SNF472 - a potential novel calcification inhibitor in CKD-MBD

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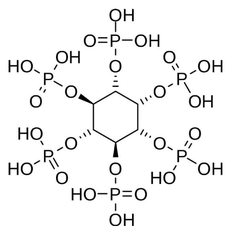
BACKGROUND

Chronic kidney disease (CKD) is associated with cardiovascular calcification (CVC) in response to mineral and bone disorder[1]. SNF472 is an intravenous formulation of the hexasodium salt of myoinositol hexaphosphate. It directly inhibits calcification by binding to the growth sites of the hydroxyapatite crystal.



OBJECTIVE

We investigated the effects of SNF472 upon vascular smooth muscle cell (VSMC)-mediated calcification triggered by high calcium and phosphate (CaPO). Cells were treated either with sodium thiosulfate (STS)[2] or SNF472.

METHODS

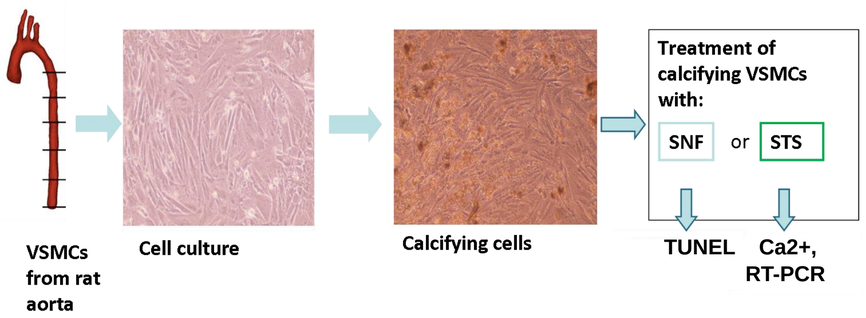


Figure 1: Isolation of primary VSMC and cell culture setup

RESULTS

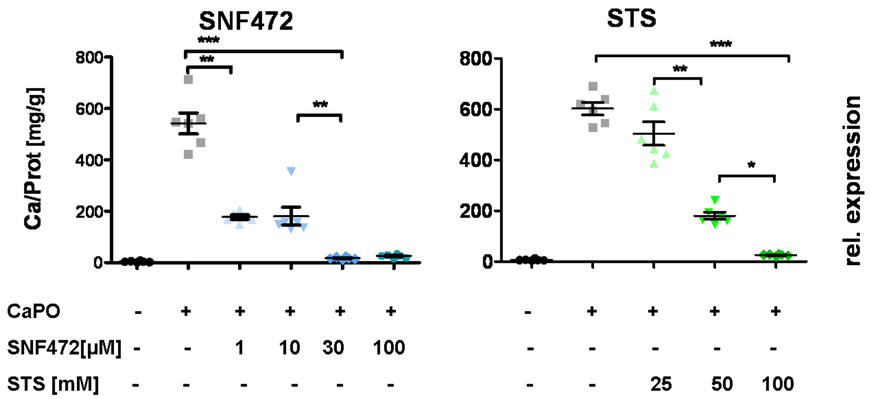


Figure 2: Dose dependeny of SNF472 and STS treatment

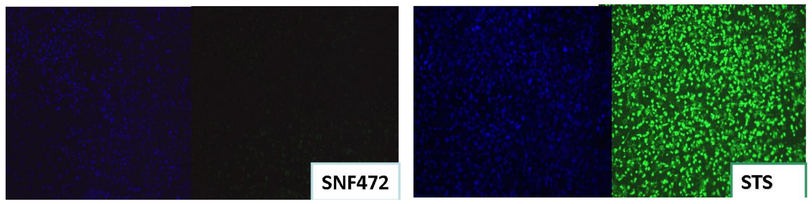


Figure 3: TUNEL staining of SNF472 and STS treated VSMCs

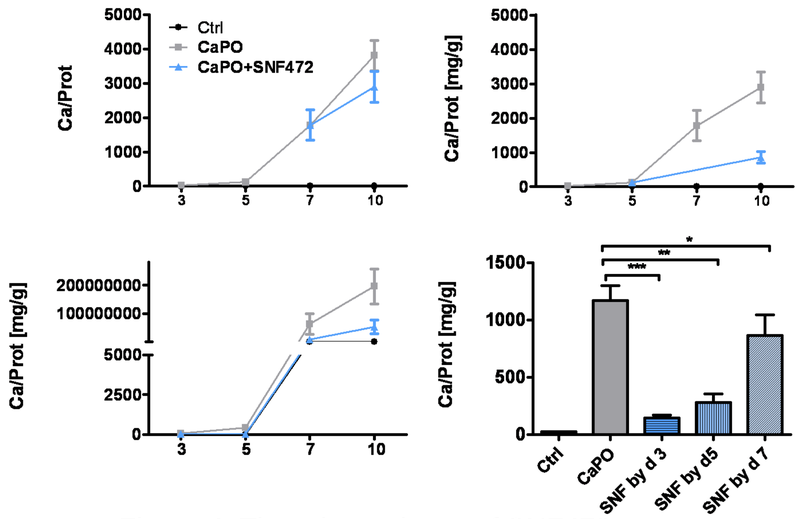
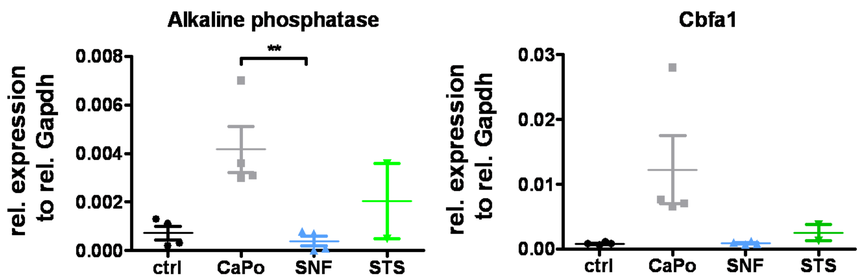


Figure 4: Time dependency of SNF472 treatment



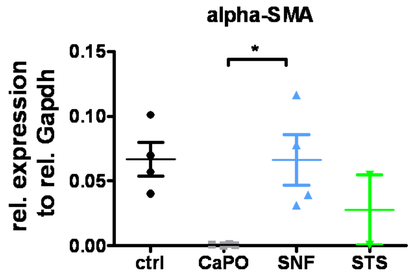


Figure 5: Relative expression of α-SMA, alkaline phosphatase and cbfa1

CONCLUSIONS

SNF472 decreased Ca deposition in rodent VSMC in a high CaPO microenvironment without inducing apoptosis and prevented upregulation of genes indicating switch from contractile VSMC to osteoblast-like cells. Hence, SNF472 qualifies as a promising research target regarding the potency to inhibit CVC in CKD patients undergoing dialysis.

REFERENCES

1. Moe,SM et al.: Pathophysiology of Vascular Calcificationin in Chronic Kidney Disease, *Circulation Research,* 2004

2.Chen, NX et al.: Adipocyte induced arterial calcification is prevented with sodium thiosulfate, *Biochemical and Biophysical Research communication,* 2014