Triggers and protectors of vascular calcification in patients with coronary artery disease

Summary

Philipp Eller, Institute of Internal Medicine, Intensive Care Unit, Medical University of Graz

Supervisor:	Prof. Dr. Philipp Eller
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 01, 2018 00:00 and September 23, 2018 23:59 (CEST)

Description

Background: The massive burden of cardiovascular disease in chronic kidney disease and diabetes mellitus is strongly associated with extensive media calcification, reduced vascular compliance, left ventricular hypertrophy, and sudden cardiac death. Media sclerosis and media calcification are regulated by a complex interaction of systemic and local triggers of vascular calcification such as hyperphosphatemia and hyperglycemia, but also critically dependent on diverse physiological protectors from vascular calcification such as fetuin A or vitamin K[1-3]. These triggers and protectors modulate the phenotype of vascular smooth muscle cells, which are not terminally differentiated cells. In this manner they can eventually react to stress, inflammation or injury by transdifferentiating from contractile to proliferative and/or osteoblastic phenotypes.

Hypothesis and Objectives: We postulate that the local microenvironment plays a central role in the phenotypic modulation of vascular smooth muscle cells. Preliminary data from our lab indicate that macroautophagy is not only essential for cellular hemostasis, but also an important protector from vascular calcification. The main objective of this project is to analyse phenotypic modulation of vascular smooth muscle cells in different arteries of patients undergoing coronary bypass surgery.

Methodology: The PhD candidate will learn how to evaluate ectopic vascular calcification using histology, molecular biology, and mass spectrometry, respectively[1-3]. The PhD student will investigate the molecular genetic determinants of phenotypic modulation in vascular smooth muscle cells. The focus of these molecular genetic analyses will be on the specific role of genes involved in vascular calcification. Ultimately we aim to modulate the vascular smooth muscle cell behaviour in primary cell culture experiments and in an *in vivo* mouse model of vascular calcification and thus prevent/treat media sclerosis and media calcification that are associated with heavy burden of morbidity and mortality in patients suffering from diabetes mellitus or end-stage renal disease.

References:

1. Potential role of regulatory T cells in reversing obesity-linked insulin resistance and diabetic nephropathy. Eller K, Kirsch A, Wolf AM, Sopper S, Tagwerker A, Stanzl U, Wolf D, Patsch W, Rosenkranz AR, Eller P. Diabetes. 2011 60(11):2954-62.
2. Regulatory T cells improve nephrocalcinosis but not dystrophic cardiac calcinosis in DBA/2 mice. Kirsch AH, Smaczny N, Riegelbauer V, Sedej S, Hofmeister A, Stojakovic T, Goessler W, Brodmann M, Pilger E, Rosenkranz AR, Eller K, Eller P. Am J Pathol. 2013 183(2):382-90.

3. Heterogeneous susceptibility for uremic media calcification and concomitant inflammation within the arterial tree. Kirsch AH, Kirsch A, Artinger K, Schabhüttl C, Goessler W, Klymiuk I, Gülly C, Fritz G, Frank S, Wimmer R, Brodmann M, Anders HJ, Pramstaller P, Rosenkranz AR, Eller K, Eller P. Nephrol Dial Transpl 2015 30(12):1995-2005.

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