Scoring of Matrix Gla protein (MGP) promoter variants within predicted transcription elements

Mohammad Najafi Ph.D[1*] and Abazar Roustazadeh Ph.D[1]

[1] Cellular and Molecular Research Center, Razi Drug Research Center, Biochemistry Department, Tehran University of Medical Sciences, Tehran, Iran
{nbsmmsbn@tums.ac.ir}

Abstract. Background: Matrix Gla protein (MGP) is known as a calcium scavenger within sub-endothelial space of vessels, so that its function is suggested to reduce the risk of coronary artery diseases. In this study, we predicted the role of MGP promoter rs1800801, rs1800802 and rs1800799 variants on the score changes of predicted transcription elements.
Methods: The gene promoter fragments flanking the polymorphic positions were selected from Ensembl Genome browser. The transcription elements containing wild polymorphic positions were found on the alignment with Jaspar profiles (similarity >80). Then, the changes of scores were statistically tested on the polymorphic modifications within the elements.
Results: The scores had not significant differences on the changes of the rs1800801, rs1800802 and rs1800799 alleles within the predicted elements (P=0.69, P=0.87 and p=0.07, respectively).
Discussion: The prediction results showed that the allele changes within the elements could not significantly affect the transcription factor scores.

1 Introduction

Matrix Gla protein (UniProtKB/Swiss-Prot: P08493) was isolated from bone, lung, heart, cartilage, kidney and smooth muscle cells. It is an 84-amino acids protein and contains five γ-carboxyglutamic residues involved in binding of calcium (1). The MGP gene (NCBI Gene ID: 4256) is located on the short arm of chromosome 12 (12p12.3) and up to 140 polymorphisms (SNPs) have been submitted in dbSNP (www.ncbi.nlm.nih.gov/snp). Several reports have shown that the number of polymorphisms within the gene promoter region may potentially affect the MGP concentration. These studies have evaluated the association between the MGP polymorphisms and myocardial infarction, coronary artery calcification and atherosclerotic vascular calcification on the hypothesis that the MGP can act as a calcium scavenger within sub-endothelial region of vessels (2). Here, we predicted the transcription factors and evaluated the variants of three promoter polymorphic sites (rs1800801, rs180802, rs1800799) within their flanking fragments using bioinformatics tools.

2 Methods

A 1800bp fragment of MGP gene promoter (ENSG00000111341) containing the rs1800801, rs180802, rs1800799 polymorphic sites was selected from Ensembl Genome browser (www.ensembl.org). The short sequences (56 bp) flanking the polymorphic sites were separated of the primary fragment and were searched against the known DNA-binding profiles (JASPAR, http://jaspar.cgb.ki.se). Then, the transcription factor elements with the complete identity were aligned using Multiple Sequence Alignment tool (Multialign, http://multialign.toulouse.inra.fr/multalin). Based on the similarity (Primary profile similarity=80%), scores were estimated on the substitutions of polymorphic variants within the transcription elements (http://mordor.cgb.ki.se/cgi-bin/CONSITE/consite).

2.1 Statistical Analyses

Statistical analysis was performed using statistical software package (SPSS 18.0, Chicago). The means of scores for the predicted elements with both polymorphic variants were reported in mean±SD form. The score differences between the polymorphic variants were evaluated by student-t test.

3 Results

We found more than ten transcription factors within the polymorphic positions based on the wild alleles (Figure 1). The scores of predicted transcription elements were calculated on the polymorphic changes. There were not significant differences in the predicted scores of rs 1800801 (P>0.6), rs1800802 (P>0.7) and rs1800799 (P>0.05) sites.

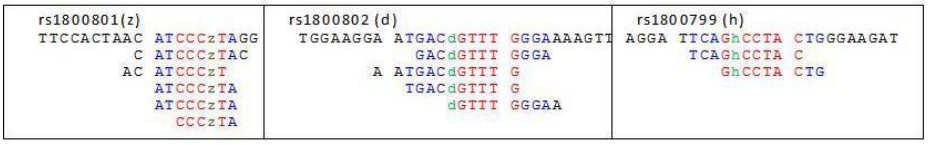

Figure 1: Multiple sequence alignment of transcription elements predicted within rs1800801, rs1800802 and rs1800799 positions

4 Discussion

In agreement with *Farzaneh-far et al.* study (3), we didn't observe the significant differences in the scores of predicted transcription factors on the allele changes. Furthermore, Herrmann et al. (4) didn't find significant differences in the polymorphic genotypes. In conclusion, we predicted several elements in the locations of polymorphic sites, using the transcription factor profiles and showed that the scores are not significantly changed using the polymorphic variations.

References

1. Proudfoot D, Shanahan CM. Biology of calcification in vascular cells: intima versus media. Herz (2001); 26:245-51.
2. Brancaccio D, Biondi ML, Gallieni M, Turri O, Galassi A, Cecchini F, Russo D, Andreucci V, Cozzolino M. Matrix GLA protein gene polymor-phisms: clinical correlates and cardiovascular mortality in chronic kidney disease patients. Am J Nephrol (2005); 25:548-52.
3. Farzaneh-Far A, Davies JD, Braam LA, Spronk HM, Proudfoot D, Chan SW, O'Shaughnessy KM, Weissberg PL, Vermeer C, Shanahan CM. A polymorphism of the human matrix gamma-carboxyglutamic acid protein promoter alters binding of an activating protein-1 com-plex and is associated with altered transcription and serum levels. J Biol Chem (2001) 276:32466-73.
4. Herrmann SM, Whatling C, Brand E, Nicaud V, Gariepy J, Simon A, Evans A, Ruidavets JB, Arveiler D, Luc G, Tiret L, Henney A, Cambien F. Polymorphisms of the human matrix gla protein (MGP) gene, vascular calcification, and myocardial infarction. Arterioscler Thromb Vasc Biol (2000) 20:2386-93.