SMOOTH MUSCLE-SELECTIVE NF-κB INHIBITION REDUCES PHOSPHATE-INDUCED VASCULAR CALCIFICATION IN MICE WITH CHRONIC KIDNEY DISEASE

Tadashi Yoshida, Maho Yamashita, and Matsuhiko Hayashi

Apheresis and Dialysis Center, Keio University School of Medicine, Tokyo, Japan

OBJECTIVES

Vascular calcification is often seen in patients with chronic kidney disease (CKD) and is associated with increased mortality, myocardial infarction, stroke, and limb amputation. Results of previous studies by our laboratory and others showed that high phosphate-induced phenotypic switching of vascular smooth muscle cells (SMCs) into osteogenic cells plays an important role in the calcification process. High phosphate is thought to be the most critical factor for vascular calcification. However, hyperphosphatemia is less prominent in the early stages of CKD, whereas the prevalence of vascular calcification is high at this stage, suggesting that factors other than high phosphate also play a role. In the present studies, we sought to determine if the pro-inflammatory NF-κB signaling in SMCs contributes to vascular calcification in CKD mice.

METHODS

SM-IκBΔN mice on the DBA/2 genetic background were generated by breeding mice expressing a truncated form of IκB (IκBΔN) following Cre activation (IκBΔN mice) and mice expressing Cre recombinase under the control of the *Tagln* promoter (*Tagln*-Cre mice). Because IκBΔN inhibits the NF-κB signaling as a super-repressor, SM-IκBΔN mice are a suitable model to determine the effect of SMC-selective NF-κB inhibition on vascular calcification.

CKD was induced in control mice and SM-IκBΔN mice, and these mice were fed a normal phosphorus diet (NPD) or a high phosphorus diet (HPD) for 10 weeks. Vascular calcification was assessed by von Kossa staining and Alizarin red staining. Aortic calcium contents were also measured.

RESULTS

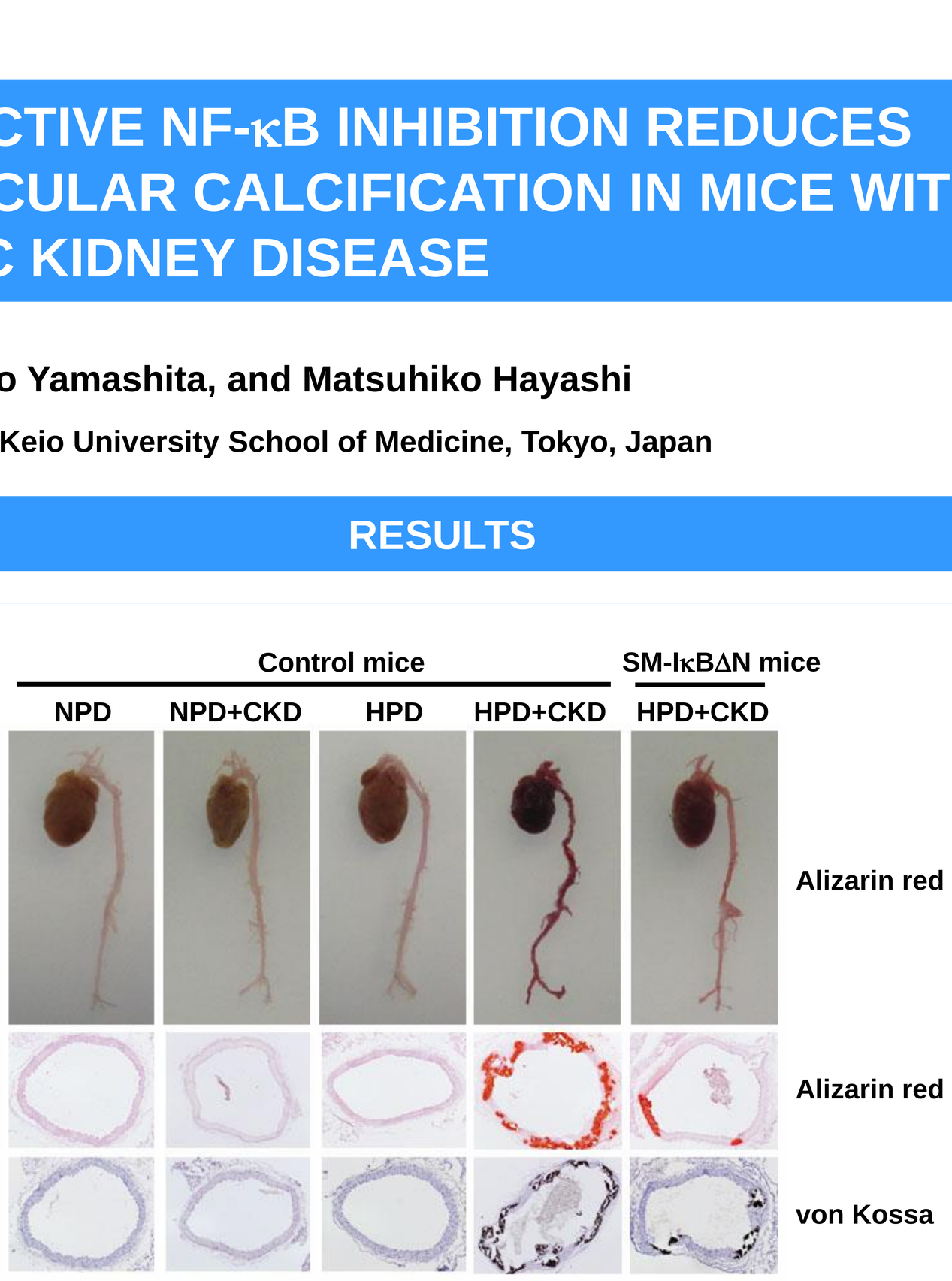

Figure 1. CKD was induced in control mice and SM-IκBΔN mice, and these mice were fed a normal phosphorus diet (NPD) or a high phosphorus diet (HPD) for 10 weeks. Vascular calcification in the thoracic aorta was determined by Alizarin red staining and von Kossa staining.

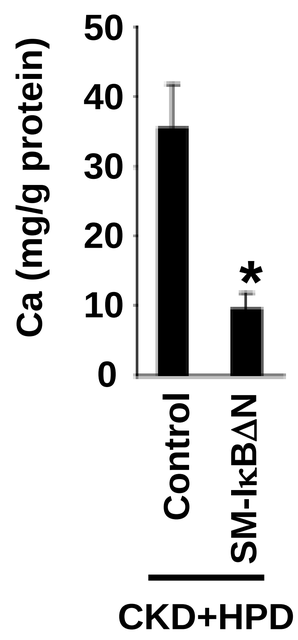

Figure 2. CKD was induced in control mice and SM-IκBΔN mice, and these mice were fed the HPD for 10 weeks. Calcium contents in the abdominal aorta were measured. *P<0.05 compared to control CKD mice fed the HPD.

SUMMARY

1. Vascular calcification was not seen in control mice, CKD-induced control mice, and HPD-fed control mice. However, severe vascular calcification was induced in CKD mice fed the HPD.

2. Vascular calcification was reduced in the aorta of SM-IκBΔN mice, as compared to control mice.

CONCLUSIONS

Results suggest that NF-κB activity in SMCs contributes to high phosphate-induced vascular calcification in CKD.

54 ERA
348--SP
CKD - MBD
Tadashi Yoshida
DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.
54th ERA-EDTA CONGRESS Madrid, Spain June 3rd-6th 2017
PosterSessionOnline.com