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Expression profile of the microRNA-142 family in uremic arterial media calcification

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Background

Vascular calcification is associated with significant cardiovascular morbidity and mortality in patients with chronic kidney disease. Our objective was to find key molecules, which regulate the phenotypic modulation of vascular smooth muscle cells. We focused on the role of microRNAs (miRNAs) and analysed the expression profile of the miRNA-142 family in detail, as it has an established role in osteoblastic differentiation.

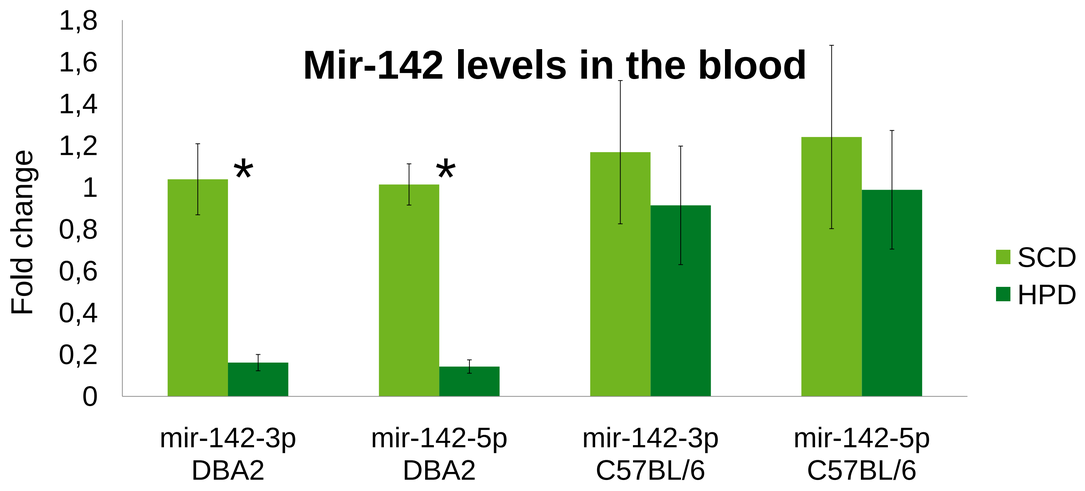

Figure 1.: miRNA levels were measured via RT-qPCR after 12 days of HPD. Mir-142-3p and mir-142-5p were downregulated in the DBA2 mice and they were not regulated in C57BL/6 mice. (*p<0,05)

Methods

For our experiments, we used DBA/2 mice which develop severe media calcification within days when put on high phosphate diet (HPD). Control C57BL/6 mice did not show any calcification on HPD within the same period of time. We measured the expression levels of different miRNAs and mRNAs via RT-qPCR in the blood and in the aortic tissue in order to determine whether changes in their expression levels were associated with progressive vascular calcification. A vascular smooth muscle primary cell (VSMC) culture was established to investigate the calcification process in vitro.

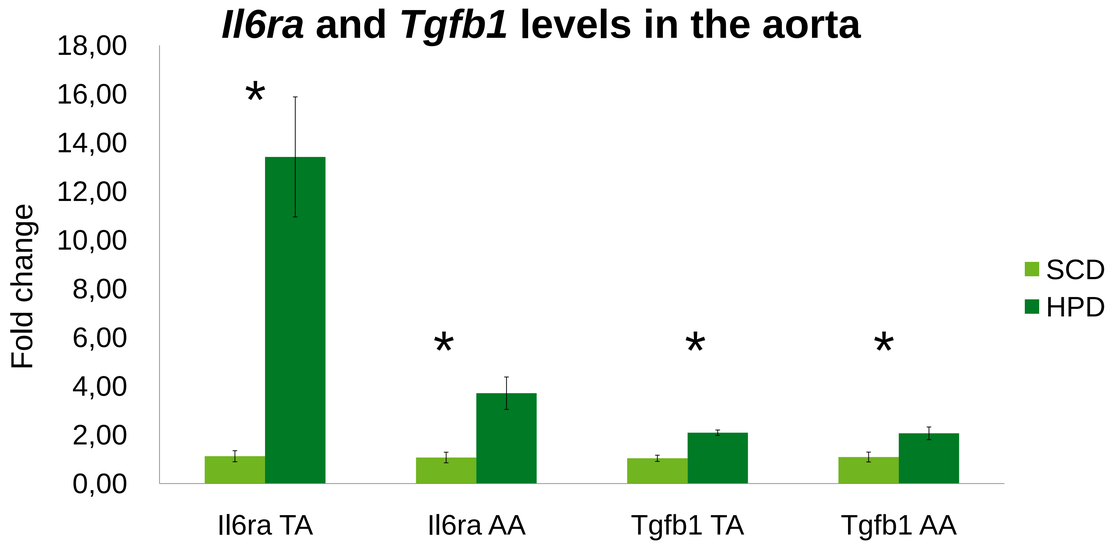

Figure 2.: *Il6ra* and *Tgfb1* were significantly upregulated in the thoracic and the abdominal part of the aorta after 12 days of HPD. (*p<0,05)

Results

The expression levels of mmu-mir-142-3p and mmu-mir-142-5p were significantly lower in the blood of the DBA/2 mice kept on HPD for 12 days. Control C57BL/6 mice on HPD showed no regulated expression of these two miRNAs. (Figure 1.)

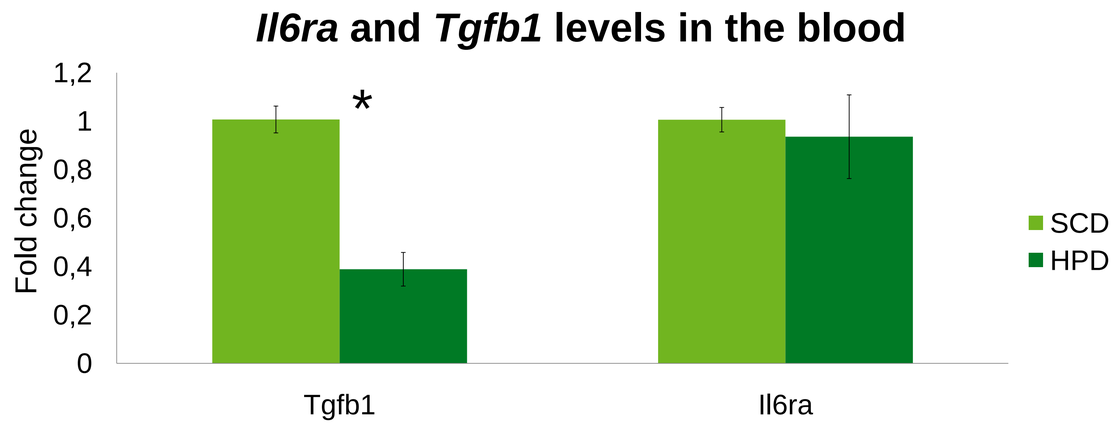

Figure 3.: *Tgfb1* was downregulated in the blood of the DBA2 mice after 12 days of HPD while *Il6ra* showed no regulation. (*p<0,05)

We examined the expression levels of potential targets of the miRNA-142 family and we found *Tgfb1* and *Il6ra* to be upregulated in the aortas. (Figure 2.) In the blood after 12 days of HPD *Tgfb1* was downregulated but *Il6ra* was not regulated. (Figure 3.) VSMCs cultured in medium with elevated phosphate concentration developed calcification in larger extent compared to cells in standard medium and are now planned to be used to study the role of the miRNA-142 family and its targets in vitro.(Figure 4.)

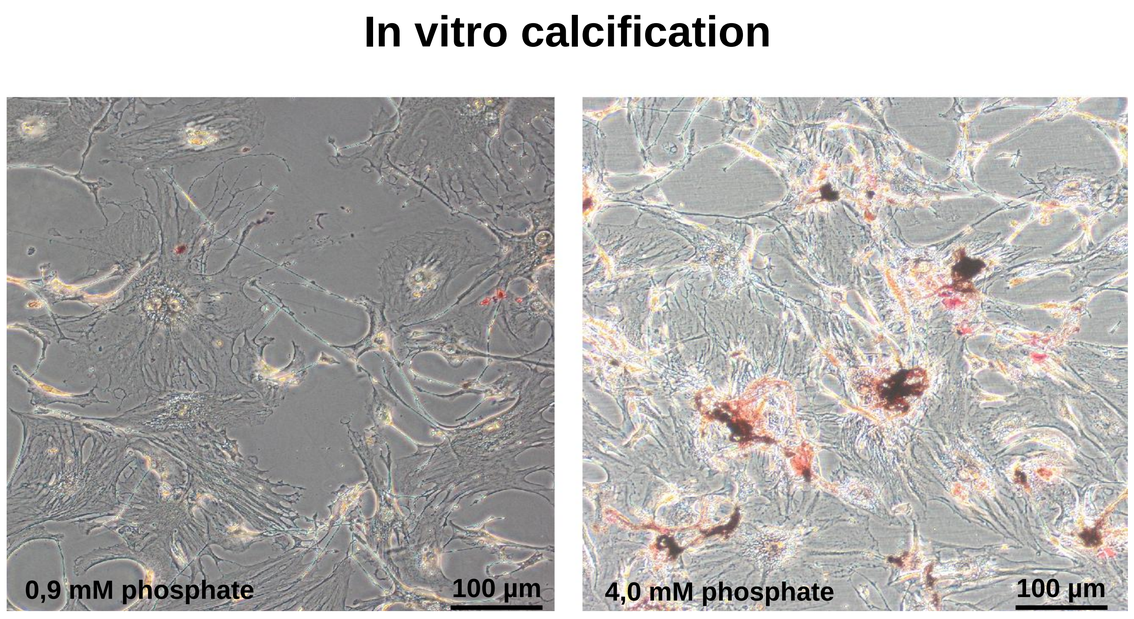

Figure 4.: VSMCs isolated from DBA2 mice develop severe calcification in high phosphate medium after 5 days. Aliazarin Red S staining.

Conclusion

These findings may indicate that the miRNA-142 family plays a role in the process of uremic media calcification and its regulation is not an effect of the dietary phosphate. Next, we plan to perform knock-down studies in order to study whether respective miRNAs play any functional role in the pathogenesis of vascular calcification in vitro and in vivo.

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