Atherosclerosis is a common cardiovascular disease responsible for high rate of patient mortality (around 17 million deaths worldwide). The disease leads to a progressive narrowing of arteries through atheromatous plaques and a reduction of oxygen flow to several tissues. Atherosclerosis is affected by many risk factors and the most important ones are feeding behavior and other environmental factors, such as smoking, along with a genetic predisposition and family history.

Following the complete sequencing of the human genome, the large amount of information and the development of high-throughput technologies have shed some light on new diagnostic and treatment approaches for human diseases. Such approaches have been applied in order to get better understanding of complex disorders featuring a genetic history. Atherosclerosis patients show a very complex genetic trait. Innumerable genes are related to the disease and they regulate several biological processes including macromolecules metabolism, such as cholesterol, detoxification of xenobiotics, endothelial function, healing and coagulation.

Recently, single nucleotide polymorphisms (SNPs) have been targeted as a form of genomic variation that could increase the understanding of human diseases, such as atherosclerosis and other cardiovascular diseases, and their influence on susceptibility and better prognostic through modulation of proteins coded by related genes. Barbosa et al. (2017) assessed 297 atherosclerotic patients regarding the T786C polymorphism of the eNOS gene. This polymorphism promotes a substitution of the nitrogenous base thymine for cytosine and reduces the activity of the eNOS gene. Barbosa’s approach showed that the TC genotype was prevalent in the population under study and the authors tested the influence of the polymorphism in patients with active risk factors related to oxidative stress.

Although a positive correlation between T786C polymorphism and atherosclerosis was found, the small sample size may not be representative and may have affected the results since it was performed on a limited number of patients. An alternative would be increasing the size of the samples considerably and analyze if the results will follow the pattern observed in the present study. Another alternative would be to invest on meta analysis and gather information published elsewhere in order to increase the sample size and obtain trustworthy results.

The conclusion of the authors lays on the fact that the presence of multiple risk factors increased the deleterious effects of the C allele, resultant of the point mutation in the position 786 within the
eNOS gene. A way to improve the statistical analysis of the present paper would be to apply a linear mixed model, for example, instead of using very simple statistical approach that could make their conclusions biased. An interesting way that could enrich the results and should be thought as a continuation of the research is the use of bioinformatics. What are the effects of the T786C polymorphism on the protein coded by the eNOS gene? Is the active conformational structure of the wild type somewhat different from the protein produced in cells carrying the mutation? In these cases, a simulation of the conformational structure of the mutated protein could be performed and compared to the wild type.

Recently, several studies on peptides have shown that these molecules are able to modulate protein function. Bioinformatic tools are been used to design rational peptides that could modulate and interfere with protein function, optimizing or inhibiting them. Besides that, peptides designed in silico and tested could be employed as a future promisor drug against atherosclerosis and other cardiovascular diseases.

Overall, the results presented by Barbosa et al. follows a pattern seen elsewhere, such as a higher prevalence of the TC genotype and that the presence of cardiovascular risk factors increase the risk of atherosclerosis associated with the C allele frequency. The T786C polymorphism is related to susceptibility to atherosclerosis and other diseases in several types of population. Their results lead to new possibilities and investigation of polymorphism and atherosclerosis susceptibility, which could in the future lead to easier diagnostic and prognostic aspects.

References