Proteomics in biomarkers discovery for Obstructive Sleep Apnea

Amélia Feliciano1,2, Vesna Bozanic2, Vukosava Milic Torres2, Rune Matthiesen2, Ana S Carvalho2, Andreia Almeida2, Bruno Alexandre2, Fátima Vaz2, Atul Malhotra3, Paula Pinto1, Cristina Bárbara1, Deborah Penque2.
deborah.penque@insa.min-saude.pt

1Serviço de Pneumologia, Centro Hospitalar Lisboa Norte (CHLN), Lisboa, Portugal; 2Laboratório de Proteómica, Departamento de Genética Humana, Instituto Nacional de Saúde Dr Ricardo Jorge (INSA.I.P.), Lisboa, 1640-016, Portugal; 3Brigham and Women’s Hospital, Harvard Medical School, Boston, MA 02115, USA.

Much has been learned on the pathophysiology and consequences of Obstructive Sleep Apnea (OSA) in the last decade’s, however the molecular mechanisms and specific pathways and proteins variants associated with such processes remain poorly defined. OSA and metabolic or cardiovascular disorders commonly coexist and therefore it is important to consider their relative roles in causing adverse clinical phenotypes and characterize their shared molecular pathways and whether there are unique ones related to OSA that mediate clinical phenotypes. Studies are also needed to estimate the reversible effects of continuous positive airway pressure (CPAP) treatment (differences pre- to post-CPAP treatment) and irreversible effects of OSA, (i.e., estimate the difference between patients with OSA after effective treatment when compared to controls).

Proteomics, the large-scale studies of protein profiles under given time/condition, has the potential to provide additional information to our understating of OSA pathogenesis that could be crucial to the identification of new diagnostic and prognostic biomarkers or therapeutic targets for OSA. In this project a prospective study that integrates clinical and proteomics associated with systems biology area has been carried out to explore the mechanisms responsible for OSA and its related metabolic/cardiovascular consequences, as well as the therapeutic benefits and side effects of CPAP treatment. Male patients (25-55 years old), with diagnosis of simple snoring, either obese or non-obese, with or without associated metabolic/cardiovascular disease have been selected for clinical evaluation and blood Biobanking. Higher throughput proteomics technologies such as 2-D Fluorescence Difference Gel Electrophoresis (2D DIGE), Liquid Chromatography associated with tandem Mass Spectrometry (LC/MS/MS) and Mass Spectrometric Assay (MSIA) combined with a Systems Biology approach have been applied to study red blood cells (cytoplasm and membrane) and plasma proteomes (morning or evening collected samples) of OSA patients (CPAP treated or non-treated) in comparison with control (simple snoring) patients. The data so far obtained will be presented and discussed. The objective is to address the mechanisms and pathways responsible for the consequences of OSA as well as the molecular effect of CPAP treatment to develop better approaches for the diagnosis and ongoing monitoring of OSA, potentially opening new avenues for OSA treatment and prevention.
Acknowledgements
To all patients that voluntarily collaborated in this study. Work partially supported by Harvard Medical School-Portugal Program (HMSP-ICJ/0022/2011), FCT/Poly-Annual Funding Program and FEDER/ Saúde XXI Program (Portugal). 2-DIGE images were capture at Instituto de Tecnologia Química e Biológica, Oeiras, Portugal. This work was approved by the Ethical Committee of INSA.I.P.-Lisboa and Centro Hospitalar Lisboa-Norte., Portugal.