Can magnesium (Mg2+) protect against vascular calcification in a mouse model of CKD?

Background and clinical relevance

In patients with chronic kidney disease (CKD), cardiovascular complications are the leading cause of morbidity and mortality. An important contributor to this phenomenon is the development of vascular calcifications in these patients, as a consequence of severely disturbed mineral metabolism. Precipitation of calcium phosphate (CaPi) crystals, in addition to active ossification of vascular smooth muscle cells (VSMC) all contribute to this complex process that ultimately leads to loss of vessel compliance and integrity. In the clinic, it still proves challenging to prevent or treat vascular calcifications in these patients.

Over the last decades, lower serum magnesium has been correlated with decreased survival in CKD patients as compared to those with a higher serum magnesium level. Indeed, multiple in vitro and in vivo studies have now shown an indisputable role for magnesium in reducing cardiovascular risk, and it has become clear that there is a role for magnesium in preventing vascular calcification. However, the mechanisms of action remain unclear.

Aim and research question

In order to delineate the mechanisms by which magnesium prevents vascular calcification, we designed a study in during which we treat CKD-developing mice with a magnesium-rich diet. In this particular model, Klotho (a gene highly involved in mineral-bone metabolism), has been knocked-out. These mice develop severe hyperphosphatemia, CKD and vascular calcifications, and is therefore an interesting model to study the effects of magnesium on vascular calcification, in the context of CKD and mineral-bone regulating pathways.

- Does a magnesium-rich diet prevent vascular calcification in Klotho knockout mice?
- What might be the mechanisms of action with respect to the pathways involved in mineral metabolism?

Internship and techniques: what to expect?

We offer the possibility to perform and present clinically-oriented research in a professional, multicultural and highly-motivating working environment with about 35 colleagues in a well-equipped department. You'll be part of the CKD/calcification research team in which you will be responsible for your own research question. Together with a PhD-student, you will be involved in the animal experiment as described above, from organ to RNA.

The skills you will acquire:

- Tissue processing for (immuno-)histochemical analysis
- A large variety of tissue staining techniques
- Imaging techniques
- RNA and protein isolation
- Gene expression analysis using RT-qPCR
- Blood serum analysis techniques
- Experience in the dynamic and fun analysis of an animal experiment!

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