

Sara Samino¹, Marta Díaz³, María Vinaixa², Miguel A. Rodríguez², Roger Mallo², Antoni Beltran², Anna Cabré², Lluís Massana², Lourdes Ibáñez³, Oscar Yanes^{1,2}

1. Spanish Biomedical Research Center in Diabetes and Associated Metabolic Disorders (CIBERDEM), Madrid, Spain. 2. Universitat Rovira i Virgili, Tarragona, Spain. 3. Hospital Sant Joan de Déu, Barcelona, Spain.

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinopathy affecting 6–10% of reproductive-aged women. PCOS is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovaries in its complete phenotype. PCOS carries an elevated prevalence of impaired glucose tolerance, T2D and metabolic syndrome. Symptoms of PCOS often manifest during adolescence making this an important time for the study of early biomarkers, recognition and intervention to prevent adverse metabolic outcomes

2. GOALS

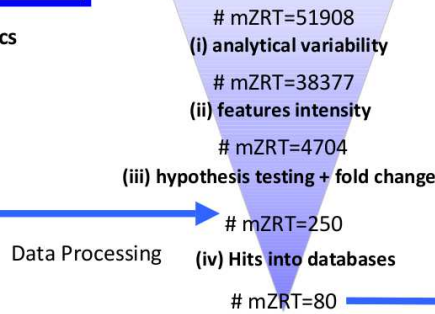
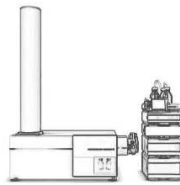
The aim of this study is to apply our metabolomic approach to discover new biomarkers of PCOS. Serum samples of young PCOS patients and healthy controls using LC-QTOF MS and NMR were analyzed.

3. MATERIALS AND METHODS

NMR lipoprotein profile
NMR metabolomic profile



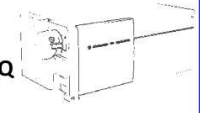
Untargeted metabolomics



Validation using LC-QQQ

11 metabolites identified

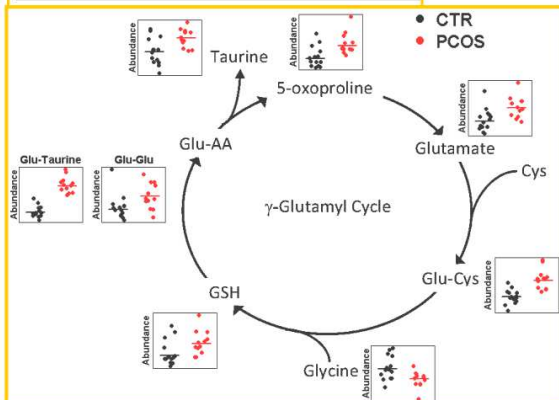
Fragmentation experiments (QTOF)



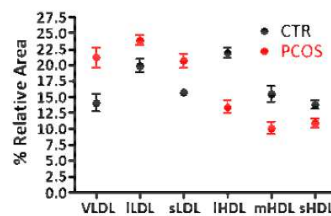
4. RESULTS

Untargeted metabolomics

	p-value	% variation
Methionine	5.04E-05	-344
Methionine Sulfoxide	1.77E-03	40
5-oxoproline	4.98E-03	39
Taurine	1.53E-02	28
Glu-Cys	1.56E-04	37
Glu-Glu	2.70E-02	35
Glutamate	4.04E-03	33
GSH	3.60E-02	34
GSH/GSSG	2.30E-02	29
Glu-Taurine*	3.03E-07	73
Glycine	3.10E-02	-18



A) Lipoprotein profile



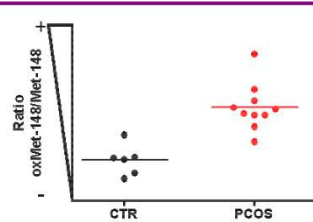
B)

	p-value	% variation
VLDL	1.29E-2	50
Large LDL	2.64E-2	20
Small LDL	2.45E-2	31
Large HDL	1.55E-5	-63
Medium HDL	5.80E-3	-52
Small HDL	2.33E-2	-20

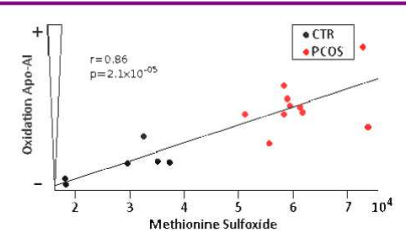
Methionine oxidation impairs reverse cholesterol transport by apoprotein AI

Met-148 residue in apo-AI changes the 3D structure of the protein impairing the LCAT activity in HDL lipoproteins

HYPOTHESIS: PCOS patients present greater oxidation of methionine residues in apo-AI relative to healthy women, and the increased levels of free methionine sulfoxide in PCOS may result from the turnover and degradation of these apo-AI protein



PCOS women shows increased levels of MetOx/Met-148 ratio in apo-AI



Levels of methionine sulfoxide in serum are positively correlated with oxidation levels of apo-AI

5. CONCLUSIONS

Untargeted metabolomic approach has revealed that γ -glutamyl cycle and oxidative stress is involved in PCOS disease.

Elevated levels of methionine sulfoxide in serum, oxidized methionine-148 in apo-AI, and the lipoprotein profile might constitute earlier biomarkers of metabolic syndrome.