SNF472 – a potential novel calcification inhibitor in CKD-MBD

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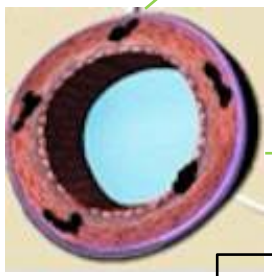
Chronic Kidney Disease – Mineral Bone Disorder

CKD kidney

Elevated:
- FGF-23
- PTH
- Phosphorus

Decreased:
- $1,25(OH)_2D_3$
- Calcium

Vascular and soft tissue calcification



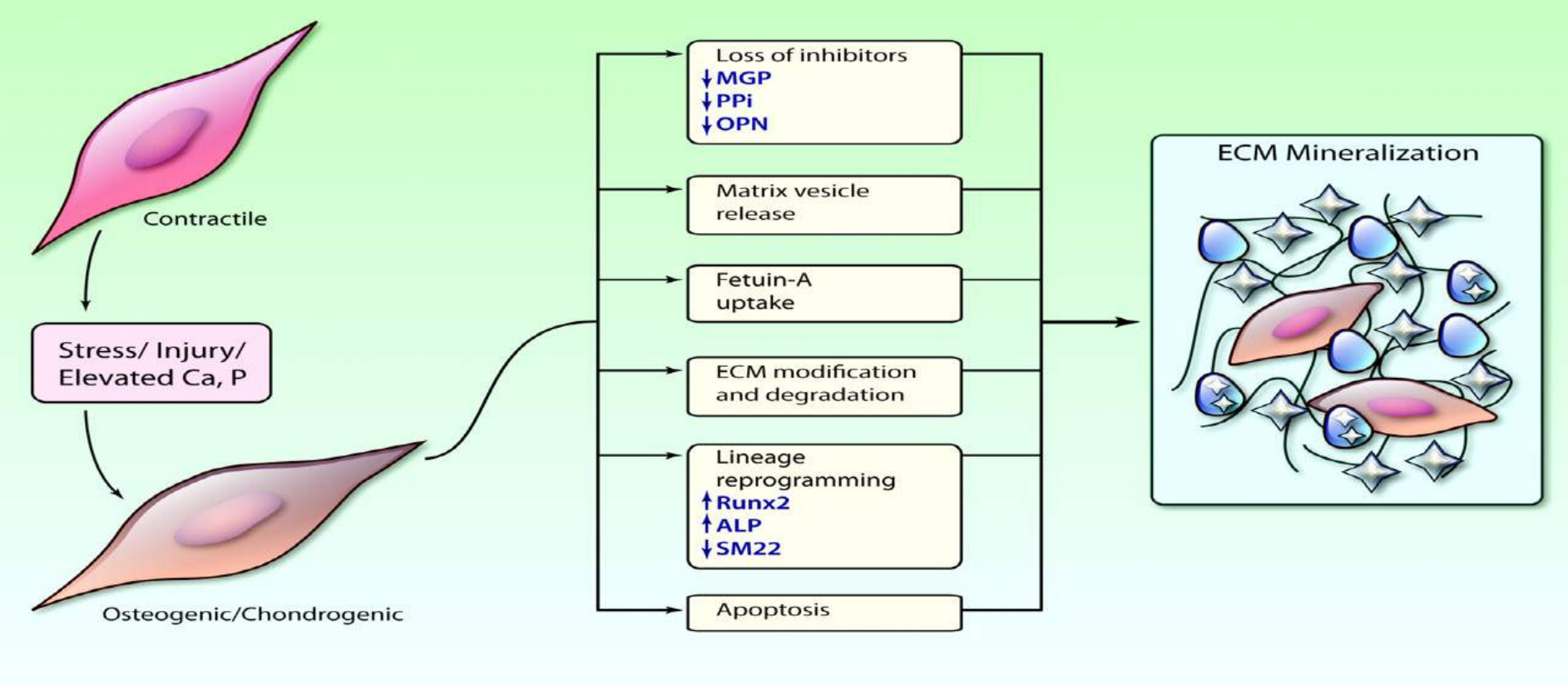
Calcification

Bone disease

Abnormal bone:
- Turnover
- Mineralisation
- Volume
- Strength

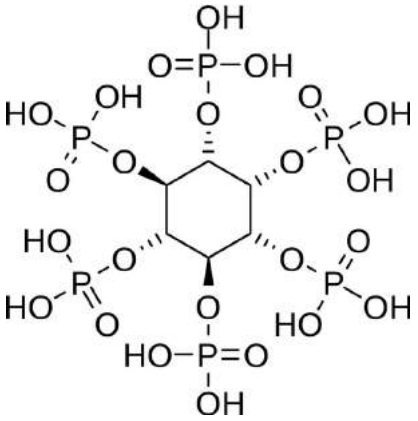
Modified from: KDIGO CKD-MBD Work Group. *Kidney Int*. 2009; 76 (suppl 113)

Vascular calcification in CKD-MBD:



What is SNF472?

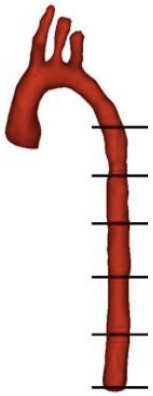
- Main component: myo-inositol hexaphosphate (IP6, phytate)
  - Natural nutritional ingredient
  - potent modulator of calcification



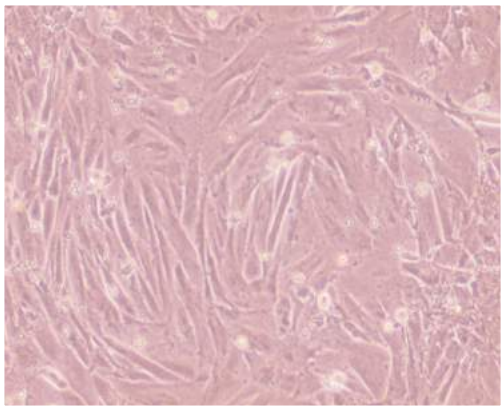
- SNF472:
  - modified IP6 salt, i.v. formulation
  - Being developed for:
    - Reducing of cardiovascular calcification in dialysis patients
    - Treatement of calciphylaxis

Grases F. et al, *Urol Res 28;*2000 , Grases F. et al *Biofactors 11;* 2000

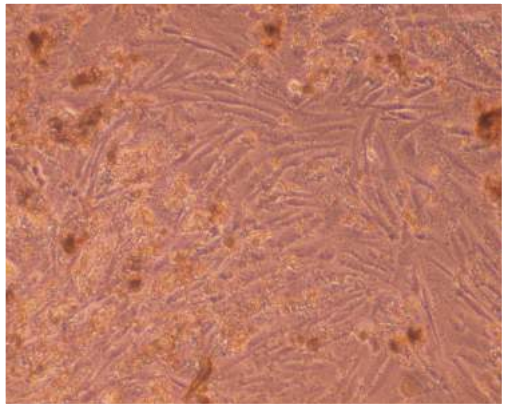
Methods: VSMC culture



VSMCs from rat aorta



Cell culture
Standard medium
- DMEM / F12 + 10% FCS



Calcifying cells
Pro-calcific medium
- DMEM / F12 + 10% FCS + 3mM Ca and PO_4

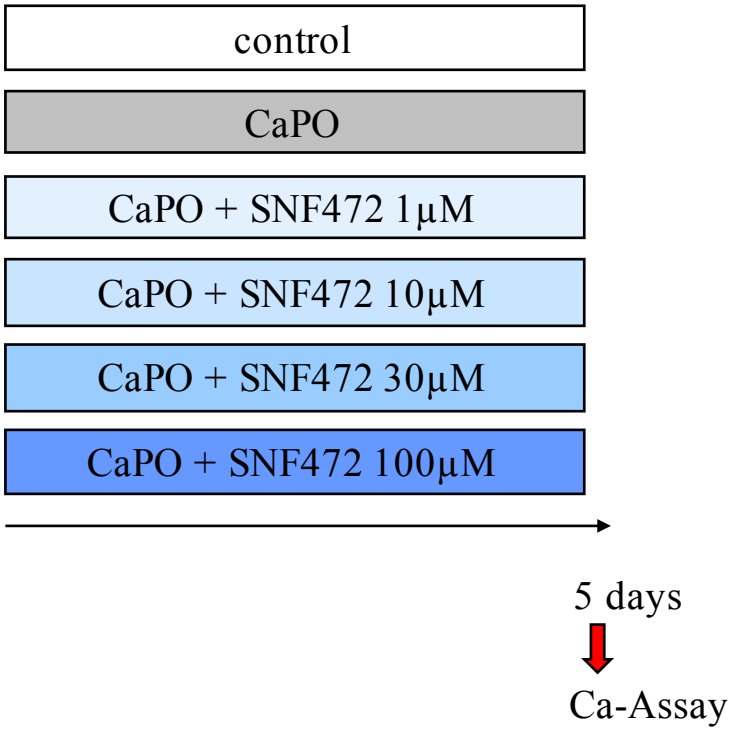
Treatment of calcifying VSMCs with:

SNF472 or **STS**

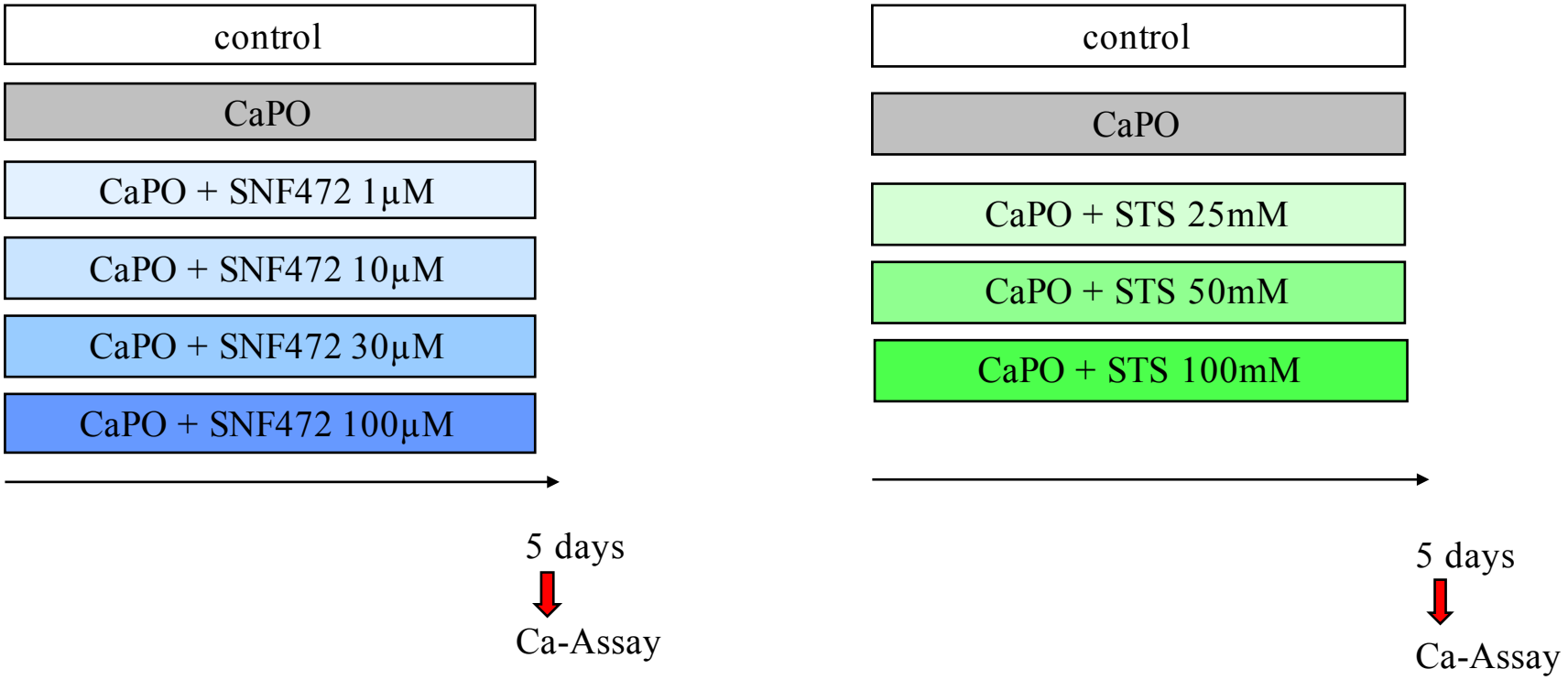
TUNEL staining

Ca-assay

SNF472:
Most Effective Dose Finding

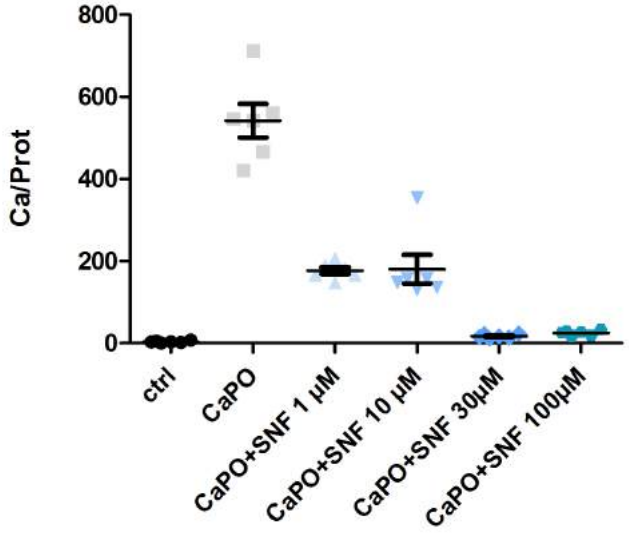


SNF472 vs STS: Most Effective Dose Finding

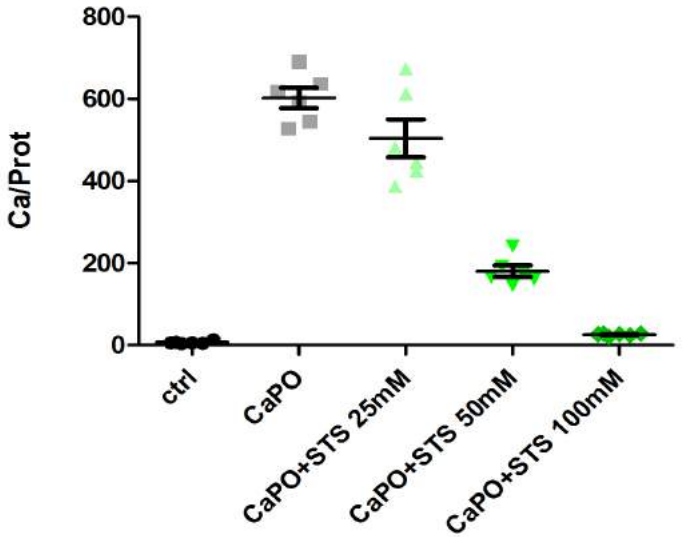


SNF472 vs STS: Most Effective Dose Finding

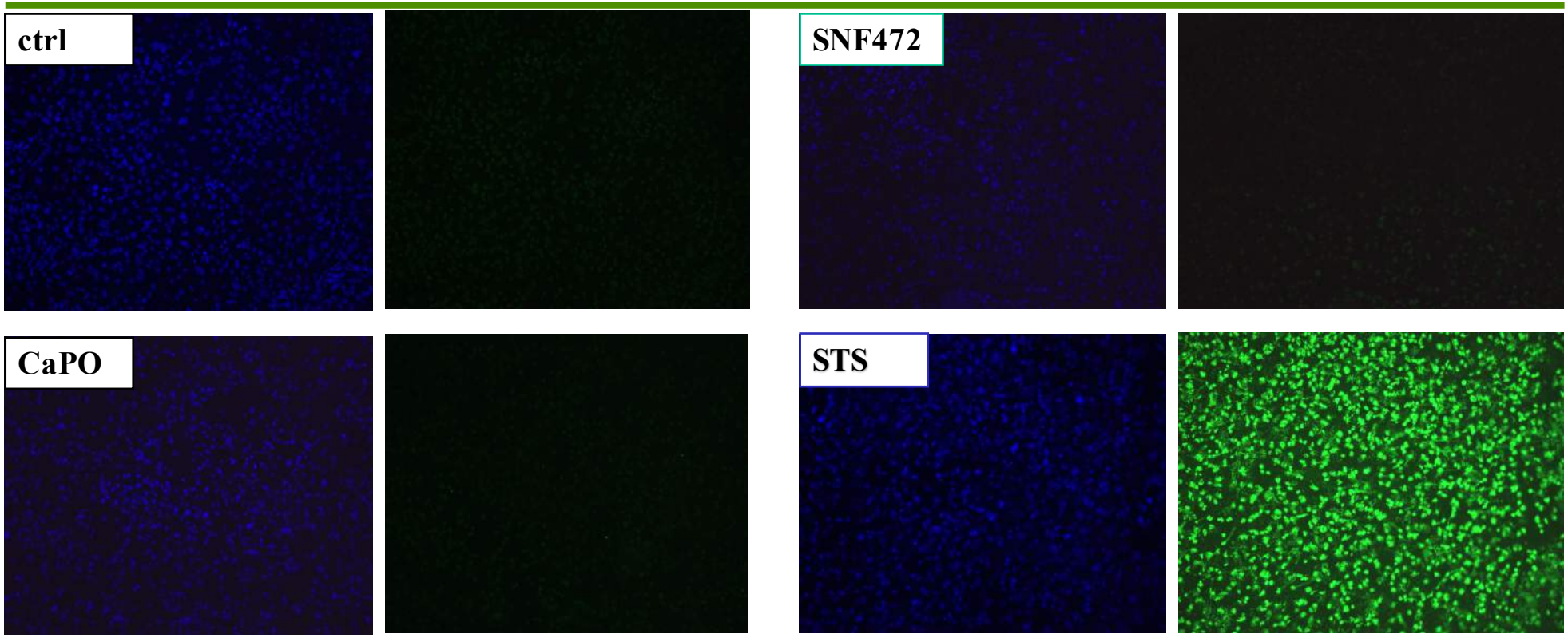
Calcium levels after 5 days SNF472 treatment



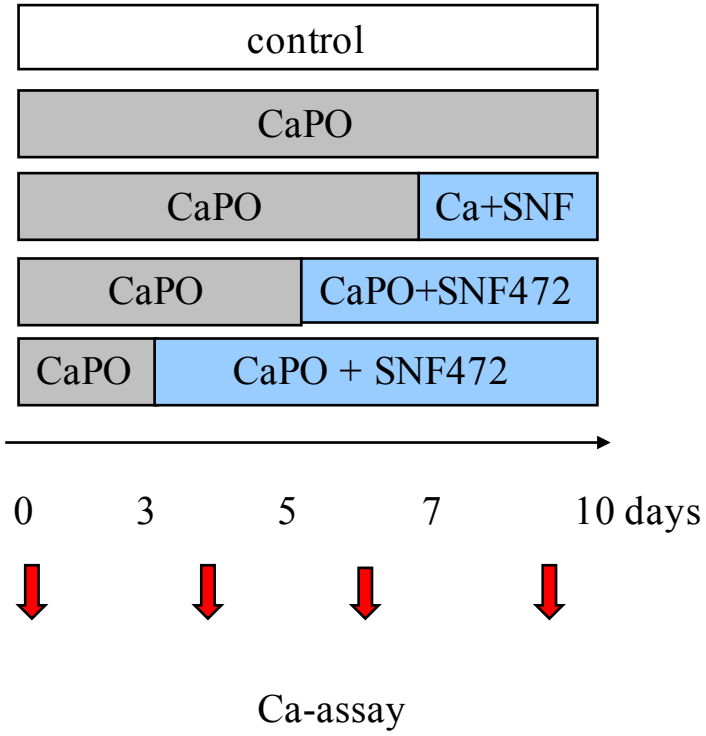
Calcium levels after 5 days STS treatment



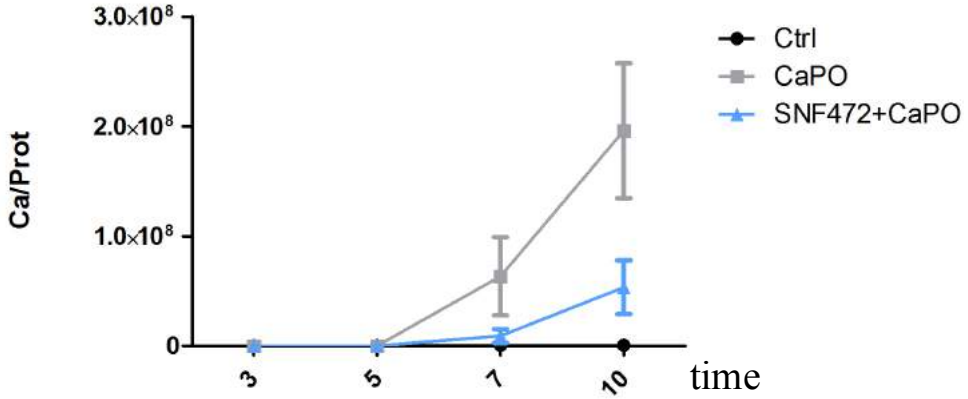
STS472 vs STS:
apoptosis rate after 7 days of treatment

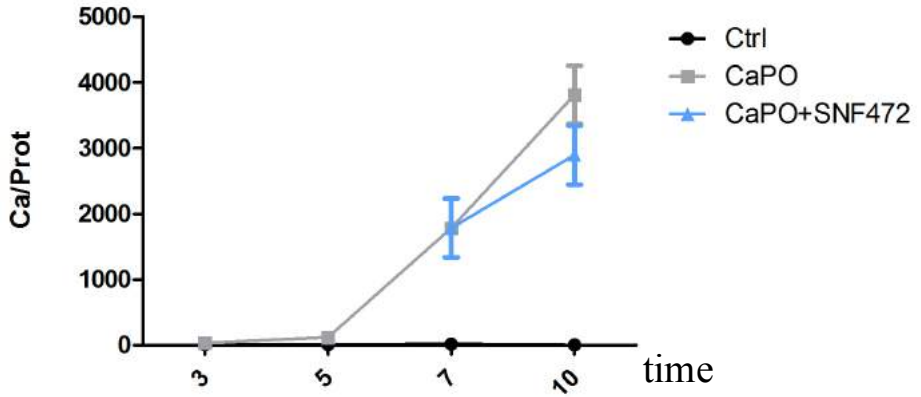


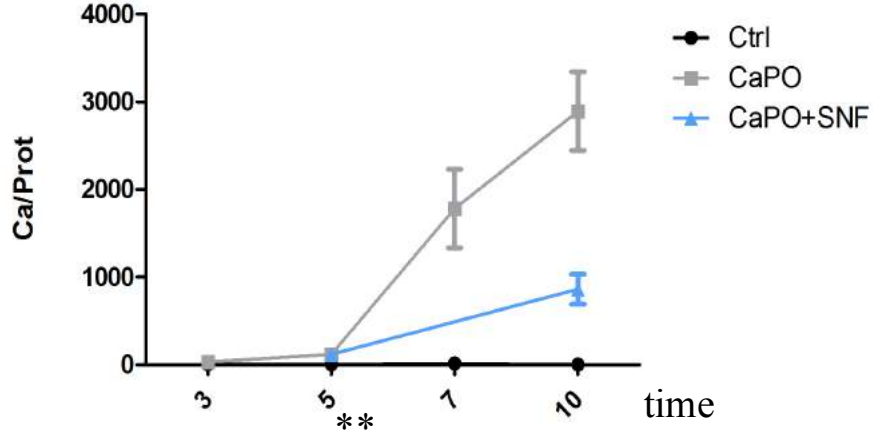
Time dependency of SNF472 treatment

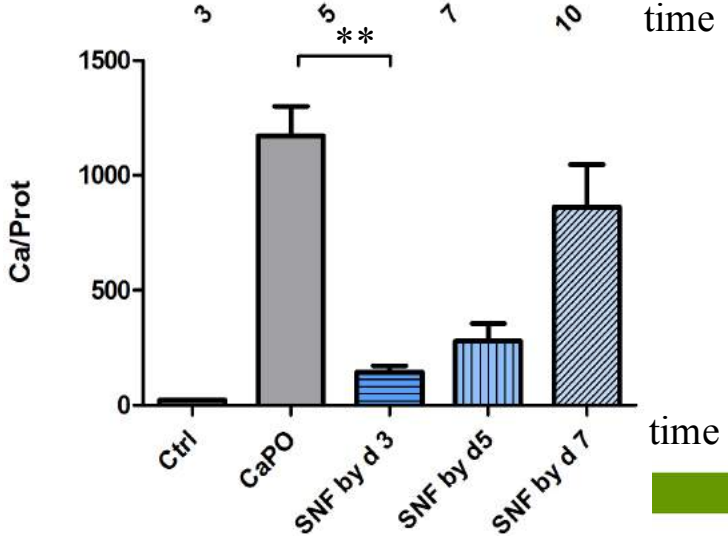


Time dependency of SNF472 treatment









Conclusions:

SNF472:

- Reduces in vitro calcium deposition of rodent VSMCs in a pro-calcific milieu
- No significant increase of apoptosis (0,8%)

STS:

- Also reduces in vitro calcium deposition of rodent VSMCs in a pro-calcific milieu
- Very high levels of apoptosis (77%)

These results are promissing on the future use of SNF472 for the inhibition of cardiovascular calcification in CKD patients

Discussion:

Thank you

for your attention!