# Variation in cardiovascular risk due to polymorphisms in lipoproteins and application of nutrigenomics

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## INTRODUCTION

Cardiovascular risk (CV risk) is determined by genetic and acquired factors. They both involve hypertension, dyslipemia and diabetes, key factors to develop cardiovascular diseases (CVD). In addition to other risk factors, lipoprotein levels are used to determine the CV risk on an individual.
However, it exists variability between individuals with the same profile. This can be explained by genetic variations that modify CV risk.
Diet is an environmental factor that involve individual variation. Different studies have been performed to analyse individual response to different diet interventions, depending on the genotype. This review collects the most relevant information about *APOE, APOA, APOB* and *LIPC* genes involving lipoprotein level variations.

## GOALS

- To analyze the connection between **polymorphisms** in genes involved in lipoprotein metabolism and **CV risk**.
- To evaluate the implication of **nutrigenomics** in the prevention or treatment of CVD in high risk individuals.

## METHODS

The search of the bibliography has been performed in the data base Medline using the key words: polymorphisms, lipoproteins and cardiovascular biomarkers. Among the 28 papers found, 12 has been used.

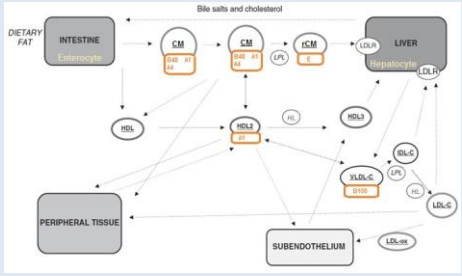


*Figure 1. Lipoprotein metabolism pathway*. In orange, apolipoproteins whose genetic variations has been described. HL variations also described.
Enterocytes get dietary fat, then cholesterol is transported to the liver by chylomicrons and to peripheral tissues by LDL particles. Cholesterol reverse transport allow its elimination by the liver through the HDL particles.

## RESULTS

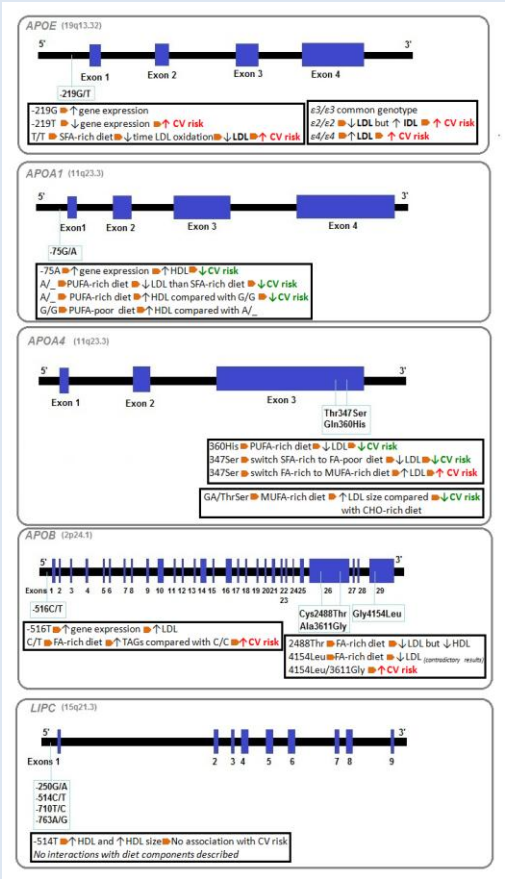


*Figure 2.* Polymorphisms associated with cardiovascular risk (CV risk) described in lipoprotein metabolism genes. CV risk vary depending on diet interventions.

Variants conferring more CV risk:
***APOE:*** -219G/T, ε2/ε2 and ε4/ε4
***APOA4:*** Thr347Ser
***APOB:*** -516C/T and Gly4154Leu + Ala3611Gly

Variants conferring less CV risk:
***APOA1:*** -75G/A
***APOA4:*** Thr347Ser and Gln360His
***APOA1 and APOA4*** *(combined):* -75G/A and Thr347Ser,respectively

## STATE OF THE ART

In the last two decades, it has been described the role of diet in individual variations, depending on the genetic profile. However, to consolidate this information, it is necessary to replicate these studies with more patients. This will clarify some contradictory results produced for the low number of subjects with uncommon variations. Currently, the knowledge is lack of soundness.

Expected short term goals:

➢To discriminate those SNPs that drive to functional protein alterations in order to **reduce wrong associations**.

➢**To predict interactions**: several genes interacting with several diet compounds lead to different phenotypes. Use of transcriptomics, proteomics and metabolomics to progress in the field of nutrigenomics.

➢To **standardize study designs** to make data collection easier, classifying the subjects depending on their characteristics.

➢To **create consortiums** to increase the number of subjects

## CONCLUSIONS

*APOE, APOA1, APOA4* and *APOB* genes showed responses to different diet interventions, but *LIPC* gene did not.

There are evidences associating polymorphisms with diet compounds, which is traduced in changes in lipid metabolism, but it is needed more information to consider nutrigenomics for the clinical practise. Genomic studies have to be performed, but also it is important not to set aside other factors, to determine CV risk and set a personalized medicine in each case, focusing specially in genetic individual variations.

It is still far reducing CV risk and, as a consequence, the morbidity and mortality of CVD, applying nutrigenomics. However, the knowledge of variants and interactions will allow to treat patients, reducing their risk factors by performing different diet interventions depending on the genotype.

### Legend

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|---|---|---|
| **B48, APOB**: apolipoprotein B48 | **IDL-C**: Intermediate Density Lipoprotein-Cholesterol | **LPL**: lipoprotein lipase |
| **B100, APOB**: apolipoprotein B100 | **VLDL-C**: Very Low Density Lipoprotein-Cholesterol | **HL, LIPC**: hepatic lipase |
| **A1, APOA1**: apolipoprotein A1 | **LDL-C**: Low Density Lipoprotein-Cholesterol | **FA**: fatty acids |
| **A4, APOA4**: apolipoprotein A4 | **HDL**: High Density Lipoprotein | **SFA**: saturated fatty acids |
| **E, APOE**: apolipoprotein E | **TAGs**: Tryacylglycerides | **PUFA**: polyunsaturated fatty acids |
| **CM**: chylomicrons | **LDLR**: Low Density Lipoprotein receptor | **MUFA**: monounsaturated fatty acids |
| **rCM**: remnant chylomicrons | **LDL-ox**: oxidated Low Density Lipoprotein | **CHO**: Carbohidrates |

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