

## ROLE OF CALPONIN IN PLATELET FUNCTION AND CARDIOVASCULAR DISEASE

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### Abstract

Calponin is an actin binding protein known to convert external mechanical signals into intracellular chemical signals in different types of cells. Calponin especially Calponin2 is found in platelets and macrophages. Macrophages play an important role in inflammatory reaction especially in the setting of atherosclerotic disease. Role of Calponin in platelet function and macrophage activity is gaining lot of attention. In this paper, we will review the role of Calponin2 on platelet activity and atherosclerotic disease.

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## INTRODUCTION

According to the WHO, Cardiovascular disease is the leading cause of death worldwide. Every year, fourteen million people die from cardiovascular disease and stroke. The number one cause of death in the United States is cardiovascular disease with over 610,000 people dying in the United States every year <sup>[1]</sup>. Cardiovascular Disease causes 1 in every 4 deaths that occur in the United States. Stroke is the fifth leading cause of death in the United States, killing nearly 130,000 Americans every year <sup>[2]</sup>. More than 17 million people die worldwide from cardiovascular disease annually <sup>[3]</sup>. Platelet inhibiting drugs and drugs which modify the progression of atherosclerosis are vital in the treatment of heart attack and stroke.

Calponin is an actin binding protein known to convert external mechanical signals into intracellular chemical signals in different types of cells <sup>[4]</sup>. The unique nature of Calponin is that it can suppress platelet activation while maintaining full activation potential. Calponin also inhibits myosin-ATPase and traction force, and stabilizes actin cytoskeleton and enhances cell adhesion <sup>[5]</sup>. In this paper we will review the role of Calponin, especially that of Calponin 2 in platelets and cardiovascular disease.

## DISCUSSION

Calponin occurs in smooth muscle cells as well as some non-smooth muscle cells such as fibroblasts, keratinocytes, platelets, etc <sup>[6, 7]</sup>. Calponin occurs in three isoforms namely h1, h2 and h3 (acid calponin). They are also identified as CNN1, CNN2 and CNN3. Calponin's function in smooth muscle cells are widely studied before but its function in non-smooth muscle cells such as platelets and vascular development are currently being investigated. Presence of Calponin 2 in non-muscle cells plays a role in cell motion and cytoskeleton integrity.

Jian Tang and others <sup>[8]</sup> studied the role of Calponin 2 in Zebrafish, showed that Calponin 2-plays an important role in the migration of endothelial cells both *in vivo* and *in vitro* and that its expression is critical for proper vascular development and they concluded that Calponin2 is critical for normal vessel development in the zebrafish.

Atherosclerosis is a chronic inflammatory condition, where macrophages play a major role in development of plaque. Since macrophages helps to maintain pro inflammatory state in vascular structure, macrophages are a good target future treatment of atherosclerotic disease. Calponin

isoform 2 is expressed at significant levels in macrophages. Inhibiting Calponin 2 have shown to increase macrophage mobility and phagocytosis, thereby reducing the incidence of atherosclerosis.

In a recent paper published by R Liu and JP Jin <sup>[9]</sup>, they concluded that in genetically modified mice with Knockout Calponin showed significantly lowered cell adhesion, and effectively attenuated the development of arterial atherosclerosis lesions with less macrophage infiltration. When Calponin in platelets is inhibited, then platelet activation and spreading will be delayed because Calponin targets the actin cytoskeleton system.

PC Hines et al <sup>[10]</sup> used microfluidic assay, and showed Calponin Knockout mice model took 2.3 times longer time to attain the same hemostasis as achieved by normal type of mice. Time to initiate rapid platelet/thrombus accumulation was longer in calponin knockout mice compared to normal type of mice. This study raised the possibility of h2-calponin as a new target for therapeutic platelet inhibition because of the ability to delay platelet accumulation without inhibiting downstream thrombotic potential.

Recently, Calponin role is being investigated in cancer too, Suppression of gastric cancer

cells in Knockout Mice shows Calponin 2 may be a therapeutic target even in treatment of cancer <sup>[11]</sup>.

## CONCLUSION

Calponin plays an important role in cellular development and migration. Calponin is also critical in development of vascular system and also control the macrophagic activity there by inflammatory response. Calponin inhibition has shown to have beneficial effects in treatment of atherosclerotic disease by attenuating the inflammatory response. Suppression of gastric cancer cells in Knockout Mice shows Calponin2 may be a therapeutic target even in treatment of cancer. Calponin is a novel therapeutic target in treatment of atherosclerotic disease as well as in development of antiplatelet medications.

## Conflict of Interest Statement-

There is no conflict of interest.

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