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## Screening of genes related to the atherosclerotic plaque stability in patients with asymptomatic carotid stenosis

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### Abstract

Carotid stenosis is the narrowing of the carotid arteries due to atherosclerosis. Our goal in this study was to search for copy number variants (CNV) in the human genome which may be related to risk of plaque formation and rupture. We obtained DNA from age matched patients at Hospital das Clínicas, in Campinas. Our cohort is composed by 15 patients with asymptomatic carotid stenosis and 15 with symptomatic carotid stenosis. All samples were genotyped using a SNP microarray and analysed. We identified various CNVs located in genes of the complement system, cytoskeletal remodelling and cell adhesion pathways. In our samples, we observed deletions in genes from both classical and lectin pathways of the complement system. Low levels of lectin binding mannose (MBL), is related to enhanced plaque formation. In addition, we found three patients with duplications in UPAR. The urokinase-type plasminogen activator receptor is part of the cytoskeletal remodelling pathway and has been previously associated to plaque rupture due to its increased expression in macrophages. Furthermore, we found a duplication in the PKC gene in one patient. It is known that Protein Kinase C, present at the cell adhesion pathway, when active stimulates the adhesion of monocytes to endothelial cells, therefore accelerating plaque formation. Overall, our results indicate that genes related to plaque formation and rupture were either duplicated or deleted in patients with asymptomatic carotid stenosis.

**Key words:** Atherosclerosis, Carotid Stenosis, Lectin binding mannose.

### Introduction

Carotid stenosis is the narrowing of the carotid arteries due to atherosclerosis<sup>1</sup>. The disease begins with an endothelial dysfunction leading to a chronic inflammatory response. In some cases, the atherosclerotic plaque may be ruptured, but the reason why some plaques continue stable remains unclear.

Our goal in this study was to screen the copy number variants (CNV) in subjects with asymptomatic carotid stenosis to access genes related to plaque formation and rupture.

### Results and Discussion

We identified various CNVs located in genes of the complement system. Many complement proteins, regulators and receptors were previously found in the atheroma<sup>3</sup>.

We observed deletions in genes from both classical and lectin pathways of the complement system. Even though the role of lectin pathway in atherosclerosis has not been completely clarified, low levels of its main protein, the lectin binding mannose (MBL), is related to enhanced plaque formation<sup>4</sup>.

Our analysis also indicated CNVs in the pathway related to the cytoskeletal remodelling. The urokinase-type plasminogen activator receptor (uPAR) is a glycoprotein involved in cell adhesion and tissue remodelling<sup>5</sup>. It has previously been associated to plaque rupture due to its increased expression in macrophages<sup>5</sup>. Previous studies displayed the correlation between plaque vulnerability and rupture with macrophage infiltration.

The cell adhesion pathway was also highlighted. Protein Kinase C (PKC) activation stimulates the adhesion of monocytes to endothelial cells, therefore accelerating plaque formation<sup>6</sup>.

### Conclusions

Overall, our results indicate that genes related to plaque formation and rupture were either duplicated or deleted in patients with asymptomatic carotid stenosis. However, a broader study is necessary to access how these genes act to maintain the stability of atherosclerotic plaques.

### Acknowledgement

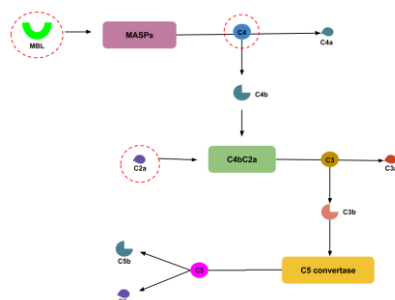


Figure 1: Lectin Pathway of the complement system. Highlighted molecules represent genes that were either duplicated or deleted.



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