Plasma Proteomics in Healthy Subjects with Differences in Tissue Glucocorticoid Sensitivity Identifies a Novel Proteomic Signature

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INTRODUCTION

Tissue sensitivity to glucocorticoids is characterized by significant inter-individual variation in terms of therapeutic response and susceptibility to several stress-related disorders (1, 2). Proteomics approaches, combined with appropriate bioinformatics analysis, offer a comprehensive description of molecular phenotypes with clear links to human disease pathophysiology (3-5).

AIM

To investigate the usefulness of plasma proteomics in identifying a proteomic signature that could distinguish glucocorticoid resistant from glucocorticoid sensitive subjects and provide clues of the underlying physiological differences.

METHODS

One hundred one (n=101) healthy volunteers were given a very low dose (0.25mg) of dexamethasone at midnight, and were polarized into the 10% most sensitive (S) and 10% most resistant (R) according to the 08.00h serum cortisol concentrations the following morning. One month later, DNA was isolated from peripheral blood mononuclear cells, and plasma samples were collected.

To identify any genetic defects in the NR3C1 gene, the protein-coding sequences and the intron-exon junctions of the NR3C1 gene were PCR-amplified and sequenced. The proteomic profile of plasma samples was determined using LC-MS/MS.

REFERENCES


CONCLUSIONS

A proteomic profile indicating erythrocyte gas exchange and platelet activation was observed in the S compared to the R group, suggesting a state of the organism that is more capable to respond to stressfull stimuli.

Our findings also indicate that a proteomics signature may differentiate the most glucocorticoid resistant from the most glucocorticoid sensitive subjects, and may be useful in clinical practice. It may also provide clues of the underlying molecular mechanisms of the chronic stress-related diseases, including myocardial infarction, stroke and Alzheimer’s disease.

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