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Developing a mouse model to investigate diabetes-related vascular calcification

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Cardiovascular calcification is commonly associated with diabetes mellitus (DM) and diabetic kidney disease (DKD), and is a leading cause of death in diabetic patients. There are several animal models to study diabetes, however, only a few develop cardiovasular calcification. In our laboratory we chemically induced Type I diabetes on an Abcc6-/- background. Our diabetic Abcc6-/- mice have hyperglycemia, increased plasma urea and creatinine, and decreased plasma albumin levels, as expected. Our diabetic model also develops more pronounced vascular calcification compared to non-diabetic Abcc6-/- controls, therefore is suitable to investigate diabetes-related arterial calcification. Mutations in the gene encoding the ABCC6 transporter result in similar cardiovascular calcification as observed in diabetic patients (without other diabetic symptoms). The protective role of ABCC6 in soft tissue calcification is thought to be due to its role in controlling plasma pyrophosphate (PPi) level. We also found that PPi levels both in plasma and in urine of diabetic mice are decreased. Interestingly we could confirm these results in human diabetic patients as well: they have decreased plasma PPi levels. We are currenlty investigating the efficacy of PPi treatment in the prevention of cardiovascular calcification developing under diabetic conditions in our animal model. This mouse model provides an excellent tool to investigate/discover important key regulators of diabetes-related vascular calcification, and therefore may help to find new targets for the prevention of vascular calcification and early biomarkers in the progression of the disease. The contribution of ABCC6 is particularly important as the estimated frequency of heterozygous carriers of ABCC6 mutations in the general population is 1 in 80.

Biography

Viola Pomozi is a biologist, obtained her PhD in the field of molecular biology. She has been working at the Institute of Enzimology (Research Centre for Natural Sciences, Budapest) since 2005. From 2015 she has spent three years at John A. Burns School of Medicine, University of Hawaii as a postdoctoral fellow. In both research groups they were focusing on an ABC trasporter protein, ABCC6. Mutations in the coding gene lead to pathological calcification in soft tissues. Using Abcc6 knockout mice they are investigating the molecular mechanisms of soft tissue calcification and are testing potential preventive treatments. Their recent findings indicate that supplementing pyrophosphate, an endogenous calcification inhibitor, is effective in the prevention of soft tissue calcification. Recently they started to investigate other pathological conditions as well leading to soft tissue calcification, including diabetes. They developed a mouse model suitable to study diabetes-related vascular calcification.