# CARATERIZATION OF RHEUMATHOID ARTHRITIS (RA) PATIENS THROUGHT 1H-NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY ($^1$H NMR).

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## INTRODUCTION

RA is an autoimmune and chronic inflammatory disease associated with a high index of morbidity and mortality by cardiovascular disease (CVD). 1H-NMR is a technique capable of determining the lipoprotein and glycoprotein profiles, to characterize dyslipidemias and to estimate the cardiovascular and inflammatory risk.

Recent studies have established the importance of **glycosylated proteins** in important biological processes:
- cell adhesion,
- transport,
- Signal Transduction
- Control of cellular inflammation

There is a technical difficulty in quantifying the glycoproteins concentration in blood plasma for lack of a fast, sensitive and high-performance technology. However, the nuclear magnetic resonance spectroscopy can detect levels of circulating glycoproteins in a quick and accurate way.

The **objective** of this study is to characterize the plasmatic lipoprotein and glycoprotein profiles of RA patients using $^1$H-NMR in order to identify patterns of the disease's severity.

## MATHERIAL AND METHODS

Blood serum of 209 RA patients

$^1$H NMR

Mathematical treatment of the signal
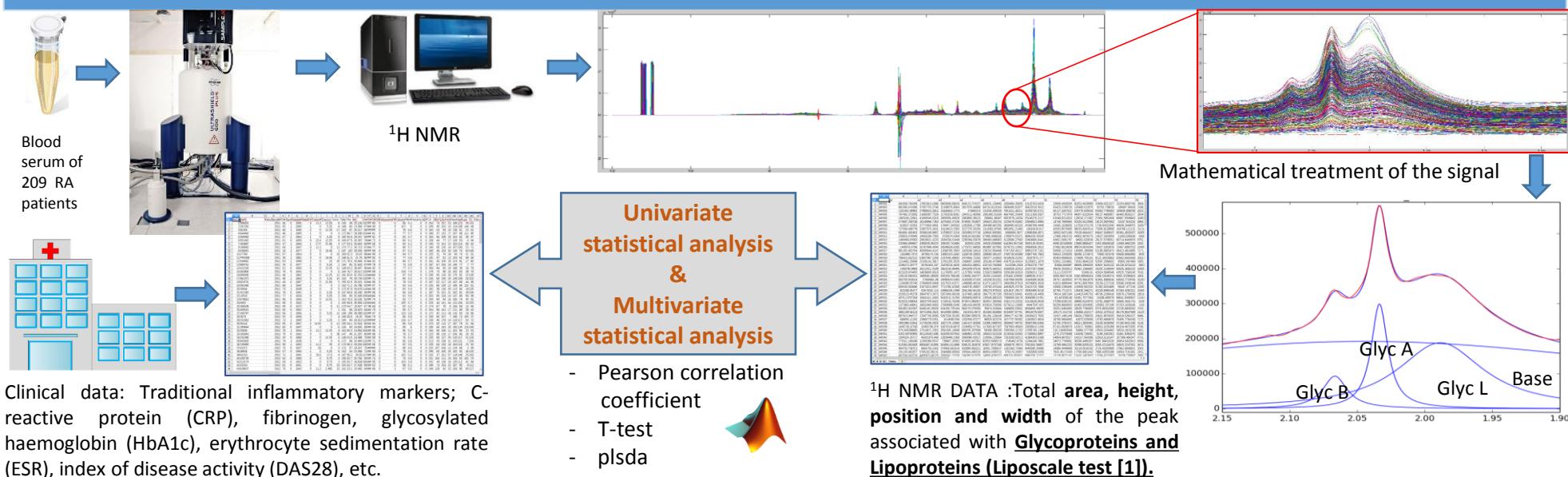
Clinical data: Traditional inflammatory markers; C-reactive protein (CRP), fibrinogen, glycosylated haemoglobin (HbA1c), erythrocyte sedimentation rate (ESR), index of disease activity (DAS28), etc.

Univariate statistical analysis & Multivariate statistical analysis

- Pearson correlation coefficient
- T-test
- plsda

$^1$H NMR DATA :Total **area, height, position and width** of the peak associated with **Glycoproteins and Lipoproteins (Liposcale test [1]).**

Glyc A, Glyc B, Glyc L, Base

## RESULTS

**Univariate statistical analysis:** Association between the inflammatory markers and the $^1$H NMR lipoprotein and glycoprotein profiles

**Table 1**: Correlation coefficient of significant values (p<0.05) between lipid variables and HbA1c and DAS28.

|  | IDL-C | VDL-TG | IDL-TG | HDL-TG | Total VLDL-P | Large VLDL-P | Med VLDL-P | Small VLDL-P |
|---|---|---|---|---|---|---|---|---|
| **HbA1c** | 0.16 | 0.17 | 0.18 | - | 0.15 | 0.15 | 0.14 | 0.14 |
| **DAS28** | - | - | - | 0.21 | - | - | - | - |

**Table 2:** Correlation coefficient of significant values (p<0.05) between glycoproteins functions and traditional inflammatory markers.

|  | ESR | CRP | Fibrinogen |
|---|---|---|---|
| **GlycB-area** | 0.14 | 0.14 | 0 |
| **GlycA-area** | 0.23 | 0.17 | 0.17 |
| **GlycB-Height** | 0.27 | 0.23 | 0.25 |
| **GlycA-Height** | 0.27 | 0.20 | 0.20 |
| **GlycA-width** | -0.22 | -0.20 | -0.18 |

**Multivariate statistical analysis:** Contribution of $^1$H NMR parameters on the index of disease activity (DAS28) categorized by quartiles
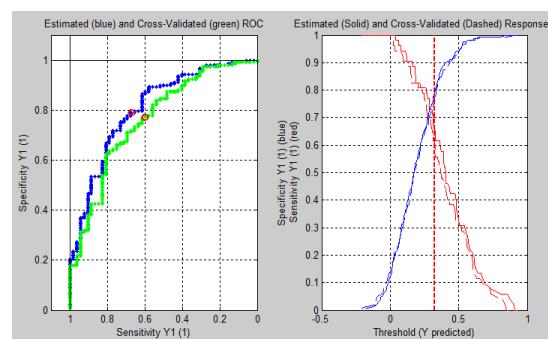
**Figure 1:** ROC (Receiver Operator Characteristics) curve predicting the behaviour of the model containing the glycoprotein and lipoprotein variables along with the RA traditional parameters of inflammation (CRP, ESR and fibrinogen).

The area under the curve (AUC) of the estimated curve (blue) is 0.8072 and the AUC of the Cross-validated curve (green) is 0.7641.
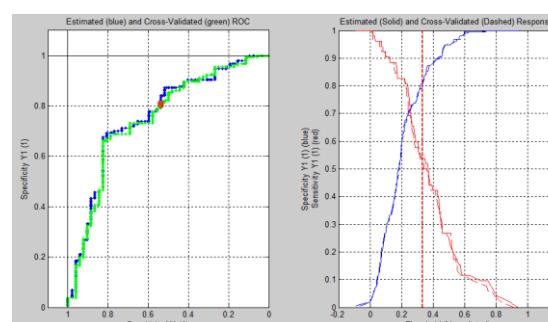
**Figure 2:** ROC curve containing only the RA traditional parameters of inflammation (CRP, ESR and fibrinogen).
The area under the curve (AUC) of the estimated curve (blue) is 0,7594 and the AUC of the Cross-validated curve (green) is 0,7506.

## CONCLUSIONS

$^1$H-RMN metabolomics is a useful tool to identify atherogenic and inflammatory profiles in patients with RA. These profiles, along with the classic AR inflammatory profiles, provide more accurate information about the severity and activity of the disease.

## ACKNOWLEDGEMENT

## REFERENCES

[1] R. Mallol, N. Amigó, M. A. Rodríguez, M. Heras, M. Vinaixa, N. Plana, E. Rock, J. Ribalta, O. Yanes, L. Masana, and X. Correig, "Liposcale: a novel advanced lipoprotein test based on 2D diffusion-ordered 1H NMR spectroscopy.," J. Lipid Res., vol. 56, no. 3, pp. 737–46, Mar. 2015.