

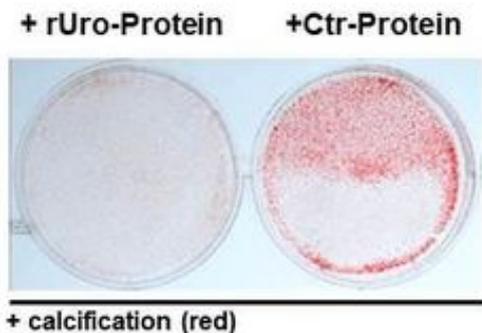
Technology Offer

Preventing Vascular Calcification in Chronic Kidney Disease

Reference Number 32-00049

Challenge

Accelerated medial arterial calcification in patients with chronic kidney disease (CKD) strongly correlates with increased arterial stiffness and cardiovascular mortality. Although the mechanism of vascular calcification is not fully understood, several lines of evidence highlight an association of low serum levels of uromodulin with elevated rates of cardiovascular mortality in CKD-patients. Current standard treatment strategies focus on hypertension and phosphate homeostasis, however, with limited success. To date, no specific treatment that can prevent or even reverse vascular calcification is available for this patient population.



Recombinant uromodulin (rUro) inhibits phosphate-induced calcification (shown by Alizarin red staining) in cultured HAoSMC (Human aortic Smooth Muscle Cells)

Technology

Recent scientific advances suggest that systemic supplementation of uromodulin can dramatically ameliorate vascular calcification. Researchers at the Center for Cardiovascular Research (Charité University Hospital Berlin) pursued this novel approach to utilize the protective function of uromodulin for CKD patients at risk of progressive vascular calcification. They successfully demonstrated that uromodulin counteracts and prevents calcification, which in turn could improve cardiovascular health progression to reduce cardiovascular morbidity for CKD patients predisposed to hypertension, coronary artery disease, diabetes mellitus and aging. This therapeutic concept shows following benefits: - Means for reducing cardiovascular risk and inflammation in CKD-patients - Utilization of endogenous protective mechanisms, reducing risk of side effects - Biomarker and therapeutic simultaneously - Novel approach to improve the cardiovascular risk management of kidney patients - Cell-based assay available for monitoring recombinant protein potency and functionality

Commercial Opportunity

The invention offers an opportunity for direct entry into translational/early stage drug development of a therapeutic protein. This opportunity is available for in-licensing or research collaboration for preclinical (co-) development towards First-in-Human. Further collaboration is especially sought to establish a cGMP production of recombinant human uromodulin and for future clinical studies.

Development Status

Proof-of-Mechanism and Proof-of-Concept have been established in various *in vitro* and *in vivo* animal calcification models. These studies provided mechanistic insights into the proposed Mode-of-Action for this novel therapeutic approach, targeting osteo-chondrogenic remodelling. Further *in vivo* studies in animal models of chronic renal failure addressing Uromodulin's anti-calcification properties are underway.

Patent Situation

This invention is subject to patent application PCT/EP2018/054839: "Uromodulin for use in prevention and therapy of pathological crystallization"; status pending.

Further Reading

Alesutan I. et al. "Circulating uromodulin inhibits vascular calcification by interfering with pro-inflammatory cytokine signalling"; in preparation Delgado G.E. et al. (2017) J Am Soc Nephrol 28: 2201–2210 Steubl D. et al. (2016) Medicine (Baltimore). 2016 Mar;95(10):e3011.