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ERA Long-Term Research Fellowship Project

G&K

Project's key info

Title of the project	Assessing the role of MRI- and MRE-based imaging biomarkers in ADTKD-MUC1/UMOD
Working Group involved in the project	Genes & Kidney Working Group (G&K)
Principal Investigator(s) of the project	Jan Halbritter (Germany) Albertien M. van Eerde (The Netherlands)
Duration	12 months, split between Germany (6 months) and The Netherlands (6 months)
Fellowship Grant	34.495,00 €
Start of the fellowship	Within 6 months after notification of the grant award to the fellow.

Receiving Institute

Name of receiving institute	1. Charité University Medicine Berlin, Germany 2. University Medical Center Utrecht, Department of Genetics, Utrecht, The Netherlands
Supervisor's name	Jan Halbritter (Germany) Albertien M. van Eerde (The Netherlands)
Supervisor's e-mail address	Jan.halbritter@charite.de a.vaneerde@umcutrecht.nl

Project's detailed description

Project description
Autosomal dominant tubulointerstitial disease (ADTKD) is a recently defined genetic entity of rare kidney disorders that is characterized by tubular damage, interstitial fibrosis and ineluctable progression to kidney failure between the 5th and the 7th decade of life. As an extra-renal hallmark, ADTKD-patients variably develop hyperuricemia and precocious episodes of gout. The four major ADTKD-genes (UMOD, MUC1, REN, and HNF1B) together account for the third most frequent genetic kidney disorder, after polycystic kidney disease and Alport Syndrome. As ADTKD is understudied and diagnosis requires access to (specific) genetic testing modalities individuals with ADTKD face many challenges related to delayed diagnosis, inappropriate workup, family burden, uncertain prognosis, and absence of specific therapies. However, this situation is about to change as personalized treatment options with small molecules have emerged on the horizon, highlighting the importance of clinical trial-readiness in ADTKD. This project wants to combine existing national cohorts from Germany (Berlin) and the Netherlands (Utrecht) for innovative phenotyping by functional magnetic resonance imaging (MRI) and elastography (MRE) readily established at Charité Berlin (in collaboration with a renowned expert in the field of kidney imaging, PD Dr. Stephan Rodrigo Marticorena Garcia, Department of Radiology, Charité Berlin, PMID:30222647/PMID:31261295). The results of the project are thought to complement the highly coordinated activities of the newly established European ADTKD-consortium (ADTKD-Net),

which is funded by the EU from 2024-2027 and is coordinated by Kai-Uwe Eckardt and Jan Halbritter at Charité Berlin (https://www.ejprarediseases.org/adtkd-net/).

Goals of the project

The overarching aim is to contribute to facilitated, non-invasive diagnosis and disease prognostication: Specifically, the project aims to:

- identify MRI- and MRE-based markers that are specific to ADTKD-UMOD and ADTKD-MUC1, the two most common entities (=diagnostic biomarker approach);
- identify MRI- and MRE-based markers that correlate with future loss of kidney function in patients with ADTKD-UMOD and ADTKD-MUC1 (=predictive biomarker approach).

For the latter, the research team will assess kidney function longitudinally and cross-compare with available kidney biopsy material. By successful implementation, imaging markers may serve as a surrogate endpoint parameter in future clinical trials (analogous to total kidney volume in ADPKD). We anticipate secondary benefits due to the paradigmatic nature of ADTKD, with relevance for the diagnosis and risk-stratification of other fibrotic kidney diseases.

Qualifications and/or expertise required to the fellow

The fellow has to have a clear intrinsic motivation and enthusiasm for the topic and the above-described types of translational questions.

The fellow should be:

- knowledgeable in nephrogenetics and have basic experience in radiology including MRI techniques (ideally plus bioinformatics);
- competent in written and spoken medical/scientific English;
- able to work with/build databases/extensive datasets, and be willing to improve skills to expert level;
- be the type that does not rest before a dataset is 100% correct;
- have proven research experience.