frequencies in middle-aged and aging patients. The hallmark of OSA is the recurrent occurrence of either complete or partial closure of the upper

airway during sleep, which is manifest by snoring, witnessed apnoeas and non-restful sleep. The latter leads to excessive daytime sleepiness, which has been linked to increases in mortality from traffic, domestic and work-related accidents, while the nocturnal hypoxic episodes resulting from upper airway obstruction are associated with substantial cardiovascular and metabolic morbidity and mortality (Garvey *et al.*, 2009; Gottlieb *et al.*, 2010; Lavie and Lavie, 2009). Therefore, considering its high prevalence, morbidity and mortality, OSA is clearly an important public health problem and, yet, only a small percentage of patients have been diagnosed (Fietze *et al.*, 2011).

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